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I – The Medical Section (for Mds)
II – The Nursing Section
(for medical staff, other than Mds)

Manner of presentation

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EDITORIAL



Prof. Aleksei Zhidovinov
Astrakhan State Medical
University, Astrakhan,
Russia

Dear Colleagues,

I am delighted to greet you on the pages of international medical journal *Archiv Euromedica*! The scope of the journal is multifaceted and embraces challenges of modern medicine. The Journal has a clinical specialization. Section *Surgery* comprises actual problems of general surgery, pediatric surgery, traumatology and orthopedics, neurosurgery, oncology, transplantology, disaster medicine, anesthesia and critical condition. As a pediatric surgeon in charge of the journal I am offering you to submit papers on the problems of pediatric surgeries and procedures, development of standards and professional training.

Special attention is paid to national priority projects in healthcare, application of high-tech therapies in different fields of pediatric surgery. We look forward to receive original articles, interesting observations, scientific reviews within the scope of the journal. The editorial board of the journal welcomes cooperation with manufacturers of medical equipment, pharmaceutical production and developers of medical technologies.

To place an advertisement on our pages is a great opportunity to share it among multinational medical auditorium and to strengthen international cooperation.

Dear Colleagues,

Traditionally publications on stomatology occupy a significant place in the journal. The aim of the section *Stomatology* — to publish the results of fundamental and applied researches, advanced and science-based effective technologies in the field of diagnostics, prevention and treatment of diseases of the stomatognathic system adhering to the modern standards of evidence-based medicine.

The principal directions of the section *Stomatology* are fundamental researches; epidemiology and prevention of stomatological diseases; dental caries; orthodontics; endodontics; implantology; gnathology; oral surgery and oral and maxillofacial surgery; innovational technologies; materials science; pediatric dentistry; geriatric dentistry, rehabilitation.

While considering and editing manuscripts the editorial board follows the ethical norms adopted by international scientific community and adheres to Recommendations on conducting, describing, editing and publicizing results of scientific works in medical journals of International Committee of Medical Journal Editors (ICMJE) and recommendations of Committee on Publication Ethics (COPE).

Our target reading audience includes dental doctors; specialists in the field of fundamental, clinical, preventive medicine as well as bridging disciplines; university teachers, lecturing on stomatology; medical residents, doctoral students for MD and PhD.



Prof. Dmitry Domenyuk
Stavropol State Medical
University, Stavropol, Russia

Dear colleagues,

We thank all authors and members of the editorial board for the co-work on preparation and release of the current issue. That is why the journal has become more interesting, actual and multidisciplinary, which lies on trend with the latest developments in modern medicine and healthcare.

I am pleased to inform you that starting from this year the Journal will be published three times a year and from 2020 — four times a year.

So we kindly ask our authors to prepare their manuscripts in advance and start submitting them for the second issue. Its release is scheduled for September.

The last but not least: in order to improve the quality of scientific papers and reputation of the journal the editorial board made the decision to increase a minimum length of an article to 4 pages.



Dr. Georg Tyminski
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Germany

EXCESSIVE BODY WEIGHT, BODY FAT, AND EATING HABITS OF STUDENTS FROM PUBLIC AND PRIVATE ELEMENTARY EDUCATION *

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ABSTRACT — **AIMS:** The objective of this study was to evaluate the prevalence of excessive body weight and eating habits among students of 3th and 4th periods of elementary school. **METHODS:** 202 children (87 girls and 115 boys) in four schools (two publics, n=104 and two privates, n=98) from Barra do Garças (MT), Brazil were evaluated. A food frequency and physical activity questionnaire was applied. After measurement of height, weight and body mass index, the body fat (%) was estimated using a bioimpedance scale. The estimation of frequencies and the statistical analysis were performed by the epitools® program. **RESULTS:** Prevalence of both overweight and obesity were higher in private schools compared to the public ones. The prevalence of overweight ranged from 18.92% to 32.43%, whereas the obesity prevalence varied from 18.2% to 36.4%. Body fat distribution was highest among girls than boys. The daily dietary intake of vegetables, legumes and fruits reached only 57.4%, 50% and 43.6%, respectively. 36.6% of the students did not drink or eat milk and its derivatives. The dietary intake of fatty foods and soft drinks 5 to 7 days per week were high, reaching 24.26% and 27.23%, respectively. The weekly consumption of sweets and candies was excessive, reaching 39.11% for 5 to 7 days. **CONCLUSIONS:** obesity was higher among students from private schools and dietary intake of vegetable foods was inadequate, whereas intake of fatty foods, sweets and soft drinks was high.

KEYWORDS — obesity, soft drinks, sedentary lifestyle.

INTRODUCTION

Recent studies have been elucidated that childhood obesity is associated to increased risk of hypercholesterolemia, high blood pressure, non-alcoholic fatty liver disease, and metabolic syndrome in children and adolescents [1–3].

The regular use of electronic devices (tablets, smartphones, games), and the time spent watching TV, raised physical inactivity, consumption of soft and sugary drinks, sleeping problems, and the risk of obesity [4].

Beyond the excessive time spent with sedentary activity, regular intake of energy and fat dense foods constitutes an important factor in determination of overweight and obesity among children and adolescents [5, 6].

It should be emphasized that those unhealthy life-styles trend to perpetuate, remaining at the adult life and posing an increased risk of obesity and correlated diseases among the adults [6, 7].

Thus, the objective of the present study was to evaluate the prevalence of excessive body weight and eating habits in students from 3^o and 4^o periods of the elementary school in two public and two private schools.

METHODOLOGY

Population and methods

During June to August 2018, 202 children (87 girls and 115 boys), of 3^o and 4^o periods of elementary school in two public and two private schools of Barra do Garças (MT) municipality were assessed.

98 students represented public schools, whereas the remaining 104 belong to private schools in Barra do Garças, MT, Legal Amazonian region.

The heights of children were measured using a portable stadiometer (MD, Brazil). After measurement of height, body weight and total body fat were evaluated by a bioimpedance scale (Tanita, TBF-551, Japan). Values of weight and height were used to calculate body mass index (Kg/m²) of each student. In addition, a food frequency questionnaire was also applied [8].

Ethical and Statistical Aspects

Before engaging the study, participants received full explanations regarding the research and signed the informed consent term. This study is a subsample of the registered study "Epidemiology and risk factors for non-communicable diseases: development and application of a health promotion scale (HPS)" which was approved by the Research Ethics Committee of the "Campus Universitário do Araguaia da Universidade Federal de Mato Grosso (UFMT)" (protocol CAAE: 62989416.1.0000.5587- 2017). The statistical analysis was performed using Epitools® software (Australia). In

* Awarded work on "Congresso Multidisciplinar Integrado às Ciências da Saúde", Campinas (SP), 2017

order to correct, standardize and balance the samples by gender, the z-test, in two-tale mode, was applied to compare two proportions. Statistical significant differences were considered when $p < 0.05$.

RESULTS

The prevalence of overweight and obesity were higher in private schools compared to the public ones. The highest prevalence of obesity was found in private school 1. The prevalence of obesity ranged from 18.92% to 32.43%, whereas the prevalence of obesity varied from 18.2% to 36.4% (fig. 1).

The body fat distribution among girls and boys is represented in the fig. 2.

The values of body fat distribution among boys were lower than the values found for girls. Thus, there was major prevalence of body fat values up to 25% among girls, which is considered unhealthy.

Although the weekly dietary intake of legumes, vegetables, and fruits had been considerable, only 57.4%, 50%, and 43.6% of children got a daily ingestion of vegetables, legumes, and fruits, respectively.

The weekly consumption of refined cereals was relatively lower, once 19.3% ingested two to four times/week and 12.4% done for five or more days.

The dietary consumption of meat and its products and milk and dairy reached 82.7% and 63.4%, respectively.

Furthermore, 36.6% of students did not drink milk or eat dairy foods according to nutritional recommendations. In respect of weekly dietary intake of vegetables, 42.6% of the students did not consume the adequate quantities.

The weekly ingestion of fatty foods was also elevated, since the consumption by two to four days, and by five to seven days were 37.13% e 24.26%, respectively.

The dietary intake of sweets, candies and confectionary foods was also excessive, reaching 37.13% and 39.11% for two to four days or five to seven days, respectively.

Another negative aspect was the consumption of soft drinks by the students, once the consumption of those drinks by two to four days and by five to seven days was 49.5% and 27.23%, respectively.

The other aspects of food intake are presented in fig. 3.

The leisure time physical activity practice by the students is presented in the fig. 4.

The frequency of students that did no physical activities was greatest amongst public schools compared to private ones ($p < 0.05$). Notwithstanding, the majority of students (65.91%), independent of school type, did not adequately practice physical activities to maintain health.

DISCUSSION

In the present study, the prevalence of overweight and obesity was greater in private schools compared to the public ones. Furthermore, prevalence of overweight ranged from 18.92% to 32.43%, whereas the prevalence of obesity varied from 18.2% to 36.4%.

Considering the ages of 8 and 9 years old, the prevalence of excessive body weight of the present study was higher even for boys than girls compared with the results found in Umuarama (PR), South Brazil, which ranged from 8.27% (overweight) to 12% (obesity) [9].

Overweight and obesity prevalence of the present study, with 8 and 9 years old students, was higher than that observed by Pinto et al. (2016) [10], with 505 students of 10 to 16 years in Ribeirão Preto (SP), Southeast Brazil. In the same manner, the prevalence of overweight and obesity was higher compared with the observed in Juiz de Fora (MG), Southeast Brazil, with a sample of 403 children, 10 to 14 years old, in which overweight and obesity were 19.9% and 10.2%, respectively [11].

In a research of São Caetano do Sul (SP), with 485 children of 9 to 11 years old, authors observed greater prevalence of overweight (45.4%) and obesity (33%) [12] than reported in the present study.

Regarding the above mentioned studies, the prevalence of excessive body weight of the present study, realized in the inner Mato Grosso (Central-Western Brazil), is so high than São Paulo State, the most developed of Brazil.

The distribution of body fat values among boys was lower in relation to the girls. Thus, there was higher prevalence of girls with body fat values above 25%, which is considered undesirable to health.

Increased body adiposity had been inversely related to cardiorespiratory fitness amongst girls in a study with 1,223 adolescents in the city of Cascavel (PR), South Brazil [13].

At least in part the excessive body weight and adiposity could be explained by unhealthy eating habits.

Therefore, in the current work the adequate daily consumption of vegetables, legumes, and fruits was 57.4%, 50% and 43.6%, respectively.

This consumption of vegetables and fruits of the current work was similar to that observed in 9 to 10 years old students in Coimbra (MG) Brazil [14]. However, the food consumption of the present study was higher than the observed in students of 14 to 19 years old in Sergipe (Northeast Brazil), whose unsuitability of fruits and vegetables intake reached 88.6% [15].

Daily food consumption of meat and its products and milk and dairy was 82.7% and 63.4%, respectively. The elevated meat consumption could also be ob-

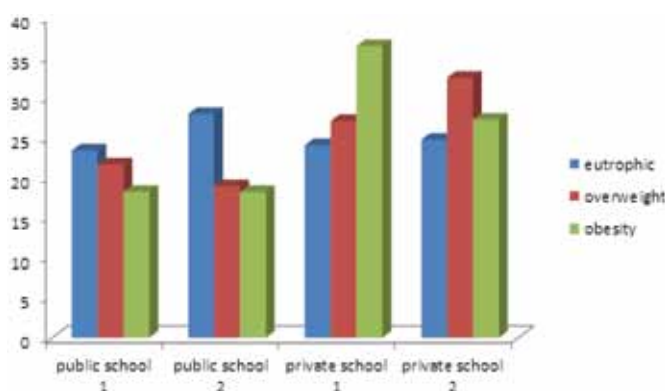


Fig. 1. Prevalence of excessive body weight among children from public and private schools of Barra do Garças (MT), Brazil

* $a \neq b$, com $p < 0.05$

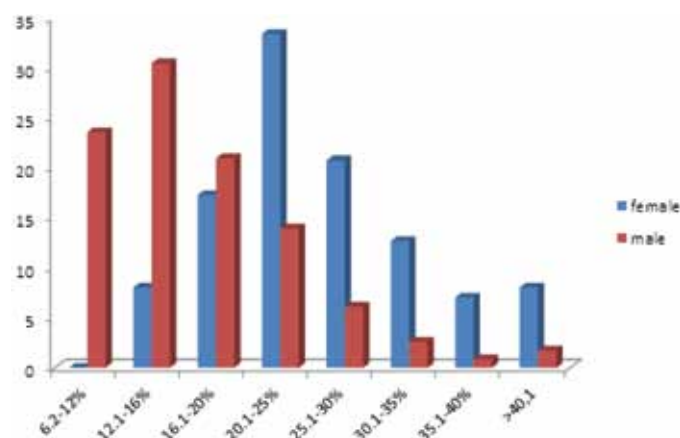


Fig. 2. Distribution of intervals of body fat, according to gender, among children from Barra do Garças (MT), Brazil

* $p < 0.04$

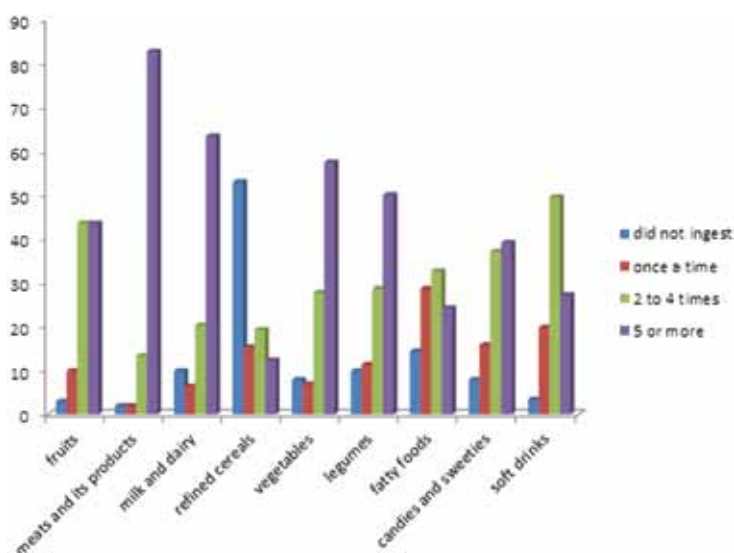


Fig. 3. Food consumption of children from Barra do Garças (MT), Brazil

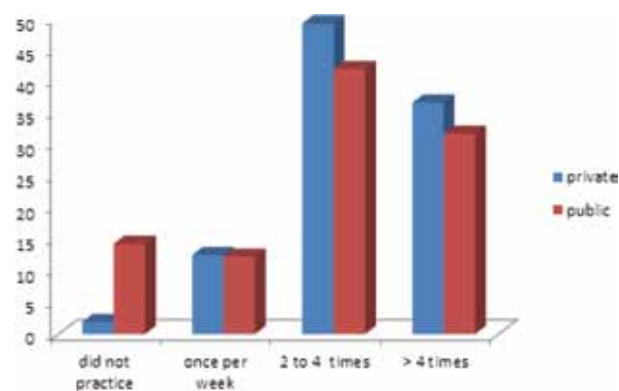


Fig. 4. Weekly frequency of practice of physical activity by students of public and private schools in Barra do Garças (MT), Brazil

* Difference between groups with $p < 0.05$.

served in other studies with children [14–16].

Beyond that, in the current work 36.6% of the students did not drink milk or eat dairy according to nutritional recommendations. This frequency of low milk and dairy intake was major than that observed in the South Brazilian municipality Ipiranga do Sul (RS), which got 20.4% of the students in a municipal school [16].

The weekly ingestion of fatty foods was also elevated, once the consumption of two to four days and of five to seven days was 37.13% and 24.26%, respectively.

Weekly consumption of sweets, candies, and confectionary foods was also excessive, reaching 37.13% and 39.11% for two to four days, or five to seven days, respectively.

A similarly elevated consumption of sweets, candies and confectionary foods was also reported in schoolchildren in many studies in Brazil and in India [10, 16, 17].

A study with children and adolescents in India reported that 61.8% did not ingest leafy vegetables once a week and that the ingestion of fried foods, fatty

foods, sweets, processed foods, and fast foods is far higher compared to the vegetables and fish intake [17].

Another negative aspect was the drinking of soft drinks by students, since the consumption of two to four days and for five to seven days per week was 49.5% and 27.23%, respectively.

A similar consumption of soft drinks was observed in children of São Paulo (Southeast Brazil) and Rio Grande do Sul (South Brazil) [10, 16], two states with highest prevalence of excessive body weight in Brazil [18].

It is known that children who regularly consume soft drinks have a major trend to consume less fruits and vegetables, practice less physical activity, and present excess of weight [15].

Notwithstanding the consumption of soft drinks which causes physiological problems in the kidney and liver, should be avoided [19].

Beyond unhealthy food habits, the time lost with sedentary activities and absence or insufficiency of regular practice of physical activity constitute other factors associated with increase of body adiposity, overweight, and obesity.

The frequency of students who did no physical activity was higher among those from public schools in relation to those from private schools. However, the majority of students, of both kinds of schools, did not practice physical activities in sufficient quantity to maintain health, which represented 65.91%.

Another study realized with 89 adolescents in many schools of Barra do Garças (MT), presented similar result found in the current study, once 65% of schoolchildren had sedentary behavior [20].

The insufficiency of physical activity observed in the present study was similar to the observed in a study with students of Sergipe (Northeast Brazil), in which 71% of them did not practice the minimum of recommended of physical activity per week [15]. The prevalence of sedentary behavior amongst schoolchildren in Pelotas (RS), South Brazil, was 69.2% [21] similar to the prevalence reported here.

In this way, a study with children demonstrated that short sleep timing, lower practice of physical exercise, and spent too much time in sedentary activities (like sitting, watching television, and using computer and electronic media) considerably enhanced the cardiometabolic risk [22].

Hortj et al. (2014) [23] demonstrated that even the time spent with sedentary activities than the lower time spent with physical activities were associated with increased risk of obesity and metabolic syndrome among 8 to 11 years old children in Denmark.

Finally, the time spent sitting was associated with increased general mortality in a study covering 54 countries [24].

CONCLUSIONS

In the current study performed in the inner Mato Grosso, at the border of Goiás State, the prevalence of both excessive body weight and sedentary behavior were very raised, whereas the intake of sweets, candies and confectionary foods, and fried foods was also higher, there was a lower ingestion of fruits and vegetables, factors that inspire future concrete actions regarding education and health promotion to school-children.

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EQUITY IN PUBLIC HEALTH POLICIES. THE PERSPECTIVE OF DIABETIC PATIENTS

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ABSTRACT — Health policies are correlated with the development of the society both nationally and locally. On the other hand, the allocation of resources for health services is a priority in regions with a lower degree of local development, where the health of the population is higher because of the more difficult access to health services, the lack of information and the postponement of the decision because of the lack of personal health care resources. Under these circumstances, investment in repairers' health policies becomes absolutely necessary in order to ensure a minimum equity of healthcare systems in that state.

KEYWORDS — Health Programs; National Diabetes Program; Chronic Care Self-Care Management.

INTRODUCTION

Depending on the socio-cultural significance given to suffering by the society, the reaction of individuals to disease and pain also varies, but also to other disconcerting physiological states, all of which have a socio-cultural determination as a result of a social construction process. The present article aims to analyse patient discourses on the national health program in the field of diabetes.

LITERATURE REVIEW

The evaluation of national health programs (Moisa, Pârvu, & Ioan, 2019) allows decision makers to review health policies in the areas mentioned in accordance with the specifics of Romanian patients (adolescents). In Romania this is a priority due to the dynamics of the health system in the last two decades: Romania (CEU, 2011) has since 2006 a national diabetes program (FENDT & IDF Europe, 2008) (whose technical coordination belongs to the National Institute for Diabetes, Nutrition and Metabolic Diseases), coordinates the annual monitoring and prevention of diabetes complications, self-monitoring, access to specific treatments, including insulin pumps and the

administration of the National Diabetes Registry, underway.

The components of the National Diabetes Program are prevention and control (Epping-Jordan, Pruitt, Bengoa, & Wagner, 2004; Everson, Maty, Lynch, and Kaplan, 2002). The responsibility (Britt, Moore, Adler, & Bartone, 1995) for patient care (Kamberi, 2018; Singh & Ham, 2006) in the case of patients with diabetes (Capplen & Norheim, 2005) non-insulin dependent patients and diabetics, according to the National Program for Diabetes, is of the general physicians, for non-insulin-dependent patients, and of the diabetologists for the insulin-dependent patients. A three-month check-up at the specialist doctor is required for every diabetic patient enrolled in the county centers. In the framework of the National Diabetes Program, we aim to investigate the actual practices in the medical system and how they influence the construction of the autonomy of individuals (CNAS, n.d.).

In the framework of prevention, the national diabetes program ensures the monitoring of persons aged over 45 or of groups at risk of illness, every three years (Order No. 1332/2018). Diabetes is considered a costly disease due to the chronic nature, the severity of the complications and the means necessary to control evolution, and poverty, illiteracy, low level of health education (Galan, 2017, Manolachi & Visitei, 2018), especially in rural areas, increase the risk of death by the complications of diabetes.

METHODOLOGICAL DESIGN

This research is a secondary data analysis applied to focus groups and interviews with diabetic patients conducted during the 2011–2013 period in the N.-E. region of Romania, which was dedicated to the Lifestyle and Health Behaviour of People with Chronic Diseases. Focus groups and interviews were attended by 6 or 4 people, of which 8 female and 2 male, diagnosed with type 1 insulin dependent diabetes, aged between 18 and 42 years.

Research objective

The purpose of this micro-research is to understand how patients with chronic diseases — diabetes

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mellitus — relate to public health policies and programs related to their illnesses.

Interpretation of data

The data interpretation was carried out in the form of content analysis, with a series of issues related to national health programs, mainly the national diabetes program, as well as aspects related to the ethical dimensions of the health program.

Discussions

Research boundaries are given by the relative age of the data collected during the 2011–2013 period. Another limit is the ratio between the number of female and male respondents in research, and the relatively small number of participants in the research. However, we believe that the data, although not a complete evaluation of the Diabetes Program, may constitute a set of benchmarks for patients' perception of the ethical dimension of this program, findings that may be useful in developing health policies and programs at the global level. We highlight the descriptive character of the analysis contained in the article, which is placed at the level of a medium-level theory of generality, without seeking to construct a complete theory with general explanatory power, but only to sketch, in an exploratory manner, a series of significant directions in the shaping of health policies in the field.

RESULTS

Chronic condition

The chronic patient experiences the chronic condition, as the normality of his life, as what defines him, or will define all his life.

You realize that a lady appeared in front of me who told me that I was to make the first injection at 1 o'clock and that I would spend all my life doing four injections a day, that I would live a normal life. It was ... How to live a normal life with 4 injections, but I got used to somehow. (FG2).

When lifestyle is essential for a proper management of self-care, accurate and timely information can be vital, constituting the difference between maintaining an approximately normal health condition within the limits of chronic patient-specific normality, and irreversible disintegration of the health condition.

I extend my life a little, I told you my girlfriends, the salon colleagues, do not live anymore. I extended my life, having the chance that my parents would have a higher education and would teach me. Since they were from the country side, they probably did not have this chance, to understand that they had to eat on time, to ... (FG2).

Right to health care

The right to health care, although a universal right in itself, depends on the level of development of the society in which the patient lives, being essentially about the fact that the limits of the possibility of a management of self-care is correlated with the inequities existing in that society.

I could tell you that in my time, the injections were made of glass with a metal needle, and I had to boil them every time. Because I was a kid and it was really hard for me to work with those ones, and because it was hard for me to always look for a stove to boil them, I would have skipped them. That was when there was insulin, when there was no insulin, I did not do them at all. That's where a lot of complications have arisen... I'd sue the Romanian State if I would get some damages, and with the money I get I buy my blood sugar tests so I can be alive for a few more years (FG2).

The quality of medication, as well as the limits within which the access to health resources is publicly ensured, are related to the level of development of the society and the health policies developed at the level of each state, even if this in practice means diminishing the chronic life expectancy of the patient.

(...) in other European countries they receive ... there are 4 tests per day free of charge, only one for us. Although we should do one before each meal or every insulin. If you want to live longer (FG2).

Health policies and level of societal development

Health policies are correlated with the development of the society both nationally and locally. On the other hand, the allocation of resources for health services is a priority in regions with a lower degree of local development, where the health of the population is higher because of the more difficult access to health services, the lack of information and the postponement of the therapeutic decision because of the lack of personal health care resources. Under these circumstances, investment in reparators' health policies becomes absolutely necessary in order to ensure a minimum equity of healthcare systems in that state.

There was no phone to call the ambulance. A little girl was saying that her grandmother was carried with a wheelbarrow when she was going into a coma, and remembered certain sequences when the wheelbarrow jumped from time to time, and she would a little bit come out of the coma... Instead of an ambulance, she was carried with the countryside wheelbarrow (FG3).

National Health Program

In the case of National Programs for eradication or control of a disease, the National Diabetes Program in Romania in this case, it is important to calibrate the allocated financial resources in order to provide quality care. The financial and material resources invested in health programs vary from state to state, depending on the philosophy behind public policies, but also on the cost-benefit ratio.

I find it very difficult not to have the exchange needles, although they are disposable and the diabetic patient gets infected very quickly. Much faster than a normal person (FG2).

The state of the chronic patient deteriorates over time, which determines at one point the need for a companion and integration into a certain degree of disability.

With many years of diabetes, all possible complications have occurred so that I no longer feel hypoglycaemia due to neuropathy. I do not sweat anymore, I do not feel anything at all, I go straight into a coma and then I should have a companion (FG2).

Persons suffering from chronic disabling illnesses are considered entitled to receive state support, including disability pension, attendant, free access to treatment, etc. When the lack of these resources jeopardizes the state of health and even the patients' lives, public health policies will always be ethically criticized, in the sense of not solving the inequities regarding access to health services and the failure to promote the right to life of patients. Obviously, no public health insurance system can necessarily solve all the inequities that have arisen, which is why it is necessary to have private health insurance. However, a number of redistributive policies based on the principle of subsidiarity in the provision of healthcare resources would be needed precisely to compensate for the structural failure in such cases of long-term chronic disabling illnesses that do not allow the patient to be insured in the contributory system.

I do not have it because he does not want to give me the right to have an attendant, money with which I would buy tests that are for the companion. My little girl is helping me. Since I gave birth, I have this problem so badly, after I gave birth, I had a bad luck that I could not take the money for two years, and then all of my savings went on blood glucose tests. Now I have no money but a 2-million and something disability pension that I cannot survive with, neither eat nor take tests. (FG2).

Equity in Health Policies

Another element of social inequity highlighted is the refusal of the public health insurance system to settle a number of treatments, especially when they are emergency treatments applied to chronic patients who have a certain degree of disability that prevents them from being ensured in contributory insurance systems. In these cases, the moral failure should be compensated by the state, which has public responsibility for the public's welfare, where they cannot secure a life within the acceptable limits of well-being at the level of that society.

I was in Vienna, I was sick, I was in a coma there, the person who was with me called the ambulance and came home with a 550-euro settlement. I went to the Insurance Houses today in Audience and they told me that I had to pay because the Romanian State would not settle the costs (...) I have insurance. Both as a disabled person and with the pension house. They do not want to settle (FG4).

When the chronic patient's incapacity for work occurs, this is reflected on the other members of the family, especially children who are forced to suffer a series of deprivations, and the result of social inactivity (Lăcătușu, 2018), where it is missing or is dysfunctional to a non-contributory social security system based on the principle of subsidiarity.

My little girl nonetheless, and I said I would give her for adoption, I was really desperate that I would not be able to feed her, really desperate that having diabetes, I should eat and thus be healthy so that I can raise her. Last year someone taught me to retire on sickness with my old age, and I would still get 3 million, but I still cannot get my tests and eat normally. As long as I have a baby and he has to eat too, he does not have a father, so it's only me. I mean, she is very much needed to help me when I'm in a coma and call the ambulance (FG2).

The chronic patient's needs significantly affect family members, especially when the patient is a parent, family provider. Close relatives will radically change their lifestyle to help the patient, going to personal sacrifices and renunciations that involve not only personal comfort, but also some aspects essential to their own development, such as school in the present case.

There are days when she does not go to school because she has to stay with me, because I am sick and afraid of going into a coma and she would return to find me dead at home, so she stays at home too (FG2).

Non-discrimination and equal treatment in health care policies

Discrimination in the employment, even if the person has all the necessary skills, and the state of health allows him to work, if he takes certain precautionary measures or if he is offered a number of particular labour conditions, can be an additional source of stress, that adds to the inconveniences caused by the illness, with negative consequences for the social integration of the chronic patient.

I tried to get hired in 2–3 companies and told them I needed a break that I could not announce in advance because I did not know the exact time. They told me that they would see, and at the end they said no (FG2).

Blood glucose control in the case of diabetic patients, based on glucose tests and the glucose meter, is a key to effective self-care management. In the absence of these, patients estimate the need for insulin after symptoms, but the tests allow dose calibration. As such, patients' access to these tests is a prerequisite for running a National Diabetes Program effective to keep disease progression under control, and avoid complications in patients. If the patient does not receive such tests, the state should be made responsible for the worsening of his or her state of health and the failure to ensure the right to life and the right to health of patients.

As long as I have tests I go on good glycaemic, when I don't — I lose control, because at night, of fear not to make hypoglycaemia over night, I eat a little more. And in the afternoon until the evening, I feel bad, bad, I have a state of depression because I had problems with these too. In the evening when I get home I feel good again (FG 6)

Chronic patients may suffer from different forms of discrimination, including employment, integration into social life, school, etc. Discrimination may be the result of a misunderstanding of the specificity of the disease, its way of transmission, or a lack of accountability for potentially hazardous situations such as accidents at work, or even conditions of illness, coma, etc. that may occur during the course of the activity.

(..) I sent the papers (for a job) and then I don't know how I told her I had diabetes and I had to go. There were a few more days. She then stopped calling me suddenly, and then I felt very bad, for a long time. (FG 5).

The importance of access to technology from the perspective of equity of the health system.

Access to communication and documentation technologies is an essential step in obtaining the real

expressive autonomy of the patient by empowering them with their own health management and self-care. On the other hand, sources of information should be carefully chosen so as not to pose health risks by applying inconsistent, miraculous therapeutic solutions that can lead to a deterioration of the patient's health. The patient's communication with other patients, online support groups, online patient communities, play an important role in maintaining appropriate tone and mutual motivation of patients to increase their therapeutic adherence, and to create true therapeutic alliances between physicians and patients.

I have seen, I've even got informed over the internet, I use the internet very often and I'm often interested in everything from abroad, it's much better about everything, especially in diabetes. I even talked to a diabetic from abroad, I do not know where from exactly, a while ago, and she told me it's like she would not have diabetes (FG 5)

Another important role of current technology is to create products that enable patients to adopt a lifestyle as normal as possible, and thus to express maximum expressive autonomy. Food technologies bring a number of lifestyle-specific products to different categories of patients, such as sugar-free sweets, and with rapid absorption in diabetic patients.

I do not really like that, for example, I drink juice and everything that is light or sugar-free, there is Pepsi, and as you know, it has caffeine, and that does not suit me too. It's a special sweet that's called, I do not know what its called. A type of glucose that absorbs very quickly, special for diabetics (FG 5).

CONCLUSIONS

The appropriate health programs for chronic patients should take into account the extent of their autonomy, not only in the decisional autonomy but also in the expressive, in other words, the patients' ability to achieve an efficient management of self-care.

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HEALTH RISKS ASSOCIATED WITH WASTE ACCUMULATION IN THE CONTEXT OF ENVIRONMENTAL LAWS OF DEVELOPMENT

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ABSTRACT — This work highlights the results of studies of environmental laws of development of urban systems that determine the cause of waste accumulation. It was disclosed that environmental pollution is an ultimative environmental factor that increases its pressure on humanity and sign of imbalance of ecological system.

KEYWORDS — environmental laws, wastes, ash and slag wastes, landfills, environmental pollution, public health.

In ecological theory, the process of urbanization can be compared with the strategy of creating safe settlements. According to this theory, the collection in a natural city has its advantages for population such as increased viability of the group (due to cooperation) as well as disadvantages such as stress caused by overpopulation of places of residence, increased competition for environmental resources, pollution and degradation. In terms of adjacent territory, the city acts as an integral formation that absorbs materials, energy and information flows from environment and produces a large number of different types of waste. These distinctions show certain features of the metabolism of cities [1, 2, 3].

Throughout its entire history, the humanity was focused on creation of production and consumption technologies, and only recently has become more attentive to waste management issues. Today, about 20–45 tons of raw materials are extracted per inhabitant per year. Almost 90–98% of these materials turn into waste. Accumulation of waste occurs in the domestic sector, where waste is 0.3–0.6 tons per person [4].

“The problem of waste in Ukraine is particularly big and significant due to dominance of resource-intensive high-waste technologies in national economy of the country as well lack of an adequate response to its challenges for a long time” [5]. So according to the data of 2016, the volume of solid waste generation in Ukraine was about 11 million tons (excluding the temporarily occupied territories, the Autonomous Republic of Crimea and the city of Sevastopol). Main

method for household waste management in the country remains their transportation and dumping at landfills (only 6% of generated household waste was recycled in 2016) [5].

Purpose of the study

The purpose of this study is to determine the effect of industrial and household wastes on environment and public health as well its environmental laws that determine causes of waste accumulation.

Materials and methods

Objects of the study were environmental laws that explain causes of waste accumulation as well as definite territories of Kyiv region (areas effected by ash and slag wastes generated by Trypilska heat power station (HPS) in Obukhiv district and landfills municipal solid waste (MSW) near Kryukivschina village in Kiev-Svyatoshinsky district). The choice of the designated territories was motivated by the fact that the inhabitants of the neighboring settlements, expressed their desire to defend in court their “right to a safe environment...”, which is guaranteed by Article 50 of the Constitution of Ukraine. In this work, we used systemic approach, as well as methods of comparative, natural and statistical analysis.

Starting position

According to M. Reimers, waste is “...type of war materials that are unsuitable for production of this type of product, as well as their unusable residues, or substances arising during the technological processes...” [1, p. 153]. “Taking into account all types of waste, the amount of useful social product is not more than 2% of extracted natural substances and energy (the remaining 98% are waste). Probably, it is impossible to reach better ratio since re-utilization leads to significant energy costs” [1, p. 153].

RESULTS AND DISCUSSION

Environmental laws of development.

The law of “impossibility of waste removal” states that “in any economic cycle results in accumulation

of waste and side effects that cannot be eliminated, they can only be converted from one form to another one or replaced in space... If there was a real opportunity to get rid of waste, this would violate the laws of conservation of mass and energy. The total amount of waste in the form of matter, energy and side effects... has become practically constant: only the place of their occurrence, the time of their generation and the physico-chemical or biological form can change in production cycles... Waste removal, as only a change physico-chemical form and the movement of pollutants in space, can give a very small overall effect since it requires considerable increase in energy costs. This approach it is quite useful on local level, but it should be mentioned that it is inefficient at regional and global level, within long period of time, that the gain obtained in one place is neutralized by the loss that occurs in some other places. This problem can be solved only by reduction of pressure of society on the environment through depopulation" [1, p. 67].

The law of "development of the system at the expense of the environment", states that "any natural system can develop only through the use of material and energy as well as information capabilities of its environment. Absolutely isolated self-development is impossible. The law is based on principles of thermodynamics. It has an extremely important, theoretical and practical significance due to its main consequences: waste-free production is impossible...; any higher organized biotic system, using and modifying the living environment, poses a potential threat to more low-organized systems..." [1, pp. 70-71]. "According to the first consequence, it is only possible to count on low-waste production, therefore, the first stage of development of technologies should be their low resource intensity (both at input and output...); The second stage is the creation of cyclic production (waste generated by some enterprises may be used as raw material for others), and the third stage is the organization of a reasonable depositing (burial) of inevitable residues and the neutralization of unrecyclable energy waste (all three stages can be simultaneous)" [1, p.71]. Consequently, "the idea that the biosphere is based on waste-free principle is false, since substances that form sedimentary rock always collect and escape from the biological cycle" [1, p.71].

The law of "ecosystem self-regulation" states that the environment provides certain population capacity for each species. Population reserve, i.e. "underpopulation" of the territory, causes growth, and its exhaustion, namely overpopulation of the territory, causes the reduction in the size of the species. This is due to the fact that increase in species number results in increase in pressure on the environment and causes

its resistance, which is aimed at maintaining ecological balance through depopulation. The excessive number of any species, including the species "homo sapiens", worsens the environment, which does not have time to recover and becomes less suitable for normal living of species, which leads to depopulation. In an ecologically balanced system, all waste products of the same species are removed by other. If this balance is violated, the waste is accumulated [1, 2, 6].

THE EFFECT OF INDUSTRIAL AND HOUSEHOLD WASTE ON ENVIRONMENT AND PUBLIC HEALTH

The purpose of works performed in State Establishment "O.M. Marzeev Institute of Public Health under Academy of Medical Sciences of Ukraine" was the determination of the effect of ash and slag waste generated by Trypilska HPS and landfills MSW near Kryukivschina village on environment and public health in Obukhiv and Kiev-Svyatoshinsky districts of Kyiv region. For this purpose, we have carried out the following studies in the areas affected by landfills of industrial and household wastes: condition of atmospheric air (with the determination of concentrations of specific pollutants); condition of soil (content of heavy metals); condition of water (in surface water bodies and water sources); morbidity of the population.

The following conditions have been disclosed at area adjacent to ash and slag disposal area excessive pollution of atmospheric air (dust with the content of silicon dioxide 20-70% to 9.2 maximum permissible concentration (MPC), chromium compounds up to 2.1 MPC), soil (cadmium up to 3 MPC), surface and ground waters and sources of decentralized water supply (cadmium up to 60 MPC, chromium up to 12 MPC, nickel up to 6 MPC, lead up to 4 MPC, manganese up to 8 MPC in comparison with drinking water indicators). Overnormative pollution of atmospheric air within 300 meters from the ash and slag landfill (smallest allowable cross-sectional sanitary area) of remains a powerful source of dust at this territory. The air pollution with chromium compounds is just a consequence that the ash at Trypilska HPS contains these compounds. Besides in atmospheric air near Trypilska HPS small disperse dust fractions were detected. Thus, an average concentration of particles is about 10 mkm (61,15 mg/m³) and significantly exceeds recommendations of WHO and EU.

It was also stated that excess of levels of morbidity of the population by different classes of diseases (respiratory, cardiovascular, allergic, oncological pathology); dynamics of key indicators of cardiovascular, oncological and respiratory diseases clearly correlates with the

distance of settlements from ash and slag disposal area. Besides, in the settlements within the influence of this object there is increase in average data on oncological pathology (in 10,4 times in town Obukhov and 1,8 times in town Ukrainka), on circulatory system diseases (in 1,8 times in town Obukhov), on respiratory diseases (in 1,2 times in willage Tripolije).

The following conditions were disclosed at the areas adjacent to landfill near Kryukivschina village excessive pollution of atmospheric air (hydrogen sulfide 1,13 MPC, ammonia 1.15 MPC, croton aldehyde 1,2 MPC), soil (nickel 1.13 MPC, cadmium 2.52 MPC, mercury 4.9 MPC, lead 2.39 MPC, chromium 2.79 MPC), ground and surface waters (nickel 5.5 MPC, cadmium 12 MPC, mercury 3.0 MPC). At the same time it was found that water pollution with cadmium, mercury and nickel in the wells of the citizens of willage Kryukovshina and in its open water basins has an unstable nature (these hazardous substances migrate in the groundwater). In our opinion a source of such pollution may be found in the MSW filtrate, which contaminates the groundwater in the surrounding territory.

Estimation of the regional morbidity among the population in the settlements near MSW revealed a tendency in a rise in number and classes of diseases closer to the landfill. Thus, closer to the landfill (village Yuriyevka – 900 metres, village Kryukovshina – 500 metres) cancer incidence in village Kryukovshina increased in 2,3 times; infectious disorders – almost twice; disorders of the nervous system - in 1,7 times; cardiovascular diseases - in 1,4 times.

CONCLUSIONS

1. Pollution, as one of the forms of environmental degradation, is an indicator of ecosystem imbalance. Pollution is conditioned by the accumulation of waste and acts as an increasing ultimate factor of reverse relation “population ↔ environment”.
2. Accumulation of wastes in the industrial and domestic sectors has negative effect on environment and public health.
3. In order to implement waste management measures, it is necessary to consider environmental laws of development.

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TEMPOROMANDIBULAR JOINT MORPHOLOGY AT ORTHOGNATHIC BITE

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INTRODUCTION

The parameters of the temporomandibular joint normal structure make an important piece of knowledge in common dental practice, primarily because it is some kind of a benchmark that allows making correct judgment concerning changes in the temporomandibular joint occurring through various diseases and prosthetic events that entail new ratios not only in the dentition area, yet also in the temporomandibular joint area [1–12].

Aim of study

To clarify the patterns of shape and size for the major morphological elements of the temporomandibular joint in case of the orthognathic bite.

Materials and methods

The study of the temporomandibular joint was conducted on 19 skulls of males and females (aged 20–44) obtained from the research craniological collection of the Human Anatomy Department, Saratov State Medical University named after V.I. Razumovsky.

RESULTS

Our study has confirmed that a normal temporomandibular joint features regular shape and size in its structural elements, namely, the articular fossa is of an elliptical shape with its anterior boundary being the articular tubercle posterior surface, the posterior boundary — the posterior articular process and the temporal bone tympanic part, from inside — with lateral edge of the main bone process, and from outside — the ridge of the temporal bone zygomatic process. The transverse diameter of the articular fossa varies between 20 and 29 mm with the average value being

24.5 mm. The articular fossa average sagittal diameter is 16.5 mm. The transverse diameter's ratio to the articular fossa sagittal diameter is 1.5:1. The average depth of the articular fossa is 8.5 mm.

The articular tubercle on the temporal bone is elliptical with a varying height, from 5 to 14 mm. The articular tubercle features three surfaces — posterior, on which the articular head travels; horizontal, representing the top of the articular tubercle and the front surface, which turns into the infratemporal fossa.

The mandibular articular head has a variable shape and features anterior, posterior and upper surfaces. The anterior surface is concave and serves as an attachment point for the lateral pterygoid muscle; the posterior surface of the articular head resembles a triangle and in all cases bears an imprint of the posterior articular process. The articular head upper surface resembles an ellipse with its longitudinal diameter of 19 mm and a transverse diameter of 8 mm. Subject to our data, the mandible articular head's sagittal diameter ratio to the transverse diameter of the temporomandibular joint articular fossa is 1:1.3, and the ratio of the transverse diameter of the jaw articular head to the articular fossa sagittal diameter is 1:2. The incongruence of the mandibular articular head against the joint articular fossa is corrected by the articular disc, which is an oval-shaped biconcave plate, with a sagittal diameter reaching 20 mm and the transverse one — 10 mm. The upper concavity matches the bulge on the articular tubercle rear surface, and the lower concavity — the upper surface of the mandible articular head. This shape of the disc compensates the incongruence of the articular tubercle and that of the articular head. Anthropometric measurements show that the longitudinal and transverse diameters of the articular disk, as well as its thickness, are different in different areas, so the articular disk in its central part seems to be pressed from below by the upper surface of the articular head and from above by the posterior articular tubercle slope. The average disk thickness in this area is 1.2 mm. The posterior part of the articular disk can be 3.5 mm — 5.3 mm thick.

CONCLUSION

Given the above, the temporomandibular joint of an adult person featuring an orthognathic bite can be described as having regular shape and size in its structural elements, while deviations from these allow

judging the occurring changes as well as monitor the treatment and observe its long-term outcomes.

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THE PECULIARITIES OF SOME INDICES OF PERIPHERAL BLOOD OF FOREIGN STUDENTS

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ABSTRACT — THE AIM of the research is: to study the morphofunctional characteristics of the peripheral blood cells of healthy young people of the same age group, taking into account the dependence on the ecological and biogeochemical factors of the external environment of the region of residence and to identify the physiological mechanisms underlying adaptation to the external environment.

MATERIALS AND METHODS. there were examined 125 students studied at the North Caucasus Federal University at the age of 18–21. For the quantitative evaluation of peripheral blood cells, 15 laboratory parameters were determined on the MEDONIK M-SERIES hematology analyzer. Leukocyte analysis was performed on the MECOS-C3 hardware-software complex.

RESULTS. The analysis of peripheral blood indices revealed significant shifts in adaptation processes in the direction of tension in the group of Indian students ($P < 0.01$) and less critical changes in the compensatory-adaptive mechanisms of the body in the group of students from Tajikistan ($P < 0.05$).

CONCLUSION. As a result of the study, new data have been obtained indicating a different spectrum of adaptive reactions of students, which allows the use of peripheral blood as a test system for assessing the influence of damaging environmental factors.

KEYWORDS — Adaptation, uniform elements of peripheral blood, erythrocyte, platelet indices, student hood, youngling, ethnicity belonging.

INTRODUCTION

The problems of the environmental conditions of society in modern conditions have become particularly acute. The ecological security of each individual

is the most important characteristic of the sustainable and stable development of society as a whole. It is known that the geographical environment acts on a person not always in direct way but indirectly go through the conditions of his life. The last fact plays a crucial role in the transformation of environmental influences on the human body and its state of health.

The relevance of the problem for this branch of knowledge is that among the problems of modernity, the assessment of the state of public health is becoming more and more relevant. This is due to the adverse effect on human health of environmental, social and economic factors.

Anthropogenic environmental pollution in many regions of the Russian Federation creates a tense environmental situation that represents a potential danger to public health. The transition from health to illness is seen as a process of gradually reducing the body's adaptive abilities. Adequate environmental conditions at the moment correspond to the properties of the biosystem but their boundaries are quite large, changes in the environment within these borders also require the inclusion of adaptive mechanisms. The whole set of adaptive reactions of a certain climatic environment is defined by the concept of an adaptive type which is the norm of a biological response to a complex of environmental conditions, providing a state of equilibrium of populations with this environment and finding external expression in morphofunctional features. One of the urgent problems of modern medicine is the problem of studying the adaptive capacity of the human body as a whole and in particular the Erythrone system, since red blood cells can be considered as a kind of total biopuncture of body tissues, they are among the first to respond to the effects of stimuli, while the first ones either return to the initial level or adapt to the changed conditions of existence. In this regard, there is a need to develop a set of methodological approaches that allow qualitatively and quantitatively assess the severity and intensity of adaptation processes in the erythron system. Improving the quality of health, the adaptive capacity of the population is possible only with the implementation of measures aimed at studying the state of health and analyzing shifts in basic indicators of health.

Youth student is a special social group, united by a certain age and specific working conditions. Adaptation to new social conditions, the ever-increasing intensification of the educational process, significant mental and emotional stresses against the background of a decrease in motor activity cause tension of regulatory-compensatory mechanisms and require a new approach to the development of scientifically based preventive measures at the university.

The scientific substantiation of the processes of adaptation of students to the conditions of study at the university is an actual problem of modern physiological science and practice. Adaptation to student life is a complex and multifaceted process that requires the involvement of all the body's reserves which is not yet fully formed in first-year students [1]. The presence of a high demand for educational and professional activities of young people requires the prediction of the functional state during the period of study at the university to ensure the effectiveness of the adaptation processes of students but the insufficient development of the physiological aspects of adaptation determines the relevance of this study [2]. Thus, the scientific substantiation of the processes of adaptation of students to the conditions of study at the university is an actual problem of modern physiological science and practice.

Clinical analysis of erythrocytes, platelets and peripheral blood leukocytes characterizes a certain moment of dynamic processes: the maturation and release of elements from the bone marrow, the lifetime of the cells, the time of their circulation in the stream. It is rather difficult to identify and correctly assess adaptive hematological reactions to the effect of damaging factors of low intensity. Small changes in the number of blood cells are easily "lost" among physiological fluctuations and limited in their direction [10]. Blood cells are sensitive to changes in the external habitat and the internal state of the human body. Since plasma is the habitat of cells, and intracellular and extracellular fluids are separated by actively functioning semipermeable cell membranes, even small changes in plasma metabolic composition should lead to disruption of cellular homeostasis and according to the laws of isosmolarity of the organism and to the disruption of cell size [2–9].

Stavropol Territory is located in the south of the temperate continental belt. It is located on the border between Europe and Asia; therefore, both European (maritime) and Asian (continental) influences are felt in the climate. The High Caucasus Mountains are located to the south of the Stavropol Territory and they do not allow warm air from Transcaucasia go into its territory and cold air masses coming from the north, on the contrary are trapped by them and spread out

over the plains of Stavropol. The ridges of the Western Caucasus isolate the land from air currents coming from the Black Sea. From the east, hot air in summer and cold air in winter plains adjoin the edge, whose influence cannot soften the air from the Caspian Sea. All this makes the climate of Stavropol more continental: with a rather large annual amplitude of temperatures (January: -2, -5° C to -30, -38° C, July: from +19, +24° C to +42, +44° C) and relatively small amount of precipitation [2, 14].

The purpose of this study was to study the morphofunctional characteristics of the peripheral blood cells of healthy young people of the same age group taking into account the dependence on the ecological-biogeochemical factors of the external environment of the region of residence and to identify the physiological mechanisms underlying adaptation to environmental conditions.

MATERIALS AND METHODS

The study was conducted during 2017–2018 on the basis of the NCFU Medical Center in the autumn period during the passage of the annual medical examination. 125 students enrolled at the North Caucasus Federal University in the following fields — Medical Biochemistry, Pharmacy, Biotechnology, Biology at the age of 18–21 students were surveyed. The subjects were found to be clinically healthy, students with acute inflammatory, infectious diseases and endocrine diseases were excluded. In the compared groups, quantitative and morphofunctional parameters of peripheral blood were evaluated. The screening of the survey of persons included: a survey of the subjects using a questionnaire that contained questions about passport data: name, gender, age; and questions about the presence of acute and inflammatory diseases. Laboratory criteria for screening were:

- the normal level of hemoglobin concentration (HB) and the number of red blood cells (ER) in all examined to eliminate anemia [12].

The preanalytical stage of laboratory studies was carried out in accordance with existing orders and recommendations of the Ministry of Health of the Russian Federation on quality control of laboratory studies, as well as established guidelines for physicians "Ways to optimize the quality of laboratory tests in endo-crinological treatment-and-prophylactic institutions" [10]. Blood sampling was carried out in the morning, on an empty stomach. For the quantitative assessment of peripheral blood cells on the hematology analyzer MEDONIK M-SERIES determined 15 laboratory parameters: the number of Erythrocytes (Er or blood cells) (RBC), volume (MCV), anisocytosis Er (RDW), hematocrit value (Ht), hemoglobin

concentration (HGB), average hemoglobin in ER (MCH), average hemoglobin concentration in ER (MCHC), platelet count (PLT), average platelet volume (MPV), platelet anisocytosis (PDW), thrombocrit (PCT), macrothrombocyte (LPCR), leukocytes (WBC), lymphocytes (LYM), granulocytes (GRAN). Measurement of the main parameters in the analyzer is based on the principles of impedance and spectrophotometry, a method of conductometric counting and based on counting the number and determining the nature of the pulses that occur when cells pass through a small-diameter opening (aperture), on both sides of which two isolated electrodes are located. Leukocyte analysis was performed on the MECOS-C3 hardware-software complex (Erythrocytometry, Blood Test, Densitormetry programs) (Fig. 1), automatic methods of preparing blood preparations were used for the study, for these purposes a high-quality smear centrifuge was used microscopy, a device for fixing and staining blood smears with built-in programmable four channel timer and drying chamber UFOMK-01 "EMKO-STEINER".



Fig. 1. Computer cytomorphometry of the uniform elements of hemopoiesis of first-year students

The results of the experiment were subjected to variational-statistical processing in accordance with the principles set forth in the manual of Lakin GF. (1990). The descriptive statistics of Microsoft Excel were used to create a one-dimensional statistical reference containing information about the central tendency and variability of the input data. The variation series obtained in the experiment were characterized by the following indicators: arithmetic average value

(M); standard deviation (σ); the error of the arithmetic mean value or the mean square error (m). Calculating the indicator of significant difference (t) and taking into account the number of measurements according to the Student's t-distribution table, the probability of differences (P) was determined. The difference was considered statistically significant, starting with P values <0.05 . In this case, the correctness of the conclusion about the existence of differences in magnitudes can be confirmed in 95% of cases [11, 13].

RESULTS AND DISCUSSION

Analysis of the morphofunctional parameters of erythrocytes of Russian students (table 1) revealed the maximum values of the following parameters: hemoglobin concentration (158.98 ± 1.79 g/l), hematocrit value ($45.35 \pm 0.73\%$), erythrocyte anisocytosis (15.29 ± 0.62), the average hemoglobin content in erythrocytes (32.13 ± 1.97) and the average concentration of hemoglobin in erythrocytes (356.11 ± 1.04 g/l) and the minimum number of erythrocytes (5.32 ± 0.085).

The group of Indian students was characterized by the highest values of the number of erythrocytes (7.59 ± 0.351) and the volume of erythrocytes (85.09 ± 1.54). The hemoglobin concentration (150.19 ± 2.01 g/l), the hematocrit value ($43.49 \pm 0.49\%$) and the average hemoglobin concentration in the erythrocytes (345.22 ± 1.85 g/l) in this group were the lowest (Table 1).

Tajik students compared with groups of Russian and Indian students had minimal red blood cell anisocytosis (13.55 ± 0.36), red blood cell volume (81.90 ± 1.45) and average hemoglobin red blood cells (28.74 ± 0.61) (Table 1). In general, if we consider the distribution of morphofunctional indicators of erythrocytes of Russian and foreign students we may see that the most similar to the indigenous population of Stavropol are Tajik students, because they are most likely due to the similarity of climatic and geographical conditions of the regions [15].

Statistically the important significant differences were found for all studied morphofunctional parameters of erythrocytes (table 1). Thus, hemoglobin concentration, hematocrit value, erythrocyte anisocytosis and average hemoglobin concentration in erythrocytes among Indian students were significantly lower compared to the same indicators of Russian students. Tajik students also had similar differences - the erythrocyte anisocytosis, the erythrocyte volume, the average hemoglobin content in the erythrocytes and the average hemoglobin concentration in the erythrocytes were significantly lower [16].

The study of morphofunctional parameters of platelets taking into account ethnicity (table 2)

Table 1. Erythrocyte morphofunctional parameters, ($M \pm m$)

Parameters	Group 1	Group 2	Group 3
HGB g/L	158,98 \pm 1,79	150,19 \pm 2,01	154,83 \pm 3,30
P1		<0,001	>0,10
P2			>0,10
RBC 10*12/L	5,32 \pm 0,085	7,59 \pm 0,351	5,41 \pm 0,096
P1		<0,001	>0,10
P2			<0,001
HCT %	45,35 \pm 0,73	43,49 \pm 0,49	43,71 \pm 1,05
P1		<0,05	>0,10
P2			>0,10
RDW - SD fL	15,29 \pm 0,62	14,08 \pm 0,33	13,55 \pm 0,36
P1		<0,05	<0,01
P2			>0,10
MCV fL	84,74 \pm 0,42	85,09 \pm 1,54	81,90 \pm 1,45
P1		>0,10	<0,05
P2			>0,10
MCH pg	32,13 \pm 1,97	29,43 \pm 0,62	28,74 \pm 0,61
P1		>0,10	<0,05
P2			>0,10
MCHC g/L	356,11 \pm 1,04	345,22 \pm 1,85	350,42 \pm 2,67
P1		<0,001	<0,05
P2			<0,05

Note: P1 — significance of differences between morphofunctional indicators of erythrocytes of Russians (group 1) and Indian (group 2) and Tajik (group 3) students; P2 — reliability of differences between morphofunctional indicators of erythrocytes of Indian (group 2) and Tajik (group 3) students

revealed that Russian students are characterized by minimal platelet count (213.60 ± 8.13), an anisocytosis index of platelets (11.63 ± 0.14), thrombocrit (0.18 ± 0.01), average platelet volume (8.57 ± 0.15) and macrothrombocyte ratio (21.41 ± 0.70).

Indian students had maximum platelet counts (290.65 ± 11.35), thrombocrit (0.30 ± 0.01) and average platelet volume (10.50 ± 0.14) (table 2). In the group of Tajik students the only indicator with the highest value was platelet anisocytosis (13.55 ± 0.36). Also, while analyzing the distribution of morphofunctional platelet indicators of Russian and foreign students, it was found that students from Tajikistan were closest to the indigenous population of Stavropol. We also associate the revealed fact with the similarity of climatic and geographical conditions of these regions.

Statistically the important significant differences were found for all studied morphofunctional parameters of platelets (Table 2). At the same time, they were significantly lower in the group of Russian students compared to the groups of Indian and Tajik students.

Table 2. Morphofunctional parameters of platelets, ($M \pm m$)

Parameters	Group 1	Group 2	Group 3
PLT	213,60 \pm 8,13	290,65 \pm 11,35	239,83 \pm 8,19
P1		<0,001	<0,05
P2			<0,001
PDW	11,63 \pm 0,14	12,44 \pm 0,29	13,55 \pm 0,36
P1		<0,01	<0,001
P2			<0,01
PCT	0,18 \pm 0,01	0,30 \pm 0,01	0,24 \pm 0,01
P1		<0,001	<0,001
P2			<0,001
MPV	8,57 \pm 0,15	10,50 \pm 0,14	10,20 \pm 0,14
P1		<0,001	<0,001
P2			>0,10
LPCR	21,41 \pm 0,70	37,09 \pm 8,93	26,68 \pm 1,12
P1		<0,05	<0,001
P2			>0,10

Note: P1 — significance of differences between morphofunctional parameters of Russian platelets (group 1) and Indian (group 2) and Tajik (group 3) students; P2 — reliability of differences between morphofunctional indices of platelets of Indian (group 2) and Tajik (group 3) students.

Analysis of the white blood cell count of Russian students (table 3) showed the maximum number of granulocytes (61.62 ± 1.52) and the minimum content of the total number of white blood cells (7.19 ± 0.32) and lymphocytes (29.88 ± 1.13). At the same time, all the specified parameters were within the reference values [13, 17].

Indian students were characterized by the opposite distribution of the content of leukocytes (table 3). Thus, the highest values were noted for the total number of leukocytes (7.59 ± 0.35), lymphocytes (34.14 ± 1.42), and the smallest - for the number of granulocytes (52.47 ± 1.51). The group of students from Tajikistan according to the nature of the distribution of the content of leukocytes repeated the trend of Indian students (Table 3). We suppose that of all the peripheral blood indices we analyzed, which reflect a change in the compensatory-adaptive reactions of the organism, is the total content of leukocytes and their separate groups. Since a similar pattern of distribution of these parameters among Indian and Tajik students was revealed [18].

Statistically the important significant differences were found for all studied leukocyte indicators (Table 3). Thus, the total number of leukocytes was significantly higher among Tajik students compared with Russian students. The number of lymphocytes was significantly higher in the group of Indian students

Table 3. Indicators of the distribution of leukocyte populations among first-year students, ($M \pm m$)

Parameters	Group 1	Group 2	Group 3
WBC	7,19±0,32	7,59±0,35	7,58±0,36
P1		>0,10	<0,05
P2			>0,10
LYM	29,88±1,13	34,14±1,42	31,04±1,32
P1		>0,05	>0,10
P2			>0,10
GRA	61,62±1,52	52,47±1,51	56,45±1,57
P1		<0,001	<0,01
P2			<0,05

Note: P1 — significance of differences between the content of leukocytes in Russian (group 1) and Indian (group 2) and Tajik (group 3) students; P2 — significance of differences between the content of leukocytes in Indian (group 2) and Tajik (group 3) students.

compared to Russian students. The quantitative content of granulocytes was significantly higher for both Indian and Tajik students than for Russian students [11, 13, 19].

Thus, the analysis of peripheral blood indices revealed significant shifts in adaptation processes towards tension in the group of Indian students and less critical changes in the compensatory-adaptive mechanisms of the organism in the group of students from Tajikistan. A significant factor shaping a similar range of adaptive reactions of the organism is the complex of climatic and geographical conditions of the Stavropol Territory and in particular of the city of Stavropol, whose climate is close to moderately cold [14, 15, 16, 20].

CONCLUSIONS

A comparative comprehensive assessment of the morphofunctional state of peripheral units of hemopoiesis, including the study of an extended blood test in a practically healthy population of one age group of young people, taking into account ethnic status, has been carried out. A search and development of evaluation and diagnostic signs of trouble among a healthy population contingent, the selection of premorbid conditions using simple, minimally invasive and at the same time most informative methods of monitoring the health of the working-age population and the younger generation. As a result of the study, new data were obtained that indicate the possibility of using peripheral blood as a test system for assessing the influence of damaging environmental factors on the organism of

children, adolescents and adults in different regions of residence. The results of the study can be used as normative characteristics of peripheral hemopoiesis and health monitoring at the stage of prenosological diagnosis and during medical examinations, including young people of pre-conscription age. Data on the relationship of the characteristics of uniform indicators of cellular composition with the degree of adaptation will allow identifying the spectrum of adaptive reactions of peripheral blood.

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VARIABILITY OF HUMAN CEREBRAL HEMISPHERES TEMPORAL OPERCULUM

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ABSTRACT — The temporal operculum is a region of the temporal lobe upper surface, which is bounded at the front by transverse temporal gyri, and from behind – by the end of the lateral cerebral sulcus.

AIM OF STUDY: to identify the shape and the dimensional features of the temporal operculum in people aged 1–21. Fixed brain preparations ($n = 47$) were used to measure the depth of the lateral sulcus at the level of the temporal operculum, and the temporal operculum length along its outer edge; the temporal operculum area was calculated as well. The studied material was divided into groups following age periodization: early childhood ($n = 8$); the first period of childhood ($n = 18$); the second period of childhood ($n = 7$); adolescence ($n = 5$), youthhood ($n = 9$). The study produced average values for the lateral sulcus depth, the temporal operculum length and area in people aged 1–21. The triangular shape of the temporal operculum has been found to be the most common. The temporal operculum area in early childhood and the first period of childhood, as well as the temporal operculum length in early childhood prevail in the left hemisphere ($p < 0.05$). Viewed from the age aspect, the depth of the lateral sulcus varies less significantly than the length and the area of the temporal operculum. The temporal operculum area correlated more with the operculum length rather than with the depth of the lateral sulcus.

KEYWORDS — temporal operculum, human brain.

INTRODUCTION

The temporal operculum (operculum temporale) is a region of the temporal lobe upper surface, which is bounded at the front by transverse temporal gyri, and from behind – by the end of the lateral cerebral sulcus (Fig. 1).

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Fig. 1. Temporal operculum layout on the temporal lobe upper surface: 1 — left temporal operculum, 2 — right temporal operculum

Within the temporal operculum, the cortical fields 41 and 42 are localized. These fields, like other fields of the temporal lobe upper surface, are linked to sound perception and are the nuclear zone of the auditory analyzer. Studying these areas of the cortex is an important task within both theoretical and practical sections of medical science, and acts as one of the basic elements for understanding age-related neuromorphology and neurophysiology [1].

Together with the parietal and frontal opercula, the operculum temporale forms the insula operculum, which hides the insular lobe (insula). Recent studies have revealed the importance of the insula in maintaining homeostasis, due to which there is a growth in the interest taken in this area of the cortex [2].

Special literature holds very few works offering a view on the size of temporal operculum. For instance, A.E. Bykanov et al. (2015) in their study provide data on the average thickness of the temporal operculum (distance between the insular posterior point and the lateral surface of the superior temporal gyrus) as equal to 32 mm (min–max = 27–35 mm) [3]. There is data showing the absence of a correlation between

the size of the temporal operculum and the length of the lateral sulcus and the brain mass [4], as well as the predominance of the temporal operculum area in the left hemisphere of the human brain [5]. The data concerning the length of the temporal operculum and the depth of the lateral sulcus, giving an idea of the longitudinal and transverse dimensions of this cortex area, is rare [4].

Aim

To identify the shape and reveal the specific dimensional features of the temporal operculum in people within the age range of 1–21.

Materials and methods

Brain preparations with no visible pathological changes were studied, which were obtained through autopsy of 47 corpses from people aged 1–21 years. The brain preparations fixed in formalin were used to measure the lateral sulcus depth at the level of the temporal operculum, the length of the temporal operculum along its outer edge. The temporal operculum outlines were marked to further calculate its surface area [2].

Subject to the age periodization (1965), the material was divided into groups: early childhood (age 1–2; 8 preparations); the first period of childhood (age 3–7; $n = 18$ preparations); the second period of childhood (boys, age 8–12; girls, age 8–11; $n = 7$ preparations); adolescence (boys, age 13–16; girls, age 12–15; $n = 5$ preparations), youthhood (boys, age 17–21; girls, age 16–20; $n = 9$ preparations).

The obtained data were processed by the variation statistical method using the Statistica 10.0 software. Due to the small number of samples, the median (Me) and the quartile range (Q25; Q75) were calculated to describe the average data, and non-parametric statistical methods were used to estimate the difference significance and the interrelational effect (U-Mann-Whitney test and Spearman's correlation coefficient).

RESULTS AND DISCUSSION

Based on the material of our study, we observed the following shapes of the temporal operculum — triangular (45%), scoop-net shaped (30%), quadrangular (15%), sickle-shaped (6%) and unidentified (4%) (Fig. 2).

The surface of the temporal operculum usually has tertiary fissures, the number of which varies from 1 to 6. The number of tertiary fissures has been noted to be prevailing in the left hemisphere.

In *early childhood*, the average depth of the lateral sulcus at the temporal operculum level has no significant bilateral differences ($p = 0.78$). The average length of the temporal operculum in the left hemisphere is 77.3% above that on the right — 28.9 [19.6; 31.4] mm and 16.3 [14.6; 21.2] mm ($p = 0.02$). The area of

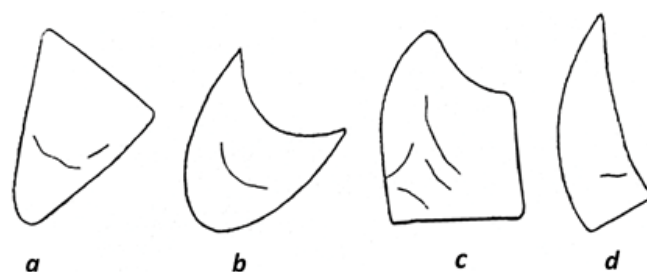


Fig. 2. Temporal operculum shapes: a — triangular, b — scoop-net shaped, c — quadrangular, d — sickle-shaped

the left temporal operculum statistically significantly exceeds that of the right (by 61.5%) — 443.9 [301.5; 492.6] mm² and 274.3 [206.1; 338.6] mm² ($p = 0.03$) (see Table 1).

In the *first childhood period*, the average depth of the lateral sulcus also reveals no significant bilateral difference ($p = 0.72$). The average length of the temporal operculum in the left hemisphere is 21.4% above that in the right one — 27.8 [25.4; 31.1] mm and 22.9 [17.6; 26.8] mm., however, the difference does not reach the level of statistical significance ($p = 0.08$). And only the area of the left temporal operculum reveals statistical significance exceeding the area of the right operculum by 26.9% — 465.9 [396.8; 503.0] mm² and 367.2 [290.1; 453.5] mm² ($p = 0.04$).

In the *second childhood period, adolescence and youth*, the studied parameters have similar values in the right and left brain hemispheres ($p = 0.10–0.94$).

No statistically significant differences have been identified in the values in the adjacent age groups. This suggests that the temporal operculum reaches its final size in the early postembryonic development stages — in the first year of life, when the most intensive growth of the brain is underway.

The correlation analysis showed a strong positive relationship between the temporal operculum length and its area ($r = 0.9$; $p < 0.001$), as well as a moderately strong positive relationship between the lateral sulcus depth and the temporal operculum area ($r = 0.4$; $p < 0.001$).

CONCLUSIONS

1. The most common shape of the temporal operculum is triangle.
2. The temporal operculum area in early childhood and the in first childhood period, as well as the length of the temporal operculum in early childhood, reveal statistically significant predominance in the brain left hemisphere.
3. From the age aspect, the depth of the lateral sulcus changes less significantly than the length and area of the temporal operculum.

Table 1. Morphometric parameters of the temporal lobe in people in the age range of 1–21 years

Age group	Parameter		n	Min-Max	Me [Q25; Q75]	p
Early childhood	Depth of the lateral groove, mm	Right	8	29,4-38,6	32,2 [30,8; 36,6]	0,78
		Left	8	30,0-36,9	32,4 [30,75; 35,0]	
	The length of the temporal tire, mm	Right	8	10,7-27,0	16,3 [14,6; 21,2]	0,02
		Left	8	16,0-35,6	28,9 [19,6; 31,4]	
	The area of the temporal tire, mm ²	Right	8	171,2-436,4	274,3 [206,1; 338,6]	0,03
		Left	8	255,0-617,7	443,9 [301,5; 492,6]	
The first period of childhood	Depth of the lateral groove, mm	Right	18	28,0-37,4	33,0 [29,8; 33,9]	0,72
		Left	18	25,6-40,4	33,2 [29,8; 35,2]	
	The length of the temporal tire, mm	Right	18	10,4-42,0	22,9 [17,6; 26,8]	0,08
		Left	18	9,6-40,3	27,8 [25,4; 31,1]	
	The area of the temporal tire, mm ²	Right	18	157,0-693,0	367,2 [290,1; 453,5]	0,05
		Left	18	170,4-830,2	465,9 [396,8; 503,0]	
The second period of childhood	Depth of the lateral groove, mm	Right	7	28,5-39,3	33,0 [29,9; 34,7]	0,74
		Left	7	23,8-40,4	32,5 [27,7; 35,9]	
	The length of the temporal tire, mm	Right	7	9,2-49,2	28,5 [15,5; 38,0]	0,94
		Left	7	10,6-51,6	31,7 [15,9; 37,1]	
	The area of the temporal tire, mm ²	Right	7	156,8-730,7	446,0 [220,9; 518,9]	0,84
		Left	7	236,3-754,4	434,1 [325,1; 501,5]	
Adolescence	Depth of the lateral groove, mm	Right	5	21,2-41,6	32,0 [28,5; 33,1]	0,75
		Left	5	25,4-35,5	32,0 [28,5; 33,1]	
	The length of the temporal tire, mm	Right	5	11,0-35,5	15,1 [12,5; 15,8]	0,17
		Left	5	12,0-43,2	25,0 [16,3; 38,7]	
	The area of the temporal tire, mm ²	Right	5	132,5-568,0	241,6 [155,6; 328,6]	0,25
		Left	5	171,0-714,9	443,7 [207,0; 619,2]	
Youthhood	Depth of the lateral groove, mm	Right	9	11,8-42,1	36,2 [27,3; 37,3]	0,75
		Left	9	29,8-45,4	35,6 [31,8; 36,8]	
	The length of the temporal tire, mm	Right	9	9,0-45,5	19,4 [10,0; 34,5]	0,17
		Left	9	15,2-40,6	31,7 [23,1; 36,7]	
	The area of the temporal tire, mm ²	Right	9	159,0-957,8	310,4 [181,0; 470,9]	0,10
		Left	9	226,5-736,6	555,7 [415,8; 669,9]	

4. The temporal operculum area correlates with the length of the temporal operculum to a greater degree than with the lateral sulcus depth. The obtained data expands and complements the information available in the literature concerning human brain temporal operculum and shall be of interest to morphologists who deal with human brain structural issues. Detailed understanding of the temporal operculum surgical anatomy offers correct intraoperative orientation and helps choose the right option ensuring surgical access.

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CONNECTION BETWEEN CLINICAL AND RADIOLOGICAL TORQUE OF MEDIAL INCISORS AT PHYSIOLOGICAL OCCLUSION

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INTRODUCTION

Lifetime X-ray and morphological diagnostics represent the major tools of research and applied value, which help solve numerous diagnostic issues faced by a number of specialists involved in public healthcare [1–9].

The growing interest taken currently in dentition morphometric studies is due to the systematization and specification of the accumulated data, which allows clinicians (dentists, maxillofacial surgeons) to compare the external maxillofacial parameters with the person's internal structural features not only in the normal status, yet also in case of pathological conditions. Besides, the effectiveness of the introduced advanced dental treatment should rely not only on improved equipment and materials, but also on better diagnostic technologies in view of the fundamental topographic anatomy knowledge, which would allow an individual approach to each case, as well as help achieve consistent and stable positive outcomes [10–15].

The individual position of the incisors has been in the focus of many researchers' works. There is plenty of detailed data regarding incisors torque, described in view of the dental and gnathic face types, and follow-

ABSTRACT — AIM. To determine the link between the clinical and radiological torque of the medial incisors in cases with physiological occlusion.

Materials and methods. A measurement of the clinical torque values was performed (whereas the torque is defined as the deviation of the tooth crown vestibular surface from the occlusal plane) in 98 people with physiological occlusion and a full set of permanent teeth. When measuring the clinical incisor torque, three methods were employed. The first method allowed studying teeth torque in relation to the occlusal plane on the cast jaw models using the Arco-Zet equipment (by Scheu Dental GmbH). The second method implied using a modified protractor, where the moving part was oriented in relation to the occlusal plane. The third method we used involved analyzing data from telerradiography and cone-beam tomograms obtained with the PaX-i3D SC digital panoramic X-ray unit (VATECH Global), which were marked with linear and angular reference points. The patients were divided into three groups depending on the incisors location: Group 1 included patients with the mesotrusive incisors location; Group 2 were patients with physiological protrusion of the incisors and a decrease in the interincisal angle, with Group 3 including patients with physiological retrusion of incisors. **RESULTS.** Regardless of the type of dental arches and the vestibular lingual inclination of the incisors, the average difference between the clinical and the radiological incisor torque values is 26°, which can be used in clinical orthodontics to develop a treatment tactics and its effectiveness in people with various gnathic and dental types as well as with various dental arches.

CONCLUSION. All methods used for measuring the teeth inclination angles in the vestibular lingual direction can be employed both in the applied and in the clinical aspect. Identifying the permanent teeth torque through cast models of dentition morphometry and through using special equipment, takes a lot of effort, time, at the same time being subject to potential measurement errors. The methods implying analysis of cone-beam computed tomography images feature high-tech reliance, precision, whereas the reproductive capacity and interpretation of the results allows using the available angular and linear parameters for evaluating the effectiveness of the respective orthodontic procedures through all the stages of treatment.

KEYWORDS — medial incisor torque, cone-beam computed tomography, protrusion and retrusion of incisors, interincisal angle, physiological occlusion.

ing the contemporary classifications of the face and dental arch types. The obtained data has shaped the basis for braces design concerning the arc equipment [16–19].

There has been a dependence identified between the inclination of the front incisors and the Schwartz facial angle (ANB), while a 1-degree change in the ANB angle results in a 1-degree or a 1-mm change in the front incisor inclination [20]. The features of the lower jaw incisors location have made the basis for adopting extraction methods in orthodontic treatment offered in case of disturbed dental arch shape and size. Following the “teeth shift” concept in orthodontics, patients with class I bite anomaly are to have their teeth removed with a deviation from the midline, crowding, bimaxillary protrusion, vertical mismatch, distal bite (overjet), and incisor inclination increase [21–26]. Currently, the orthodontic treatment planning is done reasoning from the position of the upper incisors, and not the molars or the lower jaw incisors. Given that, when planning mechanical teeth shift, some clinicians recommend placing the incisors in an ideal position to further restore the occlusal match of the remaining teeth [27–30].

Other experts offer proof to the fact that in case there is no way to provide an ideal position for the incisors, they can be placed in a “non-ideal”, yet acceptable one, and define this as an “optimal functional occlusion” using it as the basis. Identifying the angle of the incisors vestibular lingual inclination is a key task when developing methods for treating patients with maxillofacial issues through different age stages, including milk dentition bite. At the same time, identifying the incisors torque takes a detailed analysis since their location, as researchers show, is determined by various numerical values in relation to the major anatomical points. As a rule, in clinical orthodontics the upper incisors vestibular inclination determines their relation to the Frankfurt horizontal or spinal (maxillary) plane [31–34].

G.W. Arnett X-Ray Analysis (1999) identifies the upper incisors torque in relation to the occlusal plane and takes into account the gender dimorphism of this feature. For males, the angle is 58°, while for women it is 57° [35].

In clinical orthodontics, the teeth torque is identified from the position of the teeth vestibular surface against the occlusal plane perpendicular. Due to that, the torque values of the upper jaw medial incisors vary from 3 to 27°, and are expressed in such terms as “low”, “standard” and “high” teeth torque. However, the published research papers do not show what types of dental arches and faces are to be found in patients who are to use the specified braces. Mention to be made of

another opinion expressed by specialists noting that during physiological occlusion, the medial upper incisors torque values are determined by the gnathic and dental types of dental arches [36,37,38].

The variety of braces and ways of inclination angles’ measuring suggest the need for employing an individual approach and choice of optimal investigation to ensure diagnostic accuracy [39,40,41].

The instrumental methods that are used focus on the occlusal, Camper’s, and mandibular planes. These methods are effort- and time-consuming, while potential errors are complicated when applying morphometric landmarks, reference lines, comparing projection data, and involve varying anatomy of the examined tooth surface [42,43,44,45,46,47]. The leading role in determining the inclination angles of the incisors belongs to cone-beam computed tomography (CBCT), which offers high precision in identifying the inclination angles and the angles formed by antagonists (in particular, the interincisal angle) [48,49,50,51,52]. The reason behind this study is the lack of data available in the respective research literature focusing on the relationship between the clinical and the radiological medial incisors torque in case of physiological occlusion.

Aim of study

To identify the relationship between the clinical and the radiological medial incisors torque in case of physiological occlusion.

MATERIALS AND METHODS

The study involved 98 people with physiological occlusion and a full set of permanent teeth. The patients were divided into three groups depending on the incisors location: Group 1 included patients with mesotrusive position of the incisors where the interincisal angle was 125°–134°. The patients in Group 2 featured physiological protrusion of the incisors and a decrease in the interincisal angle (below 120°). In Group 3, the patients had an interincisal angle exceeding 145° also revealing physiological retrusion of the incisors. The telerradiography and cone-beam tomograms were obtained on a 21-section digital panoramic X-ray unit PaX-i3D SC featuring the functions of a computed tomograph and an FOV cephalostat with accessories (VATECH Global, South Korea) following the scanning protocol for Sim Plant. Processing, storage and export of the X-ray images involved the Ez Dent-iTM software, a multiplanar reconstruction and a three-dimensional (3D) reconstruction – using the Ez 3D-iTM tomograph software for 3D diagnostics; viewing the saved data with an importing option was performed using the Viewer™ software. The thickness of the tomographic section was 1 mm, the reconstruc-

tion step was 1 mm, the rotation step – 1 mm. In order to identify the occlusal plane, the radiographs had the major reference points applied on them. The distal point (hPOcP) corresponded to the location of the lower second molar distal tubercle. The front point (vPOcP) corresponded to the midpoint of the distance between the cutting edges of the incisors (Fig. 1).

The tomograms had a conditional median vertical of the medial incisor built on them and running from the incisor's cutting edge through the tooth neck middle. The obtained lines shaped an interincisal X-ray angle (Fig. 2).

Besides, tangent lines were drawn to the vestibular contour of the incisors crowns, which, at their intersection, made up an interincisal clinical angle. The reference points were those located at the cutting edge, near the vestibular contour of the crown, and at the top convexity point of the vestibular contour – on the tooth equator (Fig. 3).

The following were used as the major teleradiography points: N (Nasion) – located at the junction of the frontal and nasal bones; C (Condylion) – the top point of the articular head; Ar (Articulare) – the distal contour of the mandible articular head neck; T2 – the posterior lower nub of the mandible angle; Me (Menton) – the lowest point on the lower jaw contour, at the symphysis site. These anthropometric spots served as reference points for the construction of the Frankfurt horizontal (FH), the occlusal plane (OP) and the mandibular plane (MP). Besides, conditional median verticals were drawn through the cutting edge of the incisors and the tooth root apex, whereas the verticals served as guidelines for identifying the interincisal angle and for joining the maxillary incisal tomogram lines with the teleradiography facial skull plane (Fig. 4).

The clinical incisor torque was measured not radiographically only, yet also on cast jaw models. The jaw models were studied using a respective device by Scheu-Dental (Germany), which allowed evaluating the teeth torque relative to the occlusal plane. When manufacturing the cast models, the model base was in relation to the occlusal plane. The model was installed on a stage equipped with a level that allowed orienting the model in the horizontal plane. From the vestibular side of each model tooth, a conditional median vertical was drawn. A thin drill was used to make a hole in the crown center thus allowing the central probe of the device to be located in it, while the probe was connected to a measuring device to identify the inclination angle in°. The other research method was measurement using a modified protractor where the moving part was oriented in relation to the occlusal plane (Fig. 5).

The study outcomes were statistically processed using the SPSS 17.0 software package at a 0.05 signifi-

cance level. When performing quantitative description, the mean value (M) and the standard mean error (m) were used. The statistical processing was carried out using descriptive statistics, analysis of variance (Student's t-test), correlation analysis (Pearson and Spearman's paired correlation coefficients), and with nonparametric statistics methods (Mann-Whitney and Wilcoxon).

RESULTS AND DISCUSSION

The study results of the computed tomograms revealed that the inclination incisors angles in the vestibular lingual direction had features that depended on the dental arch type.

Table 1 shows the results of the study concerning the patients with physiological occlusion.

The results of studying the inclination of the upper medial incisors in the anterior-posterior direction (torque), which was measured by computed tomograms and jaw cast models, showed that in Group 1, with mesotrusive incisors arrangement, the magnitude of the clinical torque, determined through the deviation of the tooth crown vestibular surface from the occlusal plane, was $77.64 \pm 2.23^\circ$. The obtained values were close to the standard values of braces for the upper jaw medial incisors. At the same time, the vestibular lingual inclination of the upper medial incisors in relation to the occlusal plane was $51.52 \pm 3.57^\circ$, and was slightly below the values once set by G.W. Arnett (1999). The difference between the clinical and the radiographic torque at the upper medial incisors was $26.12 \pm 2.11^\circ$. The clinical torque of the mandibular medial incisor, determined through the deviation of the tooth crown vestibular surface from the occlusal plane, was $89.33 \pm 0.45^\circ$. The obtained values were close to the standard values describing the braces for the mandibular medial incisors. At the same time, the vestibular lingual inclination of the lower medial incisors in relation to the occlusal plane was $62.75 \pm 2.33^\circ$. The size of the interincisal angle, shaped by the conditional median verticals of the antagonists, in Group 1 was $134.21 \pm 3.81^\circ$. The angle made by the tangent lines to the vestibular surfaces of the antagonists was $169.34 \pm 5.94^\circ$.

In Group 2 (with protrusive position of incisors) the clinical torque was $69.56 \pm 3.61^\circ$. The obtained values were close to those of braces with a "high" torque for the upper jaw medial incisors. At the same time, the vestibular lingual inclination of the upper medial incisors in relation to the occlusal plane was $44.11 \pm 3.57^\circ$ and was significantly below the values identified in Group 1, as well as the values established by G.W. Arnett (1999). The difference in the clinical and in the

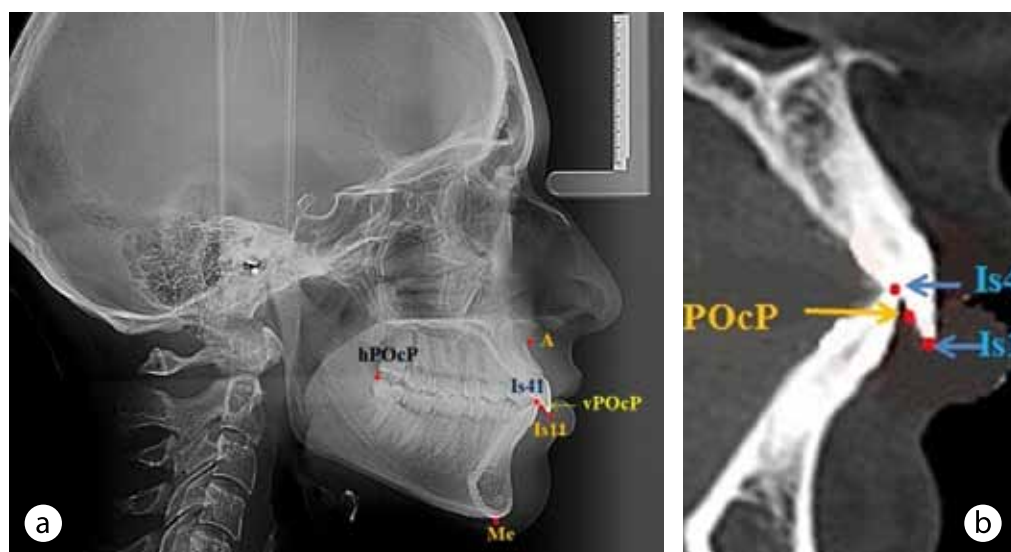


Fig. 1. Anatomical landmarks on a telegentogram (a) and a cone-beam tomogram (b) for constructing an occlusal plane



Fig. 2. Determination of cutter angle (Lii)

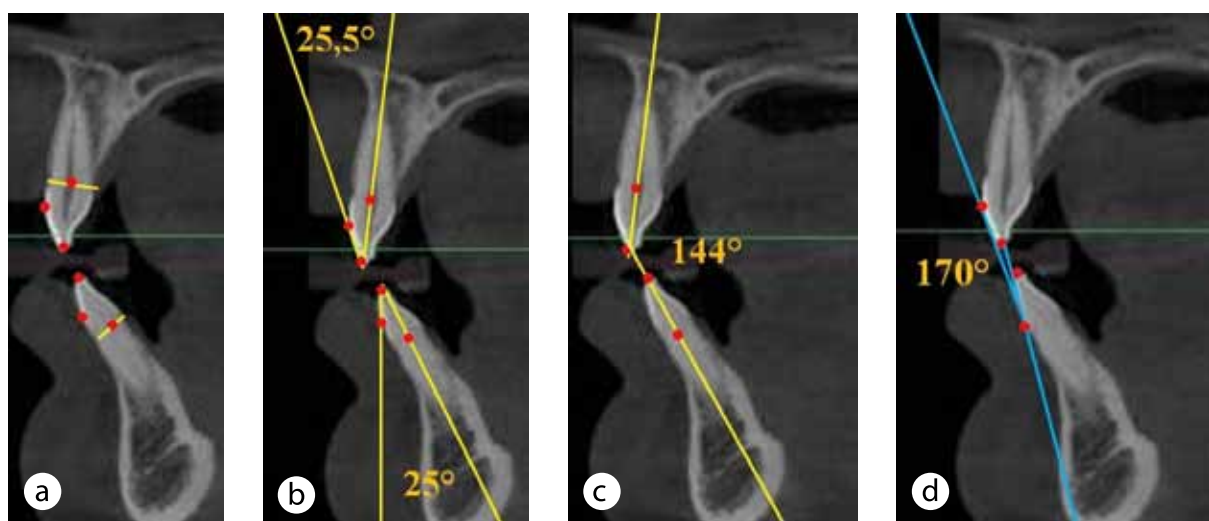


Fig. 3. Methods for studying inclination angles of incisors on tomograms: (a) main odontometric points; b — measurement of the difference in position of the reference lines; c — measurement of the intercutaneous radiological angle; d — measurement of the intercutaneous clinical angle

radiographic torque in the upper medial incisors was $26.12 \pm 2.11^\circ$. The clinical torque of the mandibular medial incisor, determined through the deviation of the tooth crown vestibular surface from the occlusal plane, was $86.03 \pm 1.14^\circ$. The obtained values were close to those for braces with a “high” torque for the mandibular medial incisors. At the same time, the vestibular lingual inclination of the lower medial incisors in relation to the occlusal plane was $60.89 \pm 1.87^\circ$. The size of the interincisal angle, shaped by the conditional median verticals of the antagonists in Group 2 was

$118.31 \pm 4.45^\circ$. At the same time, the angle made by the tangent lines to the vestibular surfaces of the antagonists was $201.07 \pm 6.27^\circ$.

In Group 3 patients with incisor retrusion, the clinical torque was $84.27 \pm 2.25^\circ$. The obtained values were close to those for braces with a “low” torque for the medial upper jaw incisors. At the same time, the vestibular lingual inclination of the upper medial incisors in relation to the occlusal plane was $57.85 \pm 2.89^\circ$ and was close to the values observed in Group 1 patients, as well as the values set by G.W. Arnett

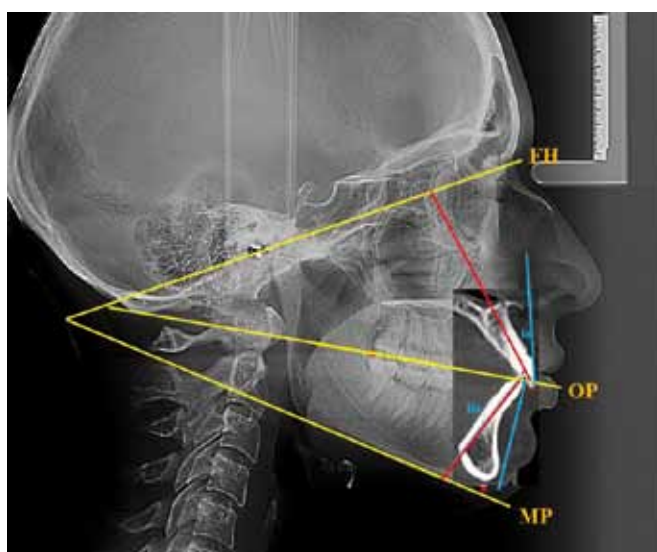


Fig. 4. The combination of teleroenogram and cone-beam tomogram with marked reference lines

Fig. 6 shows the major values of the incisors torque in the patients belonging to the groups in question.

Integrating the obtained data, we can state that visualization of the structures of the dental system and their topographic interconnection in high spatial resolution creates ground for constructing idealized, averaged models, as well as models that provide a maximum reproduction of the patient's individual features not only in view of the spatial orientation (geometry), yet also of the structure (morphology) of tissues, opening up newer opportunities in biomechanical analysis of human bone joints.

CONCLUSIONS

1. The methods employed for measuring the inclination angles of the upper and lower jaws teeth, as well as for identifying the inclination angles of the antagonizing teeth are diag-

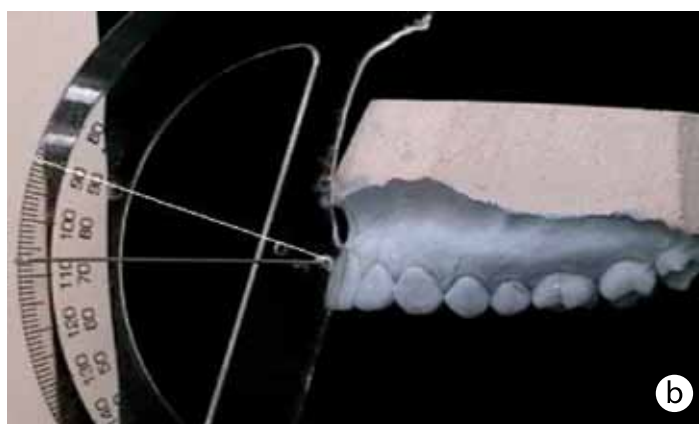


Fig. 5. Methods for the study of the clinical incisor of the incisors on a device made by Scheu-Dental (a), and using a protractor (b)

(1999). The difference between the clinical and the radiographic torque in the upper medial incisors was $26.12 \pm 2.11^\circ$. The clinical torque of the mandibular medial incisor, identified through the deviation of the tooth crown vestibular surface from the occlusal plane, was $92.09 \pm 1.16^\circ$. The obtained values were close to the standard values of the braces for the mandibular medial incisors. During that, the vestibular lingual inclination of the lower medial incisors in relation to the occlusal plane was $67.08 \pm 1.54^\circ$. The size of the interincisal angle, shaped by the conditional median verticals of the antagonists, in Group 1 was $149.89 \pm 4.24^\circ$. The angle made by the tangent lines to the antagonists vestibular surfaces was $180.26 \pm 4.12^\circ$.

nostically valuable, offer reliable data, and can be used not only to describe the physiological occlusion, but also to evaluate the effectiveness of the orthodontic treatment given to patients with dentofacial pathologies.

2. Regardless of the dental arch type and the incisors vestibular lingual inclination, the difference between the clinical and the radiological incisors torque was an average of 26° , which can be used in clinical orthodontics to design the treatment tactics and evaluate its effectiveness in people with different gnathic and dental types of face and dental arches.

3. If introduced into clinical orthodontics, the obtained results involving the reference values limits

Table 1. The inclination angle of incisors in patients of the studied groups, ($M\pm m$), ($p\leq 0,05$)

Parameters	The inclination angle of incisors (in degrees):					
	Clinical angle (people)			X-ray angle (people)		
	1 group	2 group	3 group	1 group	2 group	3 group
Tork top cutter	77,64 \pm 2,23	69,56 \pm 3,61	84,27 \pm 2,25	51,52 \pm 3,47	44,11 \pm 3,57	57,85 \pm 2,89
Tork lower tool	89,33 \pm 0,45	86,03 \pm 1,14	92,09 \pm 1,16	62,75 \pm 2,33	60,89 \pm 1,87	67,08 \pm 1,54
Cutter angle	169,34 \pm 5,94	201,07 \pm 6,27	180,26 \pm 4,12	134,21 \pm 3,81	118,33 \pm 4,45	149,89 \pm 4,24

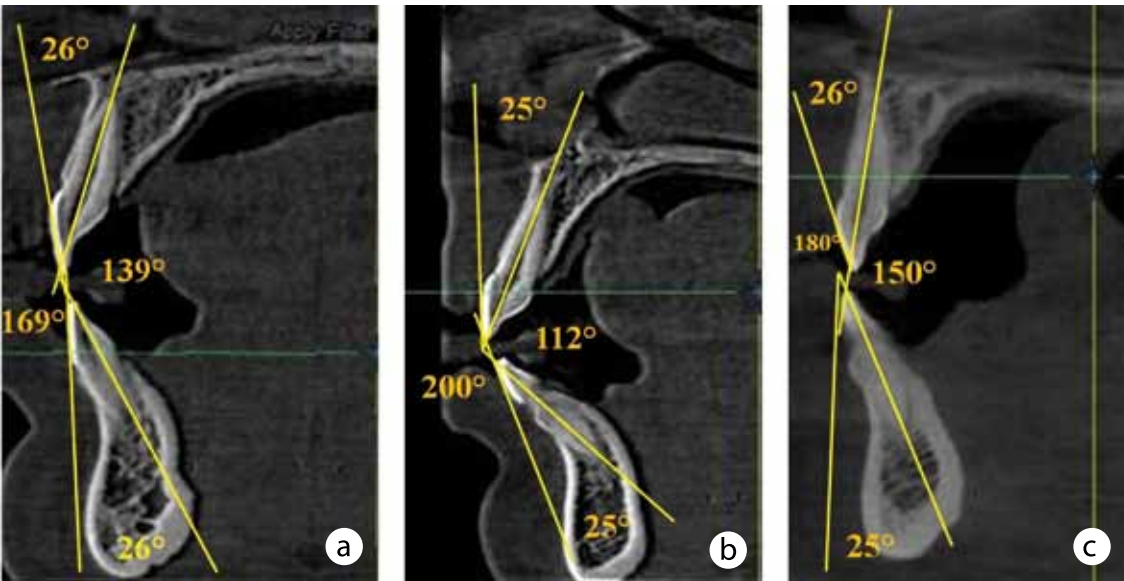


Fig. 6. Basic values of the incisor of the incisors during mesotrusion (a), protrusion (b) and retrusion (c)

and the confidence intervals of inclination angles for the upper and lower jaw teeth, as well as the inclination of the antagonizing teeth, would allow reducing the time spent on early diagnostics as well as improve the efficiency of monitoring the orthodontic correction outcomes.

4. In order to prevent the temporomandibular joint dysfunction during orthodontic treatment, special attention should be paid to the torque of the medial and lateral upper incisors, which act as guides through the mandible anterior movement.

5. Improving the available methods used to diagnose dental anomalies resulted in high-tech, high-precision, computerized methods employed to measure the maxillofacial area structures, which, when introduced, would allow not only minimizing the errors associated with instrumental measurement techniques, but also achieving better functional aesthetic outcomes due to a higher predictability of orthodontic treatment.

6. Based on the anthropometric and clinical diagnostic studies outcomes, the localization of the

standard (classical) and additional morphometric points in axial, frontal, sagittal reformats has been refined. Specifying the spatial location (topography) of the anatomical landmarks through cone-beam computed tomography allows increasing the reliability and the accessibility of measurements, standardizing anthropometric studies of human craniofacial structures, conducting a detailed assessment of their shape, as well as getting more significant amount of reliable data with high-precision dimensional features.

7. Cone-beam computed tomography employed for studying the craniofacial structures, expands significantly the current understanding of the variability of the “anatomical norm”, which is determined by individual-typological variability, gender differences, age-related changes, area of residence, etc., thus making it possible to obtain data that is of importance for personalized medicine.

8. Systematizing the data obtained through a comprehensive assessment of the individual anatomical variability of the craniofacial structures in the axial,

frontal, and sagittal planes, allows us to expand significantly the current pool of knowledge to further ensure better interdisciplinary cooperation involving areas like medical craniology, dentistry, radiology, maxillo-facial surgery, neurosurgery, otolaryngology, anatomic pathology, and forensic medicine.

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ENHANCEMENT OF RESEARCH METHOD FOR SPATIAL LOCATION OF TEMPOROMANDIBULAR ELEMENTS AND MAXILLARY AND MANDIBULAR MEDIAL INCISORS

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ABSTRACT — This item reveals the analysis outcomes for craniometric and morphometric parameters of the temporomandibular joints and incisal dentofacial segments obtained through studying 157 computer tomograms and lateral skull teleradiographies from people with physiological occlusion of permanent teeth in the first mature age period. Detailed investigation of the spatial arrangement of the craniofacial structures allowed developing, substantiating and testing a method of computer tomograms combination of the mandibular joint and dentofacial segments of the mandibular and maxillary medial incisors with head teleradiographies in the lateral projection. This algorithm allowed increasing the measurements reliability (linear, angular) in the sagittal plane, identifying the degree of complexity and justifying the choice of tactics for the planned treatment, describing the facial skull growth type (horizontal, vertical and neutral), as well as evaluating the effectiveness of orthodontic treatment at all stages.

KEYWORDS — head teleradiography; dentofacial segments; medial incisors; temporomandibular joint; cone-beam computed tomography.

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INTRODUCTION

Recently, patients have been taking significantly higher interest in restoring the aesthetic and functional standards [1–5]. A significant technological breakthrough as well as the introduction of advanced reliable techniques in orthodontics offer us newer opportunities and prospects in diagnosing and treating dentofacial anomalies [6–10]. The close attention paid by clinicians to the development of newer diagnostic methods is due to potential of achieving stable and predictable outcomes with accurate plan correction through the dynamics of dental treatment [11–15].

Neurodentistry nowadays is based on the concept of functional occlusion, which determines the direct relationship between the temporomandibular joint anatomy, the muscle-articular apparatus, the dentition occlusal surfaces morphology, and the teeth position during joining. The reconstruction of the dental arches (rows) shape and size is closely related to proper construction of the prosthetic plane in view of the individual features of the dental system based on clinical and instrumental methods of examination as well as X-ray diagnostics methods [16–20].

Physical methods for clinical examination of patients with occlusion issues (odontometry, cephalometry, dentofacial arches measurement) and functional clinical trials may not be sufficient and reliable for diagnosing and selecting a rational orthodontic treatment method. When studying the dentofacial area, of particular importance appear x-ray methods that allow precise diagnostics, adjusting the treatment plan to prevent complications, reducing the rehabilitation time, and enhancing the efficiency of dental interventions [21–26].

Virtually no one orthodontist can do without analyzing teleradiographic data. The method allows differentiating gnathic and/or dentoalveolar pathologies. The method serves a basis for developing a treatment plan including a comprehensive one, involving maxillofacial surgeons [27–29].

Teleradiography estimate the location of the temporomandibular joint elements in relation to the

Frankfurt plane and the Turkish saddle. The joint features have been the focus through numerous research works and they determine mandibular biomechanics [30–34].

A special place in the orthodontic clinics is given to the medial incisors, which, often, determine the treatment tactics for patients with occlusion issues. Their role as key teeth has been described by experts. There have been inclination (torque) angles and angulation shown, which are used to select the type of arch orthodontic appliance braces. The said angles are typically determined by the individual characteristics of facial types and types of dental arches. For certain types of dental arches, the normal position of the incisors is retrusive, for the others, on the contrary, it is the protrusive position [35–39]. Given that, still relevant are the issues implying developing methods that allow improving the accuracy of measurements and determining the position of the joint elements and the incisors, which is of particular importance in clinical orthodontics when it comes to forecasting and evaluating the treatment effectiveness.

Nowadays, there been hundreds of methods proposed for analyzing teleradiographic data, most of them being individually designed [40–42]. However, as there appeared newer details on the dental arches morphology and the dentofacial area in general, teleradiography analysis remains a relevant issue for dentistry [43, 44]. As advanced digital technologies and improved X-ray equipment have become part of the clinical practice, it allowed a widely use of cone-beam computed tomography (CBCT). The obvious advantages of CBCT include: full scanning of the object; possible 3-D examination of the object at any angle and depth; visualization of the smallest changes in the morphological structures of the respective objects; high resolution identification of the level and amount of hard tissues in the dentofacial area in any part and at any therapeutic and diagnostic stage. A series of cross-sectional images allow now diagnosing and selecting treatment methods for congenital and acquired maxillofacial pathologies [45–50].

Given the available methods, it is now possible to apply various images and combine anatomical details using computer software, which explains the aim of this study.

Aim of study: to improve the method for studying the spatial arrangement of the temporomandibular joint elements and the medial incisors, both mandibular and maxillary.

MATERIALS AND METHODS

The study included analysis of teleradiography lateral projections and computed tomograms of 157

people with no sign of dentofacial organic pathology and with permanent teeth physiological occlusion. The examinations were carried out in the age group related to the first mature period (21–35 years), taking into account the principles of bioethics and obtaining the patients' due consent.

The main points for the teleradiography included: N (Nasion), located at the junction of the frontal and nasal bones; C (Condylion), the articular head highest point; Ar (Articulare) — distal contour of the neck of the mandible articular head; T1 — posterior superior bulge of the mandible angle; T2 — posterior lower bulge of the mandible angle; Me (Menton) — the lowest point on the mandible contour, at the symphysis; Pg (Pogonion) — the mental protrusion front point. In addition, conditional medial verticals were drawn through the incisors cutting edge and the tooth root apex, which served as a reference lines for identifying the interincisal angle as well as for aligning the maxillary incisal lines with the facial skull plane.

The teleradiography and cone-beam tomograms were obtained on a 21-section digital panoramic X-ray unit PaX-i3D SC featuring the functions of a computed tomograph and an FOV cephalostat with accessories (VATECH Global, South Korea) following the scanning protocol for Sim Plant. Processing, storage and export of the X-ray images involved the Ez Dent-iTM software, a multiplanar reconstruction and a three-dimensional (3D) reconstruction — using the Ez 3D-iTM tomograph software for 3D diagnostics; viewing the saved data with an importing option was performed using the Viewer™ software. The thickness of the tomographic section was 1 mm, the reconstruction step was 1 mm, the rotation step — 1 mm.

RESULTS AND DISCUSSION

When analyzing the teleradiographic data, we found that the obtained images failed to clearly display the temporomandibular joints boundaries, where the shadows of the adjacent anatomical structures were applied, in particular the temporal bone zygomatic process. Besides, the central incisors boundaries on both jaws, on which the antimers relief is applied, were not clearly seen. At the same time, the teleradiographies featured high content accuracy for the main planes location (skull base, Frankfurt, occlusal and mandibular). The positions of the subspinal (A) and supramental (B) points were clearly visible. It was possible to measure the upper medial incisors inclination angle in relation to the Frankfurt and/or craniofacial plane, and the lower ones — to the mandibular plane. As for the computer tomograms analysis, they are significantly better compared to the teleradiographies in terms of the image clearness displaying boundaries

at different levels. It is quite possible to make precise measurements for linear and angular parameters using a package of applied mathematical software incorporated in the equipment. However, the view field of individual elements does not embrace other anatomical landmarks, which are necessary to analyze the spatial location of the studied organs. The tomograms make it hard to identify the medial incisor torque in relation to the occlusal plane. At the same time, the interincisal angle can be identified rather accurately.

Given that, we proposed a method for tomograms computer alignment for the mandibular joint and medial antagonist incisors with the lateral projection of head teleradiographies. The main references included the C points at the top of the articular process and the acoustic meatus of the tomograms, which were aligned relative to the craniofacial horizontal. When applying the incisors tomogram, the reference was the incisors conditional median verticals, which were combined with the lines shaping the teleradiography interincisal angle, as well as the face front vertical (N – Pg) and the Pg point. As a result, the study allows proposing an algorithm for comparing teleradiographies and some tomogram fragments, in particular, a fragment of the temporomandibular joint and medial incisors in an occlusal relationship. The algorithm included the following steps.

Firstly, the common points were applied: N (Nasion), C (Condylion), Ar (Articulare), T1, T2, Pg (Pogonion). These points served as a guideline for holding reference lines (planes), which we used as a reference for comparing tomogram fragments with the teleradiography. Horizontally, two lines were drawn. The upper line, which ran through the N and C points, separated the facial skull from the backskull, and we designated it as the facial skull plane or the craniofacial line (CFL). The mandibular plane (ML) passed through the Gn and T2 points. The intersection of these lines shaped the maxillofacial angle, which can be used as an indicator of the face growth type (horizontal, vertical and neutral). In the vertical direction, the N and Pg points were connected and a line resulted, which we marked as the vertical facial line. The line tangent to the mandible ramus bone (Ar – T1) with the mandibular plane shaped the mandibular angle (Fig. 1).

Secondly, the tomograms fragments were selected (Fig. 2).

Third, a combination of fragments was performed.

When combining the dentofacial incisal fragment of the tomogram, the Pg point of the tomogram was combined with the similar point of the teleradiography located on the face anterior vertical (N – Pg). At

the same time, the medial incisors conditional median verticals connecting the cutting edges with the teeth roots tips coincided with the interincisal lines. When combining the temporomandibular joint fragment, the C point of the tomogram was combined with the similarly named teleradiographic reference. During that, the location of the Ar points was used for conformity (Fig. 3).

This means that the obtained images allow performing linear and angular measurements, as well as transferring the computed tomogram data to teleradiography.

CONCLUSIONS

1. Improving the existing methods for the diagnosis of dentofacial anomalies resulted in developing a method of computed tomogram combination for the mandibular joint and dentofacial segments of the medial incisors with the head lateral teleradiographies. The method is based on aligning the C point, located at the top of the articular process and the acoustic meatus of tomograms, with the cranio-facial horizontal. When applying the incisors tomogram, the reference point was the conditional median vertical lines of the incisors, the vertical line of the face and the Pg point, which were combined with the lines shaping the interincisal angle of the teleradiographies. Using this algorithm will allow not only minimizing the errors associated with instrumental measuring techniques, yet will also lead to optimal functional and aesthetic results due to the predictability of orthodontic treatment.

2. The sum of the four angles (tetragonal indicator) including the value of the maxillofacial angle (between the ML and CFL lines), as well as the sizes of the angles shaped by the incisor lines with the ML and CFL (upper incisal, lower incisal, interincisal), may be recommended to be used as an indicator of the facial skull growth type (horizontal, vertical and neutral). An identical value, i.e. the sum of the five angles (pentagonal index), as a resultant for the upper incisal, interincisal, lower incisal, mandibular, and articular angles can also be used to describe the facial growth types.

3. Imposing the incisive dentofacial segment of a computed tomogram on a teleradiography located on the face anterior vertical allowed calculating the torque (vestibular-lingual) angles of incisors inclination towards the occlusal plane (OL). A perpendicular line drawn vertically on both sides of the OL line is a guideline for measuring the inclination angles (torques) with respect to the occlusal plane.

4. The clear (X-ray contrast) images of the temporomandibular joint elements allowed identifying the dimensions of the articular fossa in the anteroposterior and vertical directions, evaluating the ratios of

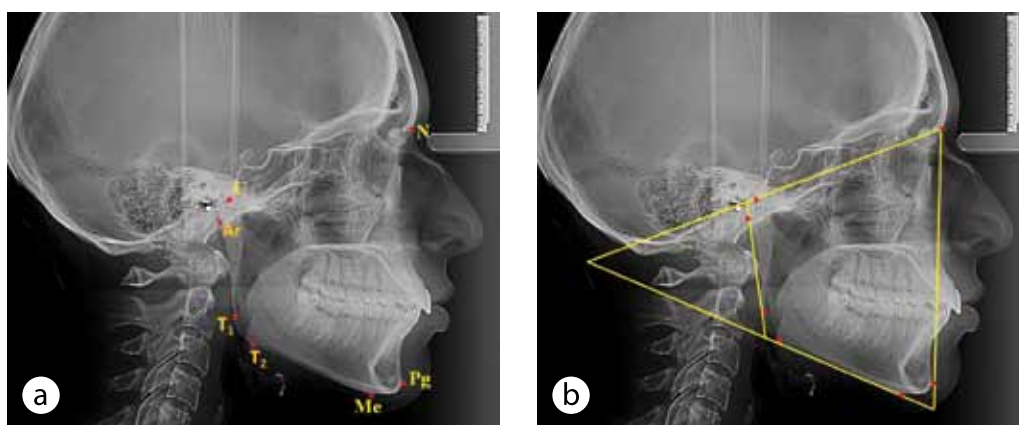


Fig. 1. The main points (a) and the line (b) used as the major reference points for comparing radiographs.

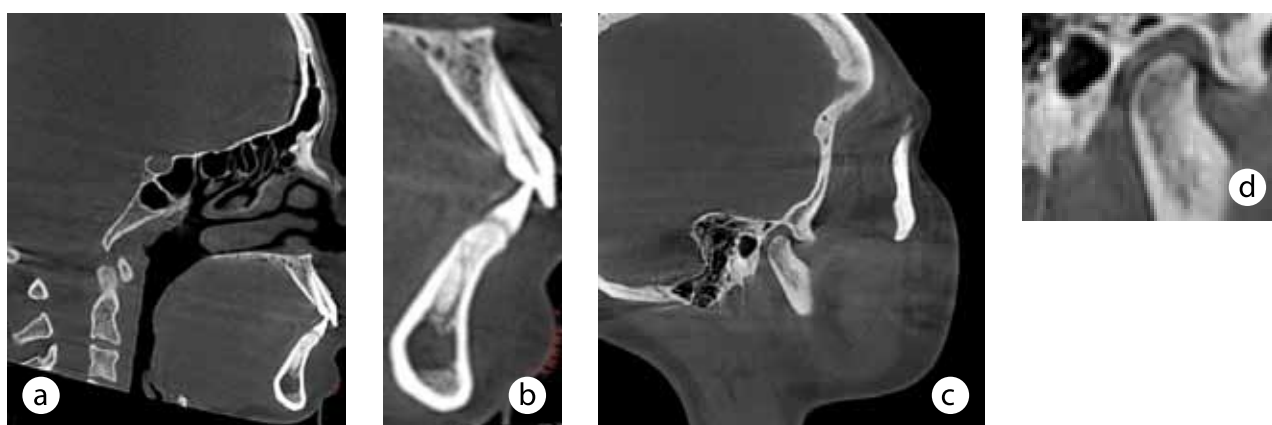


Fig. 2. Tomogram at the medial incisors level (a) and the selected fragment of the dentofacial segments (b); tomogram at the joint level (c) and the isolated joint fragment (d).

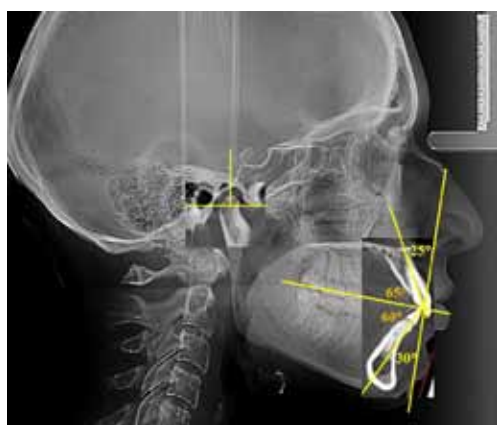


Fig. 3. Measurement of the incisors inclination angles and evaluation of the joint position on the combined radiographs

these values, calculating the index of the articular fossa, and the articular head and articular fossa size ratios.

5. The introduction of cone-beam computed tomography into integrative anatomy and dentistry can be explained by the high efficiency of this method for various in-vivo cephalometric measurements. The measurements allow analyzing the size, the shape, and the volume differences in the paired symmetric structures of the skull.

6. Using the capacity of cone-beam computed tomography in comprehensive evaluation of morphometric parameters of craniofacial structures in the axial, frontal and sagittal planes (maxillary bones, temporomandibular joint, orbits, nasal cavity, paranasal sinuses) will allow expanding the database for medical craniology, forensic medicine, pathological anatomy, neurosurgery, otolaryngology, and radiology.

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CLINICAL MEANING OF METHODS FOR IDENTIFYING VARIABILITY OF MENTAL PROMINENCE LOCATION

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The mental prominence (protuberantia mentalis) narrows at the top turning into the mandibular symphysis (symphysis mentalis), which protrudes forward as a crest. The degree of the prominence varies widely, proof to that being the results of morphological studies focusing on the dentofacial area in general and the dentoalveolar segments in particular [1–3]. There has been a proposal to evaluate the angle between the base lower edge and the protrusion. This angle has been found to have a value of 46 to 85°. However, there is no indication of the anatomical points through which the lines are drawn to build the angles [4–6]. At the same time, the available classifications of the facial shapes and dental arches are rather detailed, despite the fact that they can be very diverse even under physiological occlusion [7–9]. The features of the dentofacial area with congenital and acquired anomalies have been shown [10–12]. Clinicians evaluate the mental prominence when analyzing the facial signs of pathology, where the major anthropometric reference points and diagnostic points are located. However, the degree of the mental prominence can introduce certain adjustments to the interpretation of the research outcomes. Besides, searching through the available literature we have found no clear recommendations for identifying the mental prominence degree on the lateral telera-

diography. All of the above explains the aim and the objectives of this study.

Aim of study

To evaluate the clinical meaning of methods employed to identify the variability of the mental prominence location.

Material and methods

The material for the study included lower jaws anatomical preparations featuring various types of mental prominence. When making native preparations, a circular saw was used to cut the jaw in the chin area into segments along the interdental septa in the vestibular-lingual direction. The evaluation was done on the dentofacial segments of the mandibular medial incisors. The sides of the segments were studied relying on the anatomical and topographical approach. The specific feature of the technique was that within the medial and distal norms of each segment a line was drawn along the tooth clinical neck. Further, from the middle of the said line a perpendicular (conditional midline vertical) was drawn dividing the segment into two areas — vestibular and lingual. Next, on the vestibular surface of the segment, points of the top convexity and concavity of the mental prominence were identified to be connected with a straight line, which made an angle with the conditional midline vertical, and that we defined as the mental prominence convexity angle in the sagittal direction. In addition, telerradiographic data of the patients with physiological occlusion of the permanent teeth were studied. In assessing the telerradiography, the mandibular plane was drawn through the most prominent points of the mandible body. The medial incisor inclination axis reached the mandibular plane. The chin prominence was evaluated similarly to the first method. The mental prominence location analysis was done using the method of cone-beam computed tomography.

RESULTS AND DISCUSSION

The results of studying the dentition segments showed that the sagittal angle of the mental prominence convexity varied between 25 and 40° in case of the permanent teeth physiological occlusion. The disadvantage of this method was the complexity of

manufacturing the segments, followed by photographing and combining the linear dimensions. The analysis of lateral telerradiography allowed evaluating different intravital positions of the mental prominence as well as to evaluate the results with respect to the anatomical landmarks and the main planes, both in the horizontal and in the vertical direction. When analyzing the lateral telerradiography, we identified two location options for the mental prominence in the vertical direction. In the first case, the mental prominence touched the mandibular plane, while in the second, it was located above that. The former location of the mental prominence made it possible to evaluate its convexity in the sagittal direction between the mandibular incisor conditional midline vertical and the line connecting the mental prominence top convexity and concavity spots, while this kind of evaluation could also be obtained from the maxillary segments images.

In the second type of the mental prominence location, in addition to the sagittal angle of the convexity, the vertical angle of the prominence was also evaluated between the mandible two tangent lines. The first tangent line ran from the top convexity point of the mandibular angle to the top convexity point on the mandible body. The second line was from the top convexity point of the the mandible body to the lowest point of the mental prominence (the "Me" point). The disadvantages of this method include the difficulty of identifying some anatomical landmarks and complex measurements using various devices (calipers and protractors of various modifications). The cone-beam computed tomography method, in our opinion, combined the advantages of the two methods also eliminating the disadvantages. Besides, a software application package allowed measuring and analyzing the study outcomes directly on the computer monitor.

Conclusion. The proposed methods allow not only determining the possible gnathic and dentoalveolar types of mandibular pathology, yet also determining the methods of orthodontic and surgical treatment, which can be used by clinicians in their practice.

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PHYSIOLOGICAL AND PATHOPHYSIOLOGICAL CHANGES IN CHERNOBYL LIQUIDATORS LIVING IN HIGH ALTITUDE CONDITIONS

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INTRODUCTION

It is known that the human body living in conditions of high mountains is under the constant exposure of the environmental factors, and, in case of prolonged exposure, these factors affect the physiological functions of the body, which in many cases leads to adaptation to the given conditions. Climatic factors, such as reduced atmospheric pressure, reduced oxygen partial pressure, temperature, humidity, high intensity of solar radiation, air ionization and other factors, affect the human body through the skin, lungs, sensory organs, causing different physiological shifts. [1–5].

As it has been stated by many authors [6, 7], in mountainous conditions, a complex of adaptive rearrangements take place, firstly associated with oxygen insufficiency. The main adaptive reactions to hypoxia in *highlanders* are: somewhat increase in the respiration rate and lung ventilation; increased residual volume due to an increase of the quantity of functioning alveoles and increased perfusion of lung capillaries and rearrangement of tissue respiration [8, 9].

A number of authors [4, 10, 11] have revealed significant differences in the status of the cardiovascular system, the function of external respiration and gas exchange, as well as the blood indices, between the inhabitants of lowland areas and indigenous highlanders.

The aim of the presented study has been to reveal the differences in morbidity, changes in the functional status of different organs and systems in liquidators living on the plains compared with the residents of the highland regions of Armenia.

MATERIALS AND METHODS

The survey involved 270 liquidators — residents of Armenia, living in the high mountains, who partici-

pated in the work on eliminating the consequences of the Chernobyl NPP accident in 1986–1988. (I group). As a *control* group, 300 *lowland* liquidators were attracted (group II). All liquidators consisted in various age categories. The age of the liquidators during the period of the accident was between 20–55 years (at the age of 20–30 years — 12.6%; 31–40 years — 32.7%; 40–50 years — 38.5% and over 50 years — 16.2%).

Liquidators were divided into 3 groups: the first one comprised of individuals with external radiation dose up to 10 cGy (52.7%), the second — 10–20 cGy (41.7%), and the third — above 20 cGy (5.6%). Spirometric and immunological tests, general blood analysis (using complex unified tests) have been carried out in these liquidators. Immunological indices were studied such as white blood cells, E-rosetting (T-lymphocytes) and EAC-rosetting (B-lymphocytes): relative and absolute quantity, serum immunoglobulins G, A, M, phagocytic activity and complement titer.

Using methods of system analysis, the following indices of lung function were analyzed: Tiffeneau-Pinelli index ($IND_TIF = FEV1/VC$), forced expiratory volume in 1 second (FEV1), the vital capacity of lungs (VC), peak expiratory flow (PEF) [12].

The changes in the cardiovascular system have also been analyzed: disturbances of the nutrition of the myocardium, arrhythmia, hypertrophy of the atria, conduction disturbances, valve sclerotic changes, heart failure.

The statistical analysis of the data has been carried out by means of a number of computer programs intended for statistical processing of digital data arrays. Electronic spreadsheet Microsoft Excel and specialized statistical packages Statsoft-7, SPSS-10, MedCalc, and StatGraphics Plus were used. Correlation, regression and dispersion factor analyses were carried out [13, 14].

RESULTS

Fig. 1 shows in dynamics the morbidity by the following systems: cardiovascular and chronic non-specific lung diseases (CNSLD) in *highlander* and *plainsmen* liquidators.

As a result of many years (30 years) of research, it was found that regarding the respiratory system, the

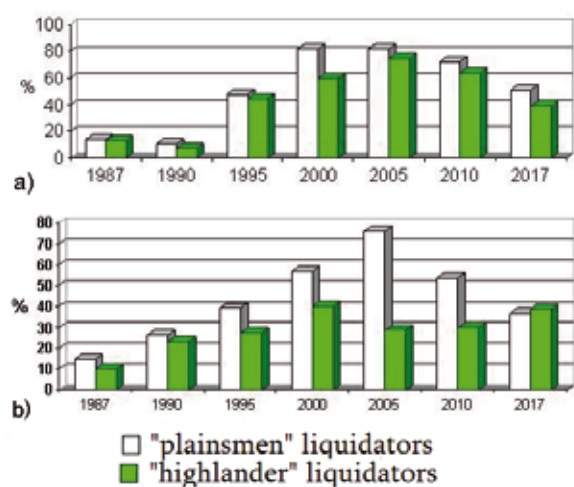


Fig. 1. Dynamics of the morbidity in "plainsmen" and "highlander" liquidators by the following systems: cardiovascular (a), CNSLD (b)

morbidity of liquidators living in high mountains was much lower throughout the whole period of the study (as compared to the *plainsmen* liquidators), which is obviously indicative of protective mechanisms in people who have long lived in hypoxic conditions. Indicators of lung function in the early post-accident period were also significantly different in the selected groups (table 1).

Using the dispersion factor analysis, the shares of the influence of the radiation factor were revealed on VC (50.57%) and FEV (34.5%) in the early and VC (20.21%) and FEV (24.13%) in the long-term periods. Only at the end of the study did the morbidity rates for CNSLD in the *highlander* and *plainsmen* liquidators become almost equal, because of the gradual predominance of non-radiation factors such as age and smoking, that affect the morbidity for the respiratory tract. Thus, the results of dispersion factor analysis (Fig. 2) showed that the shares of the effects of smoking on lung function indicators (IND_TIF; FEV1 and VC) in the late period had increased by 1.5–3 times.

Pulmonary hypertension and signs of right ventricular hypertrophy are considered to be the main adaptive changes in case of permanent residence in hypoxic conditions. The relationship of respiratory and cardiovascular disorders is particularly pronounced in the highlander liquidators. In permanent residents of the mountains, structural changes in the pulmonary vessels underlie pulmonary hypertension. The mechanism of formation of right ventricular hypertrophy is due to increasing pulmonary hypertension [15].

As for the cardiovascular system, in the early period (in 2 groups), the differences between the indices of these 2 groups were insignificant and only since 2000 a clearly marked decrease has been observed in the percentage of morbidity among the *highlander*

Table 1. Respiratory functional disturbances in "highlander" and "plainsmen" liquidators

liquidators	liquidators	VC	FEV1	FEV/VC	FVC/FEV_PEV
early period	"highlanders"	89,1±2,62	80,9±4,2	89,2±2,5	-
	"plainsmen"	81,8±2,55 p<0,05	67,3±5,23 p<0,05	82,5±2,27 p<0,05	-
late period	"highlanders"	87,4±2,8	90,7±3,69	99,0±3,34	12,8±6,22
	"plainsmen"	90,09±2,2	94,61±3,35	103,27±2,76	11,59±1,93

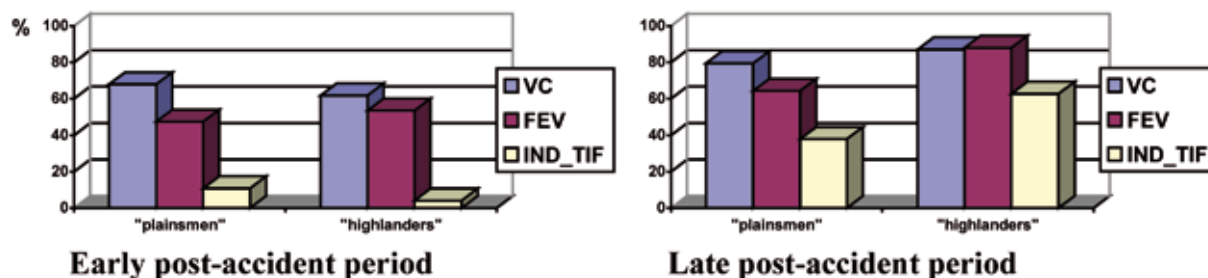


Fig. 2. Shares of influence of smoking on the indicators of the functional state of the respiratory system of "lowland" and "high mountain" liquidators in the early and remote post-accident periods

liquidators relative to the *plainsmen*. This can be explained by the fact that among the population of the mountaineers, atherosclerotic lesions of the main and peripheral vessels develop later and progress poorly. A smaller loss of elasticity of the vessels with age of the liquidators facilitates the work of the heart as well.

In liquidators who live in the highland regions of Armenia, significantly fewer cases of myocardial nutrition disorders (10.5% relative to the plainsmen - 29.1%), conduction disorders (5.3% relative to 7.6%), and arrhythmias (5.3% relative to 21.5%) have been revealed. The "highlanders" were also found to have a smaller number of such clinical cases as: myocardial infarction (in the *highlander* 5.3% relative to the *plainsmen* — 6.3%), heart failure (31.6% relative to 40.5%) and ventricular hypertrophy (36.8% relative — 39.2%). In permanent residents of highland areas, adaptive changes are formed at the tissue level. In particular, a number of authors [11, 15] indicate that in the highlanders, increased utilization of oxygen by tissues occurs as a result of increased vascularization and increased activity of tissue enzymes, and not due to the intensification of the blood flow and increased cardiac output. The presence of hypertrophy of the right ventricle of the heart in mountaineers is also noted as a decisive factor in the inclusion of the adaptive mechanisms of the body, in particular tissue factors. Of all cases of ventricular hypertrophy, in 68% of the *highlander* liquidators right ventricular hypertrophy has been observed.

Issues of the impact of mountain climatic factors on the human body in different age periods are not well understood. Revelation thereof is of interest for finding both theoretical and practical solutions to the prevention of premature aging. In permanent highland residents, the heart rate changes with age to bradycardia (found in 25.53% of highlanders relative to the plainsmen — 17.85%). At the same time, in *highlanders* the time of the systolic segment is somewhat less, and the diastolic time is longer than that in the *plainsmen*. A significant difference was found in the mean systolic pressure of the liquidators living in hypoxia (127.1 ± 3.1) and the *plainsmen* liquidators (138.2 ± 4.12). According to Alipov D.A. [16], these phenomena in mountaineers can be considered as a characteristic adaptive response that provides better filling of the heart during diastole and more economical use of the heart muscle energy.

As it is known, constant life in high altitude conditions causes persistent adaptive red blood changes. According to the works of Mirrakhimov M.M. and co-authors [17], the total number of red blood cells can be 5% higher than that in the individuals living at sea level. We found no significant differences in

the number of red blood cells in the *plainsmen* and *highlander* liquidators, although there was a tendency to increase in this number, and there was a significant direct correlation relationship between the number of the red cells and hemoglobin level (in the early post-accident period $r = 0.63$ and in the late period $r = 0.87$) in the *highlander* liquidators, throughout the period of the research. We have found a significant increase in the level of hemoglobin in the blood of the *highlanders* (164.5 ± 1.12 g/l — in the early period and 151.9 ± 1.79 g/l — in the remote period) relative to the "plainsmen" liquidators (in the early — 161.4 ± 1.15 g/l, in the remote — 146.07 ± 2.25 g/l), which is confirmed by the literature data [18], where this increase is associated with an increase in the oxygen capacity of the blood in the residents permanently living in the conditions of high altitude.

The results of the analysis of immunological indicators are presented in Table 2.

From the presented data, it can be seen that, in the early post-accident period, a significant difference was observed in T-lymphocytes (relative number — 29.71 ± 2.16 for *highlanders* and 36.67 ± 1.5 for *plainsmen*), and, in the long-term period, a significant difference was observed in almost all immunological parameters in the above-mentioned groups. In the *highlanders* in the long-term period, a decrease in the relative number of B-cells was revealed not only in relation to the *plainsmen* liquidators but also in comparison with the norm.

CONCLUSIONS

Thus, we have found that the morbidity rates by the following cardiovascular system and CNSLD, from 1995 to 2010 in *highlander* liquidators, were significantly lower compared to *plainsmen* liquidators, which indicates a presence of protective mechanisms in permanent residents of mountainous areas. In the early post-accident period, there was a significant difference between the indicators of lung function in groups I and II of liquidators.

Using the dispersion factor analysis, the shares of the influence of the radiation factor on VC and FEV (in the early (50.57%; 34.5%) and in the long-term (20.21%; 24.13%)) and smoking (in the early (64.87%; 50.64%) and in the long-term periods (83.29%; 76.19%)), which indicates that there is a decrease in the influence of radiation and an increase in non-radiation factors (age, smoking).

In the liquidators who live in highland regions of Armenia, significantly fewer clinical cases related to cardiovascular system, were found. In 68% of the *highlander* liquidators, right ventricular hypertrophy was observed, which is an adaptive change for them.

Table 2. Immunological indices in "plainsmen" and "highlander" liquidators in early and late post-accident periods.

liquidators, period		T-Cells (rel) (%)	T- Cells (abs) (uL)	B-Cells (rel) (%)	B-Cells (abs) (uL)	Phagocytosis		Comple- ment titer (%)	IgA (g/L)	IgG (g/L)	IgM (g/L)
						%	number				
early period	"highlanders"	29,71±2,16	988,91±104,9	19,24±1,75	650,86±80,02	49,28±1,58	4,09 ±0,14	36,59±1,1	1,51±0,13	12,19±1,11	0,93±0,07
	"plainsmen"	36.67±1,5 p<0.05	1143,2±84,78	18,79±0,47	561,52±18,74	48,16±0,43	4,02±0,09	36,21±0,32	1,69±0,03	12,62±0,18	0,96±0,02
late period	"highlanders"	48.7±0,79	841,2±76,54	14.5±0.71	362.33±66.38	32.2±0.31	12.2±0.2	26.75±1.75	2.4±0.2	14.4±0.21	1.8±0.1
	"plainsmen"	37.4±0.6 p<0.05	723.8±94.01	24.25±1.88 p<0.05	830.51±145.8 p<0.05	30.18±0.3 p<0.05	11.2±0.2 p<0.05	29.1±2.1	2.2±0.16	13.44±0.39 p<0.05	1.74±0.07

Significant differences in RBC and immunological parameters between *highlander* and "plainsmen" liquidators were also recorded.

Thus, the liquidators living in conditions of hypoxia turned out to be more enduring to the conditions of ionizing radiation exposure. This is explained by the physiological adaptation that has arisen throughout the life in conditions of high mountains.

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MORPHOFUNCTIONAL CHANGES IN TEMPOROMANDIBULAR JOINT CORRELATING WITH ITS MORPHOLOGICAL VARIATIONS IN PATIENTS WITH DENTITION DEFECTS COMPLICATED BY DISTAL OCCLUSION

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ABSTRACT — Dentition issues combined with distal occlusion are accompanied by structural and functional changes in the temporomandibular joint (TMJ). This study involved 180 patients with dentition defects in combination with distal occlusion. Clinical and laboratory research methods allowed identifying three variants of the TMJ morphology; the clinical and radiological features of the pathology were detected, and an algorithm for orthodontic and orthopedic treatment of this pathology was proposed depending on a particular TMJ.

KEYWORDS — dentition issues, temporomandibular joint, distal occlusion.

INTRODUCTION

Defects of the dentition in combination with distal occlusion occur through all age periods of human life and in case no timely treatment is offered, they may get complicated with secondary deformations including impaired morphofunctional ratios in the maxillofacial area [1, 3, 4, 5, 8–10, 34, 42]. Besides, they are accompanied by structural and functional changes in the TMJ, which is due to its close link with the neuromuscular maxillofacial apparatus and the pattern of the occlusal contact [2, 6, 7, 35, 41, 43]. Disturbed occlusal relationship contributes to the development of non-functional stress in the TMJ and reduces the adaptive capacity of its structural elements, which leads to restricted mandible movements, ten-

sion and pain and, subsequently, degenerative changes in its structural elements [25, 26, 36]. Clinical dentists often see dentition defects combined with muscle and joint dysfunction symptoms; however, the correlation between the occlusion pathology and the TMJ issue is not always clear. Yet, normalization of the occlusal contact is known to improve or facilitate the physiological function of the TMJ elements [31–33].

Treating adult patients with impaired occlusion has its own specifics. For instance, the specific features of treatment of adult patients with dentofacial issues and deformities are due to the complete growth of the facial skeleton, which makes it difficult to restructure the bone tissue under the influence of the active elements of orthodontic equipment, and hence the medical approach tactics is of great importance [11–18, 22, 24, 44, 45]. The diagnostics and comprehensive treatment of patients with impaired occlusion combined with a TMJ pathology has been quite the focus of attention currently [19–21, 23, 27–30, 37–40]. At the same time, the issue of changes in the TMJ with dentition defects depending on its structure appears of interest.

Aim of study

to increase the efficiency of treatment offered to patients with dentition defects combined with distal occlusion, depending on the TMJ morphology type.

Materials and methods

The study included 180 patients who were undergoing orthopedic treatment for dentition defects combined with distal occlusion.

Diagnostics, planning and selecting the most appropriate treatment method was done based on the outcomes of clinical, laboratory, radiological and graphic research methods. Based on the clinical examination, the degree of muscle & articular dysfunction was identified. For this purpose, the clinical dysfunction M. Helkimo index was modified. Studying functional occlusion, installation and preparation of the functionograph for operation, manufacturing orthodontic appliances and orthopedic structures — all this was done using an articulator. The anatomical and topographic status of the

TMJ was assessed through zonograms obtained with a universal radiological installation *Orthophos 3*. Studying the function of the TMJs, masticatory muscles, as well as the detection of occlusal disorders was performed using a functional analyzer by M. Kleinrok and V.A. Khvatova, which is based on intraoral recording of mandibular movements with a functionograph. An electromyographic study allowed the assessment of the functional status of the masticatory muscles. To register the masticatory muscles electrical potentials, an interference (surface) electromyography method was employed. The masticatory muscles electromyographic activity was assessed with a *Neuromian* electromyograph.

RESULTS AND DISCUSSION

The zonogram analysis allowed identifying the parameters of the mandible head, mandibular fossa and the articular tubercle. Systematization of the obtained data helped identify three main types of TMJ:

First — a narrow mandibular fossa and a mandible head of medium width; the mandibular fossa of medium width and the mandible head of a large width (i.e., when the structure of the mandible head was larger than the mandibular fossa structure) (Fig. 1).

Second — a narrow mandibular fossa and a small width of the mandible head, the mandibular fossa and the mandible head of medium width, a wide mandibular fossa and a wide mandible head (i.e., when the mandible head structure corresponded to the mandibular fossa structure) (Fig. 2).

Third — the mandibular fossa of medium width and a small mandible head, a wide mandibular fossa and a medium-wide mandible head, a wide mandibular fossa and a small width of the mandible head (i.e., when the mandible head structure is smaller than the mandibular fossa structure) (Fig. 3).

Following the selected TMJ types, all the patients were divided into three groups.

The clinical examination allowed identifying that the symptoms of muscle & articular dysfunction were observed in 97.3% of Group 1 patients. As for the patients in Groups 2 and 3, they revealed the muscle & articular dysfunction symptoms 10.1% and 17% less frequently, respectively.

Analyzing the teeth occlusal contacts in the studied groups revealed that 83.4% of the cases in Group 1 accounted for premature occlusal contacts, in Group 2 this index was 82.9%, and in Group 3 — 80.3%. During laterotrusive mandible movement, 80.6% of Group 1 patients had disturbed *canine guidance*. In Groups 2 and 3 laterotrusive mandible movement revealed impaired *canine guidance* in a fewer number of cases (by 6.1% and by 15.2%, respectively).

When doing occlusography, the occlusogram index was identified, which was 34.91 ± 3.49 in Group 1; 41.31 ± 1.69 — in Group 2, and 38.50 ± 3.50 — in Group 3.

Depending on the TMJ type, the zonograms showed two degrees of the mandible head posterior displacement within the mandibular fossa. In Group 1, the central position of the mandible head in the mandibular fossa was observed. Patients of Group 2 revealed potential posterior mandible head displacement up to 2 mm (first degree). In Group 3, the posterior mandible head displacement could be up to 4 mm (second degree).

Functionograms in the studied groups showed that the patients had disturbed Gothic angle and Gothic arc. The Gothic angle revealed asymmetry, disturbed straightness and length of the sides, and in Group 1 was smaller — by 20.20° ($p < 0.001$), in Group 2 — by 15.40° ($p < 0.01$), and in Group 3 — by 15.80° ($p < 0.01$).

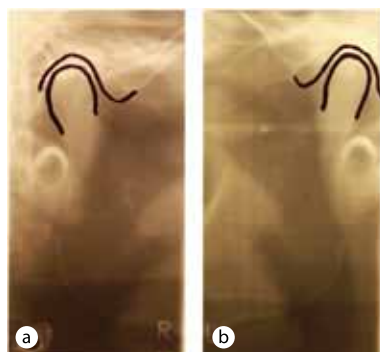


Fig. 1. TMJ zonogram, patient K. Large size and central position of the mandible head with a medium width of the mandibular fossa on the right (a) and left (b)

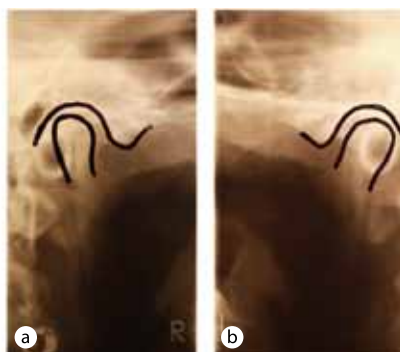


Fig. 2. TMJ zonogram, patient D. The average size and distal position of the head of the mandible with an average width of the mandibular fossa, right (a) and left (b)

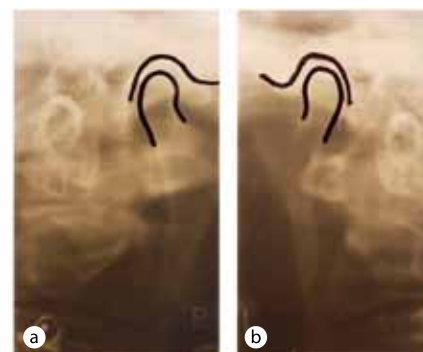


Fig. 3. TMJ zonogram, patient C. Small size and distal position of the mandible head with a medium-width mandibular fossa, right (a) and left (b)

As for the Gothic arc, the functiograms showed their shortening of one or two sides, the asymmetry and curved lateral movements, as well as asymmetry of the occlusal field location.

Analyzing the amplitude of the masticatory muscles biopotentials during the jaws compression in conventional occlusion showed its link with the degree of muscle & articular dysfunction. The patients of the studied groups manifested a decrease in the biopotentials amplitude of the masticatory and temporal muscles, and an increase in the biopotentials amplitude of the suprahyoid muscles.

This means that the analysis of the maxillofacial area in the studied groups allowed identifying morphological and functional disorders of the TMJ, masticatory muscles and occlusion as well.

Treating adult patients in the groups was planned in view of the muscle & articular dysfunction degree. In case of patients with mild muscle & articular dysfunction, for instance, orthodontic or orthopedic treatment was immediately started, while cases of moderate or severe muscle & articular dysfunction required killing the pain syndrome and coordinating the masticatory muscles function first.

In case of pain syndrome, symptomatic treatment was performed first, which was aimed at eliminating the pain symptoms. Medication and physiotherapy were used to relieve pain. Drugs and physiotherapeutic treatment were selected individually, taking into account the clinical image of the disease and the patient's individual tolerance of drugs and physiotherapeutic treatment.

To identify the mandible optimal position, as well as to improve the topographic relationships of the TMJ elements and to restore the *canine guidance*, occlusal splints were made.

Once the pain in the TMJ and masticatory muscles was eliminated, orthodontic and orthopedic treatment was started. When planning treatment, the TMJ morphology and the mandible head position in the mandibular fossa were taken into account as decisive.

In Group 1, orthodontic and orthopedic treatment implied dental alveolar compensation of the main pathology and prosthetic measures without displacing the mandible and changing the topography of the TMJ elements (Fig. 4).

In Groups 2 and 3, the comprehensive treatment involved the stage of displacing the mandible forward along with the mandible head displacement to the posterior slope of the articular tubercle, keeping the joint gap in the anterior part at not less than 2 mm (Fig. 5).

The magnitude of displacing the mandible head forward to the posterior slope of the articular tubercle

keeping the joint space in the anterior part of not less than 2 mm was determined at the stage of developing a constructive bite, and was controlled by zonograms. Then, the mandible position was corrected with respect to the maxilla, taking into account the normalization of the dentition occlusal & articulation relations, the functional status of the masticatory muscles, and the topography of the TMJ elements. The outcome of restored occlusal disorders was improved relation of the dentition in static and dynamic occlusion, with developing *canine guidance*, as well as *canine protection* or *group guiding function* on the working side. A sign of restored functional status of the masticatory muscles was their coordinated work, which was to be seen from an electromyographic study. Besides, these changes were controlled through analyzing the Gothic angle based on the results of functiograms.

Orthopedic treatment was performed in two stages. The first stage included making temporary prosthetic constructions with restoring the *canine guidance*, which facilitated the patient's adjustment to the new conditions of the maxillofacial functioning. The main criterion of adjustment was improved functional status of the masticatory muscles based on the data from functiography and electromyography. At the second stage, permanent dental prostheses were made.

A clinical examination done after treatment allowed diagnosing the signs of muscle and articular dysfunction in 59.7% of Group 1 patients. In Groups 2 and 3, symptoms of dysfunction were less common (by 18.2% and 20.4%, respectively). In 40.3% of patients of Group 1, 58.5% of patients of Group 2, and 60.7% patients of Group 3, there were no signs of muscle & articular dysfunction detected. In addition, the treatment helped decrease the number of patients showing symptoms of moderate and severe degrees of muscular and articular dysfunction in the studied groups.

As a result of the treatment, the occlusogram index increased in Group 1 going from 34.91 ± 3.49 up to 63.84 ± 1.10 ($p < 0.01$); in Group 2 — from 41.31 ± 1.69 to 69.55 ± 1.05 ($p < 0.001$), and in Group 3 — from 38.50 ± 3.50 to 71.29 ± 1.90 ($p < 0.05$). The *canine guidance* was observed in 58.3% of the patients in Group 1; 79.8% of the cases in Group 2, and in 85.2% of the patients of Group 3, which is 38.9%, 54.3% and 50.8% above for the same indicator prior to the treatment, respectively.

Due to the treatment, the functiographs showed an increase in the Gothic angle in Group 1 — from $85.04^\circ \pm 2.730^\circ$ to $98.37^\circ \pm 1.820^\circ$ ($p < 0.001$); in Group 2 — from $89.84^\circ \pm 4.420^\circ$ to $103.47^\circ \pm 3.280^\circ$ ($p < 0.05$), and in Group 3 — from $89.37^\circ \pm 3.390^\circ$ to $104.86^\circ \pm 2.480^\circ$ ($p < 0.001$), which indicated restored coordinated activity in the masticatory muscles.

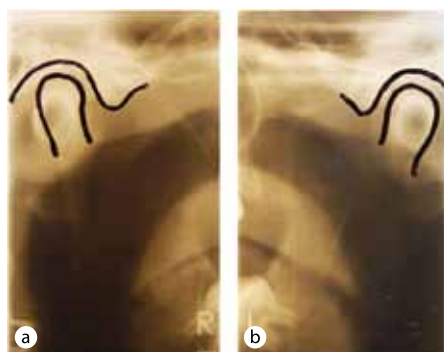


Fig. 4. TMJ zonogram, patient D. The anterior position of the mandible head after the treatment, right (a) and left (b)

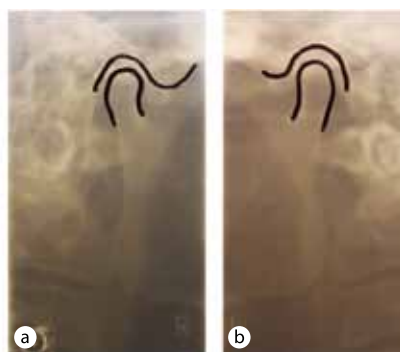


Fig. 5. TMJ zonogram, patient C. The central position of the mandible head after the treatment, right (a) and left (b)

The electromyographic study allowed us to record changes in the masticatory muscles through the course of treatment as well as to identify the moment of the masticatory muscles adjustment to new functioning conditions. The treatment resulted in changed biopotentials amplitude of the masticatory, temporal, and suprahyoid muscles. Electromyography done in the studied groups revealed recovered biopotentials amplitude of the masticatory muscles with a mild degree of muscle & articular dysfunction and its approximation to the normal parameters in cases of moderate and severe degrees of dysfunction.

Comparison of data from the respective literature with the results of our own research on the issue in question suggests that diagnostics and treatment methods for adult patients suffering from dentition issues combined with distal occlusion reveal features depending on the morphological variation of the TMJ and the degree of the muscle & articular dysfunction.

CONCLUSION

Given the zonogram data, depending on the ratios of the mandibular fossa width and the mandible head in the antero-posterior direction, three types of TMJ were identified in patients with dentition defects combined with distal occlusion. The major criterion for selecting comprehensive treatment methods of adult patients with dentofacial issues and deformities was the displacement degree of the mandible head forward to the posterior slope of the articular tubercle while keeping the articular gap in the anterior part of not less than 2 mm at the stage of formation of the constructive bite, which was controlled by zonogram. In Group 1, orthodontic and orthopedic treatment included dental alveolar compensation of the main pathology and prosthetic measures without displacing the mandible and changing the topography of the

TMJ elements. In Groups 2 and 3, comprehensive treatment implied mandible anterior displacement with shifting the mandible head to the posterior slope of the articular tubercle keeping the joint gap in the anterior part of not less than 2 mm. Adjustment of the masticatory muscles to new functioning conditions in adult patients has been confirmed with a change in the biopotentials amplitude of the masticatory, temporal, and suprahyoid muscles on electromyograms. Adult patients feature recovered biopotentials amplitude of the masticatory muscles in case of a mild degree of muscle & articular dysfunction and its approximation to the normal parameters in case of moderate and severe dysfunction.

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CARDIOVASCULAR ADAPTATIONS OF FOREIGN STUDENTS TO CLIMATIC AND GEOGRAPHICAL CONDITIONS OF STAVROPOL REGION

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ABSTRACT — PURPOSE OF RESEARCH: studying adaptive opportunities of the cardiovascular system of foreign students to the climatic and geographical conditions of Stavropol region.

METHODS: The data sample included the Stavropol and foreign students, natives of the countries of the Southern Asia, the Western Asia and Africa in the youthful period of ontogenesis and the first period of a maturity. In total 218 students, from them the Russian students were examined: youths — 73 persons, men — 55 people; foreign students: youths — 36 people, men — 54 persons.

RESULTS: Stable and compensatory adaptive reactions are characteristic to youths and men from the Southern Asia and to men from the Western Asia. A condition of the critical tension (excessive tension) are characteristic to first-year students and senior students from Africa.

FINDINGS: It is established that the greatest stress of adaptation mechanisms is experienced by students from Africa.

KEYWORDS — adaptation, mathematical analysis of the heart rhythm, variational pulsometry, foreign students, Stavropol region.

INTRODUCTION

There are a lot of publications in modern scientific literature, which reflect the issues of adaptation of foreign students to different living conditions in Russia. These are issues of adaptation to different climatic and geographical conditions, to sociocultural conditions, and to the learning process. Moving foreign students to Russia is accompanied by the expressed

morphofunctional reorganization of all systems of an organism. Against this background, the effects of stress experienced by students during the study period make high demands on their bodies leading to significant changes in the cardiovascular system [9, 10, 14]. In addition, it is necessary to consider possible action of a desynchronosis, absence at an organism of experience of adaptation to a new food and a number of other factors, new to an organism.

Climatic and geographical conditions in the new area influence population in two aspects. The first of them is actually physical-geographical – the certain combination of landscape and climatic conditions characteristic of this area, favorably or adversely influencing the human body adapted to other physiographical conditions. The second aspect is medical geographical combination of disease with natural nidity which is localized in this area and telling him as the habitat certain medical geographical specifics [3, 7].

In the most general sense, human diseases are the result of a violation of historically developed forms of communication of the organism with the environment. However, in the process of adaptation with very strong or prolonged exposure to adverse environmental factors, or in case the adaptation mechanisms in the body are weak, there is a disadaptation (disturbance or disruption of adaptation) and morbid conditions develop. It is called "adaptation diseases".

Disadaptation and development of morbid conditions happens step by step [1]. The initial stage of a border area between health and pathology is a condition of functional tension of mechanisms of adaptation. Its most characteristic sign is the high level of functioning which is provided at the expense of the intensive or long tension of regulatory systems [19, 25].

The later stage of the border zone is a state of unsatisfactory adaptation. It is characterized by a decrease in the level of functioning the biosystem, mismatch of its individual elements, the development of fatigue and overwork. The state of unsatisfactory adaptation is an active adaptive process. The body tries to adapt to excessive conditions of existence by changing the

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functional activity of individual systems and the corresponding voltage of regulatory mechanisms. However, due to the development of insufficiency, violations extend to energy and metabolic processes, and the optimal mode of operation cannot be provided.

The condition of disruption of adaptation can be shown in two forms: preillness (Premorbidity) and illness. Preillness is balance between health and illness or manifestation of initial symptoms of diseases. This condition contains information about the localization of possible pathological changes. This stage is reversible, since the observed deviations are functional in nature and are not accompanied by a significant anatomical and morphological restructuring [21, 24].

The leading sign of the disease is to limit the adaptive capacity of the organism. The insufficiency of general adaptation mechanisms in the disease is complemented by the development of pathological syndromes. It is associated with anatomical and morphological changes, which demonstrates emergence of the centers of local wear of structures. Despite the specific anatomical and morphological localization, the disease remains a reaction of the whole organism. It is accompanied by the inclusion of compensatory reactions, representing a physiological measure of the body's protection against the disease [20, 23].

To determine the effectiveness of adaptation processes, criteria and methods for diagnosing the functional states of the body were developed. Baevsky R.M. suggested to consider five main criteria: level of functioning physiological systems; degree of tension of regulatory mechanisms; functional reserve; extent of compensation; steadiness of elements of a functional system [1].

Diagnostic methods of functional states are directed to assessment of each of the listed criteria. Level of functioning physiological systems is defined by traditional physiological methods. Degree of tension of regulatory mechanisms is investigated the next ways: by methods of the mathematical analysis of a heart rhythm, by studying secretory function of salivary glands, daily fluctuations of physiological functions, etc.

To prevent premorbidity (prenosological conditions), it is important to control the functional state of the body of students. An effective method of assessing the state of health is a mathematical analysis of heart rhythm. Thanks to this method, physiological indicators have been established, the magnitude of which most clearly responds to the loss of health during the development of the disease [5, 11, 13, 22].

For this reason, purpose our research was studying adaptive opportunities of the cardiovascular system of foreign students to the climatic and geographical conditions of Stavropol region.

MATERIALS AND METHODS

Stavropol and foreign students were included in the cross-sectional study. The age of people is 17–21 years (the youthful period of ontogenesis) and 22–28 years (the first period of mature age). Foreign students are natives of the countries of the Southern Asia (India), the Western Asia (Cyprus, Kuwait, Lebanon, Palestine, Syria) and Africa (Morocco, Sudan). In total 218 students, from them the Russian students were examined: youths — 73 persons, men — 55 people; foreign students: youths — 36 people, men — 54 persons.

To analyze the heart rhythm, we used the method of variation pulsometry using a clinorostatic test on the Varicard 2.5 diagnostic device (Institute of Introduction of New Medical Technologies RAMENA) using the "Iskim 6.1" software.

The clinorotostatic test is a widely used test for studying the reserves of the autonomic regulation of blood circulation. It consists in registration the heart rate and blood pressure when a person moves from a lying position (horizontal position) to a standing position (vertical position). Analysis of the cardiointervalogram during the clinorostatic test with the calculation of the Stress Index allows us to estimate the vegetative reactivity. We used the STATISTICA 10 software package for data processing (StatSoft, USA). Differences were considered statistically significant at $p < 0.05$.

RESULTS AND DISCUSSION

In the horizontal position, youths from the Southern Asia in comparison with the Stavropol students are characterized by authentically big sizes of the Stress Index and amplitude of fashion (Table 1). Youths from the Western Asia and Africa illustrate the minimum values of mode, Standard deviation and variation scope. These results it is reliable below the specified parameters of youths of Stavropol Territory, and standard deviation of the African youths is significantly more same indicator of West Asian students. Analysis of stress index values for students from different climatic and geographic regions showed that their vegetative homeostasis, as well as among local youths, is within the normal range, but South Asian students have some tension of compensatory mechanisms, a higher level of functioning the sympathetic level and the central contour of heart rate regulation. Men of the Western Asia have a decrease of function of the central contour in the management of heart rate, as well as an increasing influence of the parasympathetic division.

Men from West Asia in a horizontal position are characterized by reliably maximum values of the stress index, the amplitude of the mode and minimum values of the standard deviation (Table 2). The maximum

Table 1. Results of the mathematical analysis of the heart rhythm of students of the youthful period of ontogenesis in the lying (horizontal) position, ($M \pm m$)

Statistical significance (P-value)	Stavropol Region	South Asia	West Asia	Africa
Stress Index				
	58,2±9,39	135,6±20,11	81,1±29,52	104,2±26,79
P1		<0,001	>0,10	>0,10
P2			>0,10	>0,10
P3				>0,10
Mode, s				
	822,6±20,47	634,2±18,48	692,8±32,82	534,8±116,97
P1		<0,001	<0,001	<0,02
P2			>0,10	>0,10
P3				>0,10
Amplitude of the mode, %				
	30,6±1,52	42,8±4,22	38,6±2,59	35,2±7,30
P1		<0,01	<0,01	>0,10
P2			>0,10	>0,10
P3				>0,10
Standard deviation, s				
	86,1±4,30	69,6±15,68	50,1±8,50	109,3±21,66
P1		>0,10	<0,001	>0,10
P2			>0,10	>0,10
P3				<0,05
Range, s				
	789,8±57,30	303,7±33,77	395,0±83,17	269,7±65,57
P1		<0,001	<0,001	<0,001
P2			>0,10	>0,10
P3				>0,10

Note: P1 — Significance of differences of indicators of South Asian, West Asian and African youths in comparison with the Stavropol youths; P2 — Significance of differences of indicators of West Asian and African boys compared with South Asian men; P3 — Significance of differences of indicators of African youths in comparison with West Asian youths.

values of the variation range were found in Stavropol students in comparison with men from the Western Asia. South Asian men in horizontal position have significantly lower values of mode, standard deviation and variation range than among representatives of the Stavropol region. All senior students have vegetative homeostasis in the normal range, this is confirmed by the values of the stress index. However, students from Western Asia have the highest tension of compensatory mechanisms, a high level of functioning the sympathetic part of the autonomic nervous system and the central contour of heart rhythm regulation. Stavropol men students have a decrease of role of the central contour in managing the heart rhythm, and in the autonomous contour they have a restructuring the relationship between the sympathetic and parasympathetic systems. As a result, we can see that the influence of the parasympathetic division increases.

Moving from horizontal to vertical position of students from South Asia and Africa, caused significant changes in the parameters of the cardiovascular system — an increase of variation range, indicating the activation of the parasympathetic division of the autonomic nervous system. Moving from a horizontal to a vertical position of students from Western Asia, caused significant changes in the parameters of the cardiovascular system — increase amplitude of the mode, indicating the activation of the sympathetic System, what provides the stability of hemodynamics in the vertical position. In the vertical position, South Asian youths have an increase of the stress index, low values of mode, low values of standard deviation, low values of variation range and high values of amplitude of the mode. At the same time, compared with students from South Asia, we can see significantly higher diastolic blood pressure values, large values of mode and low

Table 2. Results of the mathematical analysis of the heart rhythm of students of the first period of a maturity in the lying (horizontal) position, ($M \pm m$)

Statistical significance (P-value)	Stavropol Region	South Asia	West Asia	Africa
Stress Index				
	58,7±10,90	104,1±23,07	129,0±20,26	107,2±24,99
P1		>0,10	<0,01	>0,10
P2			>0,10	>0,10
P3				>0,10
Mode, s				
	831,4±22,30	692,0±24,73	731,1±22,26	587,0±72,05
P1		<0,001	<0,002	<0,002
P2			>0,10	>0,10
P3				>0,10
Amplitude of the mode, %				
	34,8±2,03	39,1±4,11	48,8±3,81	42,8±5,64
P1		>0,10	<0,002	>0,10
P2			>0,10	>0,10
P3				>0,10
Standard deviation, s				
	94,9±5,25	60,1±10,88	51,0±4,61	108,0±21,05
P1		<0,01	<0,001	>0,10
P2			>0,10	>0,10
P3				<0,01
Range, s				
	849,2±70,33	341,1±42,91	371,2±46,99	234,3±41,17
P1		<0,001	<0,001	<0,001
P2			>0,10	>0,10
P3				<0,05

Note: P1 — Significance of differences of indicators of South Asian, West Asian and African students in comparison with the Stavropol students. P2 — Significance of differences of indicators of West Asian and African students in comparison with the South Asian. P3 — Significance of differences of indicators of the African students in comparison with the West Asian.

values of stress index at West Asian and African students (Table 3).

In group of foreign senior students moving to horizontal position caused reliable changes of parameters of a cardiovascular system — it is increase amplitude of the mode at representatives from the Western Asia, which exceeded the same indicator at the Stavropol, South Asian and African men. Also we can see increase value of variation range at students of Africa, decrease the mode at the Stavropol students and decrease values of variation range at West Asian men. It demonstrates activation of sympathetic part of the autonomic nervous system at local senior students and parasympathetic — at African (Table 4). However, the stress index in a standing position among senior students from Africa was significantly lower than that of Asian representatives.

The assessment of vegetative reactivity revealed among the first-year students from South Asia the

prevalence of the asympathicotonic (pathological) variant — 50.0%, among the boys from Western Asia — equally hyper — and asympathicotonic variants (37.5%). The difference is African students had only asympathicotonic variant of vegetative reactivity. Assessment of autonomic reactivity in students of the first period of maturity, meaning a rapid restructuring the peripheral apparatus of the autonomic nervous system during performing a clinorotostatic test, also revealed three variants. Stavropol students (41.8%) had a normal reaction to the test. Asian students had hypersympathicotonic vegetative reactivity (50.0% — South Asia and 40.7% — West Asia), with an excessive connection of the sympathoadrenal system. Students from Africa had asympathicotonic (pathological) autonomic reactivity (72.7%).

Table 3. Results of the mathematical analysis of the heart rhythm of students of the youthful period of ontogenesis in the vertical position, ($M \pm m$)

Statistical significance (P-value)	Stavropol Region	South Asia	West Asia	Africa
Stress Index				
	76,4±11,75	106,8±15,41	70,9±8,46	51,8±10,43
P1		>0,10	>0,10	>0,10
P2			<0,01	<0,01
P3				>0,10
Mode, s				
	715,2±17,58	616,8±25,00	627,4±45,25	689,0±19,86
P1		<0,001	>0,10	>0,10
P2			>0,10	<0,05
P3				>0,10
Amplitude of the mode, %				
	32,7±1,68	48,9±4,07	56,5±6,14	39,7±7,96
P1		<0,001	<0,001	>0,10
P2			>0,10	>0,10
P3				>0,10
Standard deviation, s				
	86,5±4,45	55,4±7,98	52,8±6,07	66,2±6,83
P1		<0,001	<0,001	<0,02
P2			>0,10	>0,10
P3				>0,10
Range, s				
	670,5±46,74	490,6±63,60	460,6±39,62	650,3±118,36
P1		<0,05	<0,001	>0,10
P2			>0,10	>0,10
P3				>0,10

Note: P1 — Significance of differences of indicators of South Asian, West Asian and African youths in comparison with the Stavropol youths. P2 — Significance of differences of indicators of West Asian and African youths in comparison with South Asian youths. P3 — Significance of differences of indicators of the African youths in comparison with West Asian youths.

CONCLUSIONS

On the basis of indicators of a heart rhythm we found out that in horizontal position of the youths of Stavropol Krai have parasympathetic influence on a heart rhythm, and students of the I period of a maturity — sympathetic influence on a heart rhythm. In horizontal position South Asian youth and men have prevalence of a sympathetic part of the autonomic nervous system in regulation of a heart rhythm. Youth from West Asia and Africa have a predominance of parasympathetic influences, and men from the same regions have sympathetic influences. The data obtained by us coincides with the data of references [4, 6, 12]. In a horizontal position, all students have an activation of the sympathetic part of the autonomic nervous system in the regulation of heart rhythm, which is a normal reaction of the organism to a clinorotostatic test. The exception is made by the

African students who have increased parasympathetic influences.

Evaluation of autonomic reactivity revealed the following: African youths, South Asian youths and African men have more pronounced asympathicotonic reactivity among foreign students. The examined youths and men of the Western Asia have pathological options of vegetative reactivity (hypersympathicotonic and asympathicotonic). We can think about the individual specificity of the identified vegetative response, which has a constitutionally determined pattern of vegetative response, because students from Stavropol, South Asia, West Asia and Africa respond to the same stimulus with various changes in vegetative indicators.

During analyzing the indicators of the heart rhythm in the prone position and in the standing position, three types of adaptive responses of the vegetative regulation system were identified:

Table 4. Results of the mathematical analysis of the heart rhythm of students of the first period of a maturity in the vertical position, ($M \pm m$)

Statistical significance (P-value)	Stavropol Region	South Asia	West Asia	Africa
Stress Index				
	82,3±12,51	155,9±37,89	151,4±35,48	65,5±6,88
P1		>0,10	>0,10	>0,10
P2			>0,10	<0,05
P3				<0,02
Mode, s				
	711,7±18,91	626,8±31,91	609,4±26,62	536,0±45,52
P1		<0,05	<0,002	<0,001
P2			>0,10	>0,10
P3				>0,10
Amplitude of the mode, %				
	38,3±2,29	46,5±3,83	66,1±3,19	46,4±6,27
P1		>0,10	<0,001	>0,10
P2			<0,001	>0,10
P3				<0,01
Standard deviation, s				
	85,5±5,11	52,3±5,40	56,1±7,02	83,2±19,37
P1		<0,001	<0,001	>0,10
P2			>0,10	>0,10
P3				>0,10
Range, s				
	643,8±50,87	449,9±90,00	494,1±48,12	642,6±81,09
P1		>0,10	<0,05	>0,10
P2			>0,10	>0,10
P3				>0,10

Note: P1 — Significance of differences of indicators of South Asian, West Asian and African students in comparison with the Stavropol students. P2 — Significance of differences of indicators of West Asian and African students in comparison with South Asian students. P3 — Significance of differences of indicators of the African students in comparison with West Asian students.

1. Stable adaptive response, characterized by a balanced influence of the part of the autonomic nervous system on the heart rhythm and the preservation of hemodynamic homeostasis, typical mostly of Stavropol youths and men, and South Asian youths.
2. Compensatory response, manifesting by increased activity of the sympathetic part of the autonomic nervous system in the regulation of heart rhythm (youths and men from South and West Asia have it)
3. The condition of critical tension, expressed in the inhibition of the activity of the autonomous contour of the control and the decrease in the functional reserve of the circulatory system (it is typical for African boys and men).

Identifying the types of adaptive reactions of the vegetative regulation system allows us to estimate the

spectrum of the prenosological conditions of the body of students from different climatic and geographical regions from a stable adaptive response (young men of Stavropol and South Asian young people) to a condition of critical tension (African boys and men).

Thus, the vegetative homeostasis, indicating the adaptive abilities of the organism, reflects the state of health of students in the youthful period of ontogenesis and mature age (I period) in different climatic and geographical regions of the world. After assessing the level of health, the next stage is development of criteria for identifying risk groups, taking into account the already identified signs of possible pathology and disadaptation.

The results we obtained confirmed the greatest difference between the variational pulsometry index of African students and Stavropol students and confirmed the greatest similarity (and therefore adapta-

tion) of South and West Asian students to the climatic and geographical conditions of the Stavropol region, because the most optimal adaptation effect is achieved when morphofunctional parameters are similar (according to N.A. Agadzhanian) [2, 8].

Foreign students in South Asia, West Asia and Africa have the opportunity to adapt to the conditions of Stavropol, it depends on the period of ontogenesis (youth and adulthood). It can assume that the optimal adaptation effect is achieved by South Asian youths and West Asian men. The basis of the adaptation effect is the greatest similarity of the morphofunctional characteristics of nonresident and indigenous people. With some caution, we can talk about the unsatisfactory nature of the adaptation process among students from Africa. The results of this study allow to approach the task of purposeful management of the adaptation process, since adaptation to any factor is associated not only with the waste of energy, but also the structural resources of the body.

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SPECIFIC FEATURES OF MAJOR ANGULAR PARAMETERS OF CRANIO-FACIAL COMPLEX IN MALES AND FEMALES WITH MESIAL OCCLUSION IN THEIR FIRST MATURE AGE

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INTRODUCTION

Uneven growth, leading to an abnormal ratio of the upper and lower jaws, underlies the development of various occlusion issues [1, 2, 3]. The respective literature holds it that the dental anomalies variability in different areas ranges from 11% to 90%. The high prevalence of occlusion issues should be attributed primarily to the difficulty associated with their correct and timely diagnostics [4, 5, 6, 7]. The research carried out to identify occlusion anomalies reveal the lack of a decrease trend, which means there are stable mechanisms triggering the development of this pathology, which keep its prevalence at a stable level [8, 9, 10]. Besides, this pathology is complicated with occlusive and musculo-articular disorders [11, 12].

Aim

to study the variability of the major angular parameters of the cranio-fascial complex in males and females with mesial occlusion in their first adult period.

MATERIALS AND METHODS

The material of the study included 50 lateral head teleoradiographs of young men and women with mesial occlusion in their first mature age. For age periodization, we used the classification adopted at the 7th Research Conference on Age Morphology, Physiology, and Biochemistry (Moscow, 1965). The material was divided into two age groups: 1) males aged 22–35

(n = 26); 2) females aged 21–35 (n = 24). The teleoradiographs had the following cranio-cephalometric points applied: Nasion, Sellion, Orbitale, Porion, Spina nasalis anterior, Spina nasalis posterior, Incision superioris, Incision inferioris, Molare superior coronare, Molare inferioris coronare.

Through the cranio-cephalometric points, planes were drawn further used to measure the angular parameters: 1) the angle of occlusal plane inclination towards the skull base plane (NSe – OcP); 2) the angle between the Camper horizontal and the occlusal plane (Pc – OcP); 3) the angle of the occlusal plane inclination towards the Frankfurt horizontal (H – OcP); 4) the angle between the maxillary plane and the occlusal plane (SpP – OcP); 5) the angle between the mandibular plane and the occlusal plane (Mp – OcP).

The teleoradiographies analysis was done subject to the A.M. Schwarz method (1961).

Results. The average angle of occlusal plane inclination towards the skull base plane in males was $13.3^\circ \pm 1.4^\circ$ ($A = 1.5^\circ - 19.0^\circ$), and in females – $12.4^\circ \pm 0.7^\circ$ ($A = 1.0^\circ - 17.5^\circ$), which made a statistically significant difference ($P < 0.05$). In all the groups, the parameter was subject to significant variability ($CV = 42.2 - 44.4\%$). The angle of the occlusal plane inclination towards the Frankfurt horizontal for males was an average of $8.4^\circ \pm 1.5^\circ$ ($A = 1.0^\circ - 18.0^\circ$), and for females aged 21–35 it was $9.1^\circ \pm 1.7^\circ$ ($A = 1.0^\circ - 18.0^\circ$). The prevalence of the average angle H – OcP in women was statistically insignificant ($P > 0.05$). The parameter was subject to significant variability in both males and females ($CV = 63.8 - 70.1\%$).

The angle between the Camper horizontal and the occlusal plane in males was an average of $8.6^\circ \pm 1.5^\circ$ ($A = 2.5^\circ - 20.0^\circ$), and for females – $9.1^\circ \pm 1.7^\circ$ ($A = 2.5^\circ - 20.0^\circ$). The prevalence of the Pc – OcP angle in young females was statistically significant ($P < 0.05$). The angle is subject to a significant degree of variability in both males and females ($CV = 68.3 - 66.2\%$).

The average values of the angle between the occlusal plane and the mandible body plane in males and females were about identical ($P > 0.05$). The average

value for males was $20.9^{\circ} \pm 0.6^{\circ}$ ($A = 18.5^{\circ} - 24.5^{\circ}$), and for females – $20.8^{\circ} \pm 0.7^{\circ}$ ($A = 18.5^{\circ} - 24.5^{\circ}$). The parameter in question proved not very variable, be that males ($CV = 11.5\%$) or females ($CV = 12.3\%$). The angle between the the occlusal plane and the mandible body plane revealed a statistically significant predominance in males ($P < 0.05$). Its average value for males was $8.5^{\circ} \pm 1.3^{\circ}$ ($A = 1.5^{\circ} - 14.0^{\circ}$), and for females – $7.9^{\circ} \pm 1.5^{\circ}$ ($A = 1.5^{\circ} - 14.0^{\circ}$). The parameter manifested high variability in both males and females ($CV = 62.4^{\circ} - 68.9\%$).

CONCLUSIONS

The above means that almost all the investigated angular cranio-fascial parameters in males and females with mesial occlusion in their first adult period, except the Mp-OcP angle, are subject to great variability, which proves their significant individualization. This issue should be taken into account when developing an examination and treatment plan for patients belonging to this group.

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ANALYSIS OF SOME COMPONENTS OF BLOOD PROTEOME IN “HEALTHY POPULATION” OF RUSSIAN MEGAPOLIS

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ABSTRACT — THE AIM OF THE STUDY was to study some components of blood proteome in *healthy* megapolis population.

METHODS: The study included 2025 people examined in the framework of preventive medical examination and referred to its results to 1–2 groups of health (the category of *healthy people*) and did not have at the time of examination of chronic and acute diseases. The age of the examined persons was in the range of 20–50 years (median — 34.8 years). Total protein level, plasma concentrations of C-reactive protein, ferritin and homocysteine were selected as markers of blood proteome.

RESULTS: Our screening study allowed establishing that a significant part of the population of the megapolis, classified as practically healthy persons, has deviations from the physiological interval for a number of proteome components. This is most evident in shifts in plasma concentrations of C-reactive protein and ferritin. So, in more than half of the individuals levels of C-reactive protein was outside the normal range. The distribution structure for ferritin shows the opposite trend.

KEYWORDS — blood proteome, C-reactive protein, ferritin, homocysteine.

INTRODUCTION

Currently, proteomics, being one of the most widely known synthetic biological disciplines, is considered as a fundamental basis for the development of personalized laboratory diagnostics [1, 7]. In whole, proteome is a set of all protein components of a biological sample [3]. It is shown that proteomic methods can study the protein structure of both biological fluids and various tissues of the body [3, 5]. This allows us to distinguish biomarkers of a number of pathological conditions and diseases, carrying out their molecular diagnosis, including — at an early stage of their formation [5, 8, 9]. The most commonly analyzed biological sample for proteomic analysis is serum or plasma [6–10].

In most cases, proteomic analysis involves a mass spectrometric study of biological substrates [7, 12, 15], but it is also possible to selectively evaluate individual components of the proteome by biochemical analysis

of the concentration of metabolites [2, 3, 8, 11]. This is especially important for cohort studies that are performed as part of screening testing of a large population [2, 5, 9].

In recent decades, the emphasis of medicine has gradually shifted from *diseases treating* to preventive medicine [12–14, 17]. This is due to the high frequency of prenosological conditions that require timely correction. In turn, such a statement of the problem is determined by the need for a detailed study of the prevalence of metabolic disorders, including shifts in proteome components in the population classified as *healthy individuals* [5, 11, 12, 17].

In this regard, the aim of the study was to study some components of blood proteome in *healthy* megapolis population.

METHODS

The study included 2025 people examined in the framework of preventive medical examination and referred to its results to 1–2 groups of health (the category of *healthy people*) and did not have at the time of examination of chronic and acute diseases. The age of the examined persons was in the range of 20–50 years (median — 34.8 years).

All people included in the study, after obtaining informed consent, were subjected to extensive laboratory testing. Total protein level, plasma concentrations of C-reactive protein, ferritin and homocysteine were selected as markers of blood proteome. All these parameters were determined by standard laboratory methods. All patients were tested in the morning.

The gradation of the level of indicators was made according to the existing standard (reference) laboratory intervals. Additionally we used a quartile approach, highlighting the reduced and increased level of the parameter and four quartiles. The normal distribution of the trait values corresponding to the Gauss distribution was taken as the population norm. The structure of distribution of values of the parameter, essentially different from the last, was considered deviating.

The data were processed in the software package Statistica 6.1.

RESULTS

The quartile analysis of the formed group of people allowed to establish that the structure of the distribution of the values of the selected proteome components differs significantly from the standard Gauss distribution (Fig. 1–4). Thus, the level of total protein is found at low values in 14.93% of the examined individuals (Fig. 1). In addition, attention is drawn to the fact that this parameter is recorded at the lower limit of the norm corresponding to 1 quartile in 33.79% of people.

Interesting data were obtained with respect to the level of C-reactive protein in blood plasma (Fig. 2). It was revealed that among the examined people, referred to the results of preventive examination to the category of *practically healthy* persons, in 54.81% of cases there was an increased level of the indicator. In addition, in 14.97% of the examined people the concentration of C-reactive protein was fixed at the upper limit of the norm corresponding to the 4th quartile.

The most significant deviation from the standard distribution structure was revealed for the main iron – transport blood protein-ferritin (Fig. 3). It was found that the reduced level of this indicator was typical for 26.87% of the surveyed group of people, and in 47.65% of cases it was at the lower limit of the norm (1 quartile).

According to the homocysteine concentration, the formed group corresponded to the Gauss distribution to the greatest extent, however, a certain shift was observed for this parameter as well (Fig. 4). Thus, 11.68% of the surveyed persons had a reduced value of the indicator, and it was at the lower limit of the norm in 31.31% of cases. On the contrary, an increased level of homocysteine was recorded in 5.79% of people.

DISCUSSION

Laboratory biomarkers are known to be the basis of personalized medicine [1, 3, 5, 8, 12, 14]. These include components of the proteome such as C-reactive protein, ferritin and homocysteine.

C-reactive protein, which belongs to the category of acute phase proteins, is one of the markers of inflammatory reaction [4, 5]. In addition, its level is considered as a predictor of various chronic diseases, including cardiovascular disease and degenerative diseases of the musculoskeletal system [16, 17]. In our study it was found that more than 54% of the population of the megapolis, belonging to the category of *healthy* persons, has an increased level of the indicator. This indicates the need for their in-depth study for diagnosis and early correction of prenosological conditions.

Also, the study showed that a significant part of the population of a large city (about 27%) has devia-

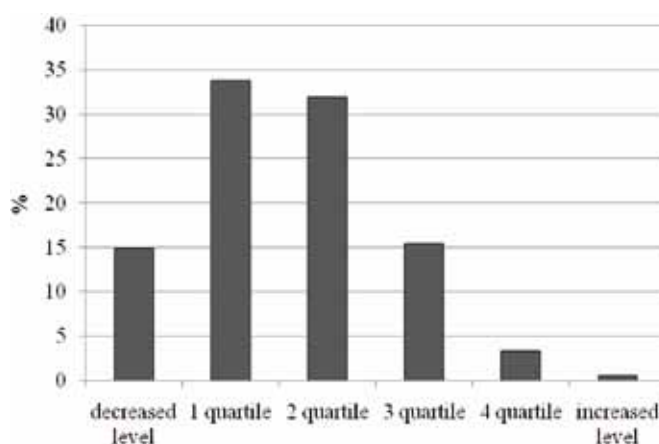


Fig. 1. Quartile structure of total level of blood protein in healthy people

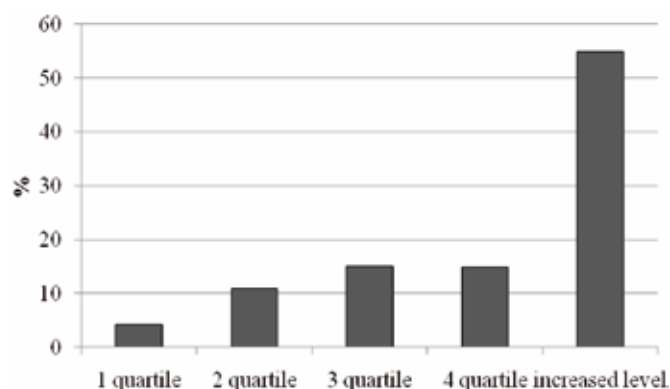


Fig. 2. Quartile structure of C-reactive protein level in the blood of healthy people

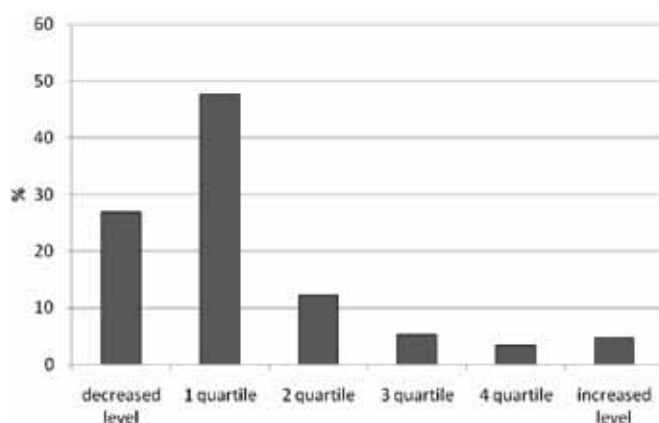


Fig. 3. Quartile structure of ferritin level in the blood of healthy people

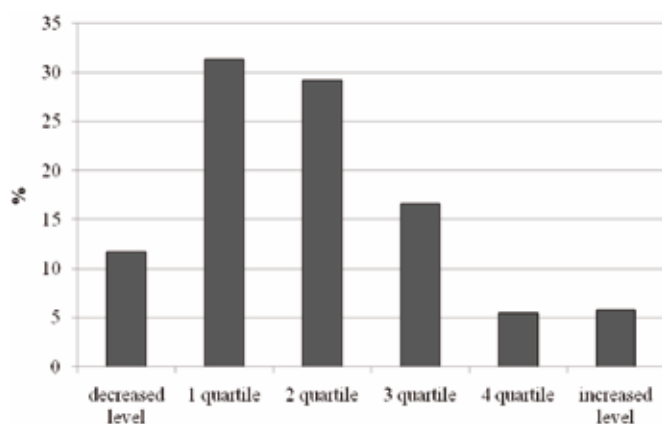


Fig. 4. Quartile structure of homocysteine level in the blood of healthy people

tions of ferritin concentration from the physiological level, and about half of the people demonstrate the trend to reduce the level of this metabolite. Such data confirm the literature data on the heterogeneity of the population according to this criterion [11], and there is evidence that both the increase and decrease in the level of this parameter is associated with an increase in the risk of cardiovascular disease [8, 11].

Similar shifts are shown by us for the concentration of homocysteine in the blood plasma of residents of the megapolis. In total, about 43% of the surveyed people had a reduced value of the parameter or located at the lower limit of the norm. It is also considered as a negative criterion, which is a potential marker of prenosological disorders, including neurological disorders (in particular, Alzheimer's disease [10], sleep disorders [2]) and even sexual dysfunction [13].

Thus, an extensive study has demonstrated the presence of significant shifts in the plasma concentration of a number of proteome components, which requires further in-depth analysis for personalized correction.

CONCLUSION

Our screening study allowed to establish that a significant part of the population of the megapolis, classified as practically healthy persons, has deviations from the physiological interval for a number of proteome components. This is most evident in shifts in plasma concentrations of C-reactive protein and ferritin. So, more than half of the individuals having levels of C-reactive protein outside the normal range. The distribution structure for ferritin shows the opposite trend.

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HISTOMORPHOLOGIC CHANGES IN LYMPH NODES WITH LYMPHOTROPIC IMMUNOSTIMULATION IN EXPERIMENT

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ABSTRACT — The research deals with the study of histomorphologic changes in the lymph nodes of rats arising from the lymphotropic and intramuscular administration of acidic peptidoglycan. The authors investigated histologic changes and applied the morphometric method including the determination of the average size of the lymph nodes, the size of the germinal zones, the density of the lymph nodules. It is stated that the restructuring of the lymph nodes during lymphotropic administration occurs at different times in comparison with its intramuscular administration. The lymphotropic method provides a relatively earlier and prolonged onset of an immunostimulating effect. This made it possible to conclude that the method of administering immunomodulators should differentiate depending on the phase and form of the disease progression.

KEYWORDS — lymph nodes, lymphotropic administration, immunostimulation, immunodeficiency, peptidoglycan, murein.

INTRODUCTION

Currently, doctors in their practice increasingly confront with a state of secondary immunodeficiency which is caused by the influence of many external and internal factors [1, 2, 3]. These factors include malnutrition, helminth infection, chronic infectious diseases, injuries or surgeries, endocrine dysfunction, intoxication of various origins, etc. Doctors are equipped now with a huge number of immunostimulating drugs that are included in the treatment of diseases [4, 5, 6]. One of the groups of such drugs are those based on murein, acid peptidoglycan (APG) — a component of the cell wall of bacteria or some algae. Despite the fact that these drugs have been used for several decades, histomorphologic changes in the immune system in response to this type of immunostimulation have not been studied enough. One of the methods of *targeted* drug delivery to the lymphatic system is the lymphotropic method. It allows to create a high and long-lasting concentration of drugs in the lymphatic system [7, 8]. The research objective was to experimentally study the nature and timing of histomorphologic

changes in the lymph nodes during lymphotropic immunostimulation using APG.

MATERIAL AND METHODS

The study was conducted in a certified laboratory in 20 male rats of the Wistar line at puberty, weighing 150–170 g. All the studies were carried out in accordance with the European Convention for the Protection of Vertebrate Animals used for experiments or for other scientific purposes (ETS N 123). The research has been granted a permission of the Astrakhan SMU Bioethics Committee (the protocol N 3 of 31.10.2011). The animals were divided into 2 groups — observational and experimental, 10 animals each. Immunostimulation modeling, in groups, was performed by administration of APG with a molecular weight of 1000–40 000 kDa in a dose of 0,3 U. In the observational group, the drug was administered intramuscularly, in the experimental group — lymphotropically on the day 1, 2, 3, 8, 9, 10 of the experiment. Hyaluronidase was used as a lymphotropic substance in a dose of 0,07 U. Withdrawal from the experiment was carried out on the day 1, 3, 7, 14 and 30. The sampling, fixation of lymph nodes and the manufacture of paraffin blocks were carried out according to the standard technique of working with lymphoid organs. The samples were stained with hematoxylin and eosin, and azure II-eosin staining was used to identify the cells. Details of the histological structure were studied using a hardware-software complex including a Leica MZ 12,5 stereomicroscope, Pixera television cameras, and a Leica DM-1000 microscope using the Morpholog computer program. Linear lymph node indicators were recorded by creating an *object-distance* between two points. The cross-sectional areas of the structural components of the lymph nodes (cortical, medullary substance and paracortical zone) were determined by the method of *masking*. Morphometric calculation was performed in six fields of view of each slice, six slices from each object being analyzed. Statistical data processing was performed using variation statistics with Statistica 6.0 software.

RESULTS AND RESEARCH

Histological examination of lymph nodes in both groups showed an increase in the number and hyperplasia of the follicles in the subcortical zones, the formation of *light centers* with the proliferation of cellular elements. There was also noted a filling of the lumen of the sinuses with lymphoreticular cells. See fig. 1. Our attention was attracted to a pronounced proliferation of lymphoreticular cells. We registered the formation of follicles with designated *light centers* by the effect of lymphoblasts and hemocytoblasts. See fig. 2. In the group with lymphotropic administration of APG, on the 3rd day, there was a significant increase in the density of lymph nodules per surface unit of the sample, as well as the size of the germinal centers, which increased by 36% and 32%, respectively. Lymphatic nodules appeared not only in the cortical, but also in the medullary substance. See fig. 3. There was also a slight increase in the average size of the lymph nodes, which was within the margin of error. Lymphatic cells filled the lumen of the follicles. On the 30th day, the density of the lymph nodules and the size of the germinal centers decreased by about a third and amounted to 19% and 20%, respectively. In the observational group, an increase in the studied parameters was observed on the 7th day of the experiment. Lymph nodes' growth was found to be 25%, the germinal centers and density of lymph nodules increased by 31% and 28%, respectively. On the 30th day, the above changes almost came to initial values. See fig. 4.

DISCUSSION

Analyzing the obtained results, it can be stated that the introduction of APG causes stimulation of

immunoregenerative processes in the lymph nodes. There were differences in the timing of the formation of an immunostimulating effect depending on the method of administration. With lymphotropic administration, the effect occurred earlier (on the 3rd day), and with intramuscular administration — on the 7th day. The duration of the immunostimulating effect after intramuscular administration was leveled by the 30th day, and in the experimental group it was preserved, which resulted in a more prolonged effect.

CONCLUSION

The lymphotropic administration of APG, in contrast to intramuscular administration, provides an earlier and more prolonged onset of an immunostimulating effect. The data obtained may allow the doctor to prescribe a rational treatment regimen, depending on the characteristics of the clinical course of the disease and to obtain the optimal effect.

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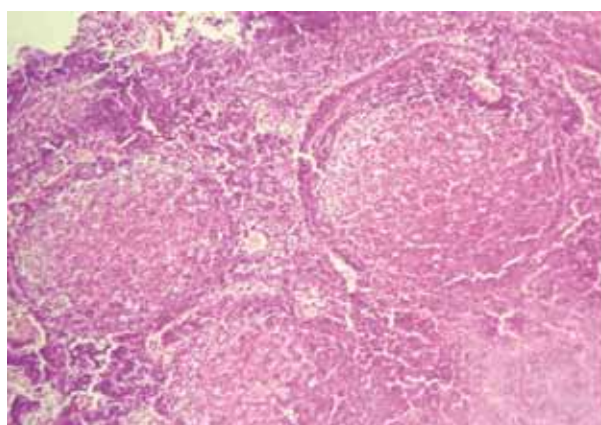


Fig. 1. A large number of hyperplastic follicles in subcortical zones, «light centers» with proliferation of cellular elements. Lymphoreticular cells fill the lumen of the sinuses. Stained with hematoxylin-eosin $\times 100$

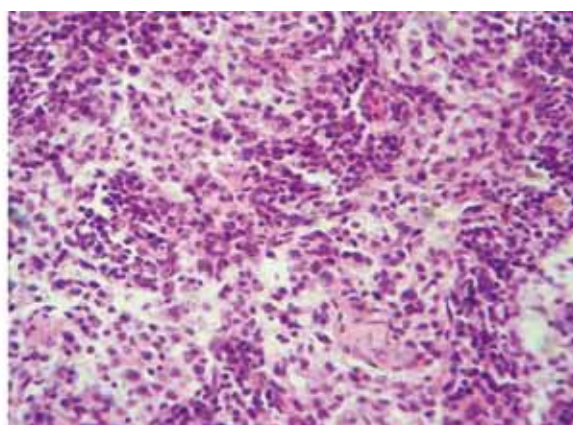
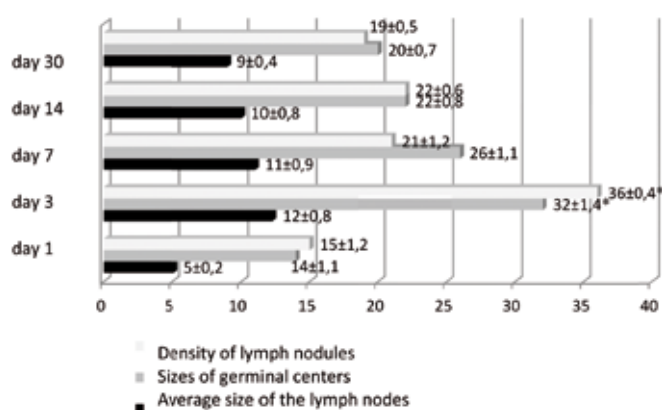
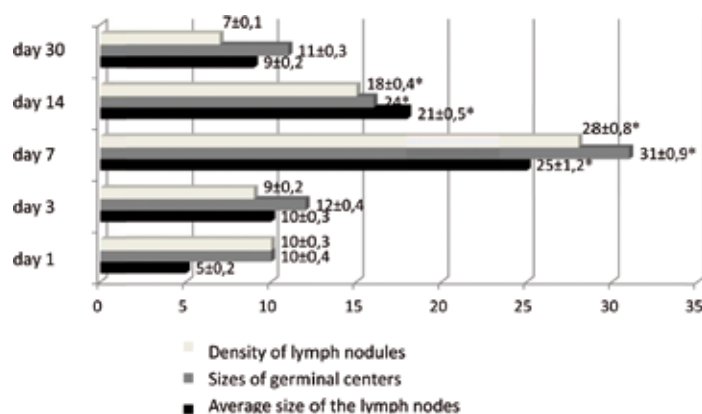


Fig. 2. Proliferation of lymphoreticular cells. Lymphoblasts, hemocytoblasts form follicles with designated «light centers». Stained with hematoxylin-eosin $\times 400$



*Fig. 3. Dynamics of morphofunctional changes in lymph nodes with lymphotropic administration of HGP at different time of observation (%); * — statistically significant differences at $p < 0.05$*



*Fig. 4. Dynamics of morphofunctional changes in lymph nodes with intramuscular administration of HGP at different time of observation (%); * — statistically significant differences at $p < 0.05$*

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POSTMORTEM PATHOLOGICAL FEATURES IN LIVER TISSUE OF HIV PATIENTS

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ABSTRACT — Study of morbid anatomy material from dead patients suffering from HIV-related illnesses, including hepatitis C, provided an opportunity to identify substantial pathological changes in the structural elements liver that suggested other pathogenetic mechanism of development changes in patients with HIV and hepatitis C associated with impaired metabolism in erythrocytes that are collapsing, hemoglobin in the plasma of blood vessels of the liver. As a result of the destruction of erythrocytes, free, not associated with erythrocytes, hemoglobin cannot carry carbon dioxide from cells, hypoxia ensues the structural elements of the liver and cells are forced to use the free dissolved in plasma oxygen, which further exacerbates the occurrence of hypoxia and Anoxia and then the appearance of intoxication of the massive destruction of hemoglobin and the advent of plasma transferrin. The last captured by macrophages. The free hemoglobin in the bloodstream increases its toxic effect on tissue cells, causing cell death in the resultant ischemia, thus worsening the oxygen supply of them. As a result of the subsequent destruction of haemoglobin are formed its decay products in the form of iron porphyrin, bilirubin, The latter contributed to the development of jaundice or acute porfirii owing to the death of hepatocytes, which manifest is to develop cirrhosis or cancer.

KEYWORDS — HIV, hepatitis c, ischemia, cirrhosis, cancer.

RELEVANCE

It is known that HIV-associated AIDS is one of the frequent causes of mortality in young age [1,2]. Many authors consider hepatitis c HIV infection and chronic hepatitis, precipitating factor in the defeat of the structures of the liver and in the subsequent development of cirrhosis [3,4]. According to Rodríguez-Nóvoa S, Morello J, González M, et al. (2008), the use of antiviral drugs causes hemolysis and increases

bilirubine [5, 6, 7]. This group of scientists conducted a study on the treatment of HIV/hepatitis c-infected patients showed increased bilirubine with 9% to 45% after the start of treatment of HIV-infected patients with hepatitis c. overall, according to many authors, efficiency standard antiviral treatment does not exceed 50–80%. However, despite the emergence of large quantities of drugs for the treatment of HIV infection, pathogenesis of HIV infection are not fully disclosed. Conducted on atherosclerosis plaques assays materials perished from HIV while also not given complete replies to the nature of the investigated processes occurring in the body, HIV-infected, leading to death. The majority of patients with hepatitis c, including HIV-infected, develops resistant anemia, decreased intake of toxic antiretroviral drugs [8]. Anemia at the present stage is not an exhaustive justification pathophysiology as disclosure mechanisms reduce the hemoglobin in the blood of patients with hepatitis c and HIV infections. It is expected that the anemia has multifactor nature, which explains the cases of failed attempts of empirical application of erythropoietin in treatment of patients with hepatitis c and HIV infections [9, 10, 11].

Therefore, the study of the pathological features of HIV infection should be considered relevant because it is necessary to address the issues of early Diagnostics, treatment, rehabilitation, taking into account the early accession opportunistic infections, leading to the defeat of various organs and systems of the patient, emerging when the pathology study and the emergence of new data on pathogenesis mechanisms in the development of HIV/AIDS infection.

MATERIAL AND METHODS

The materials used autopsy 9 HIV-infected children from 3 months. up to 12 years and 35 adult patients from 30 to 38 years, deaths from HIV infection and opportunistic diseases, obtained in accordance with the regulations of the Helsinki Declaration (2000) and with the permission of the Ethics Committee of the Federal autonomous State educational institution of higher education, Ministry of science and higher education of the Russian Federation far eastern Federal University". The monitoring group amounted to avoided material 17 patients who died as a result of

injuries that are incompatible with life, ranging in age from 12 to 76 years (Table 1).

Coloring samples of liver tissue produced in hematoxylin-eosin, and microbiology characteristic structural elements were evaluated at liver histological sections as you increase lens $\times 200$, $\times 400$. In doing so, made Microscope Olympus-Bx82 and Cdh digital camera with proprietary 82 IT software.

presence of brown pigment in the system of blood outflow.

We found that the dark pigment accumulation in the cytoplasm of macrophages corresponds to transferrin, product exchange lysed RBCs and hemoglobin destroyed. At the same time found that pathological process in the structural elements of the liver infection hepatitis c virus (HCV) infected with HIV starts with

Table 1. Material distribution

#	Age groups	Control	Pathology			Material
			Hepatitis C	Hepatitis C+ HIV infection	HIV infection	The liver, kidneys, lungs
1	3 months–12 years	3		3	6	9
2	30–33 year	3	7	4	3	14
3	34–35 year	3	3	3	3	9
4	36–38 year	8	3	5	4	12
TOTAL		17	13	15	16	44

RESULTS AND DISCUSSION

The result of the study material to avoided material liver was revealing in the liver parenchyma of the morphological picture of acute hepatitis c with explicit leukocyte infiltration between lobule fabric, the presence of biliary extension ducts, determination of apoptosis of hepatocytes, fatty liver, cirrhosis, necrosis (fig. 1, 2, 3, 4, 5).

In the lumen of blood vessels are identified by macrophages, whose cytoplasm is filled with transferrin (fig. 6).

We believe that the pathological changes in the liver of patients with HIV infection associated with hepatitis c and pathology study material related to erythrocyte hemolysis, the destruction of hemoglobin and the subsequent emergence of processes cellular Anoxia. Moreover, we found that some patients show signs of acute hepatitis c is characterized by the typical picture with around between lobules and infiltration zone tetrads, but saving the structure of the hepatic lobules; other patients identified the transition of acute hepatitis in chronic, with signs of the formation of false hepatic lobules, increased outflow of bile system, apoptosis of hepatocytes, antitheses of common perceptions about pathogenic changes in structures.

Based on our research, found that besides the well-known symptoms of pathological changes in organs, submitted by many authors (hyperemia parenchyma, apoptosis and degeneration, fibrosis, cirrhosis and later joining local necrotic changes with leukocyte infiltration) we have identified all the bodies of the

hypoxia. The latter, as a result of subsequent manifestations of intoxication, leading to apoptosis, and necrosis of cells due to Anoxia due to aggressive destruction of erythrocytes and the release of free plasma hemoglobin in the blood vessels of the liver, which is even more adding to the ischemia due to its toxicity, thereby worsening the oxygen supply to the tissues of the liver.

Collapsing, hemoglobin allocates degradation products in the form of a porphyrin, bilirubin, iron, transferrin, which invade macrophages.

In ischemia of hepatocytes and, as a consequence, their deaths, declining elaboration of all constituent of erythropoietin, disturbed Mrr erythropoiesis and regeneration, control over the breeding of metabolites. This is indirectly confirmed by numerous studies have referred to lower hemoglobin in the peripheral blood of patients with hepatitis c and HIV-positive, but it does not explain mechanism of anemia.

Particularly high risk for the development of processes such as cirrhosis of the liver in patients with hepatitis c and HIV-infected in the absence of a pathogenetically justified treating anaemia, and understanding of mechanisms of pathogenesis, which is what leads to undesirable complications, so There is a need to develop a randomized trials of high methodological quality assessment for strategic effects on anemia in persons infected with hepatitis c virus and human immunodeficiency.

Thus, we believe that a key factor in the mechanisms of systemic damage to the walls of blood vessels, including the participants of hematological and tissue

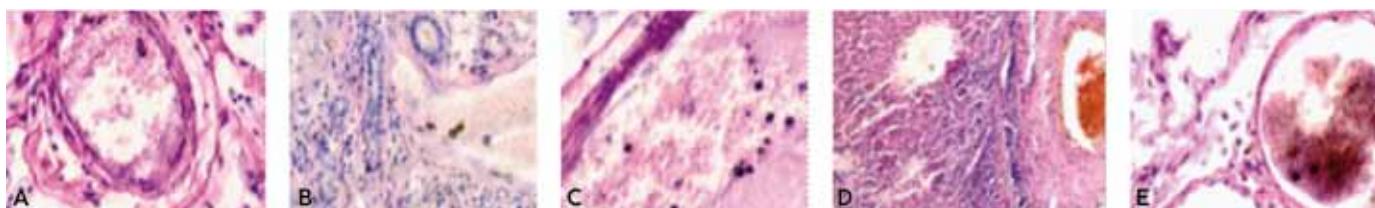


Fig. 1. Human Liver — a, b, c, d) with a pigment in cytoplasm of macrophages in the lumen of the vessels; e) pigment in the cytoplasm of macrophages and diffusely located in the lumen of the vessel. Coloring g/e. Mikrofoto. HCS. $\times 200$

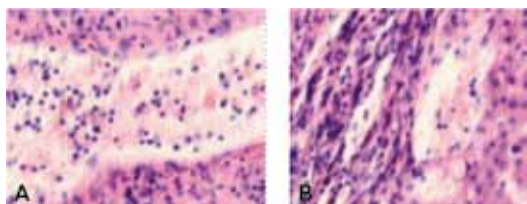


Fig. 2. Liver Parenchyma in patients with hepatitis c in HIV-infected. Pseudodolka liver — a, b) leukocytes in pronouncing the lumen of the vessel. Coloring g/e. Mikrofoto. HCS. $\times 200$

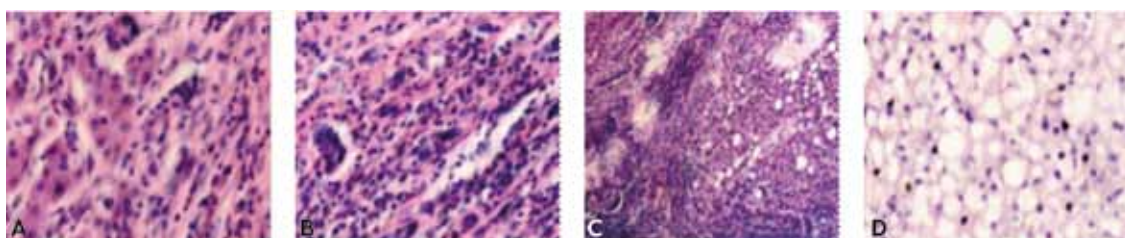


Fig. 3. Liver Parenchyma in patients with hepatitis C in HIV-infected. Pseudodolka liver — a, b) infiltration mezhdolkovyh structures; c, d) steatosis/ Coloring g/e. Mikrofoto. HCS. $\times 200$

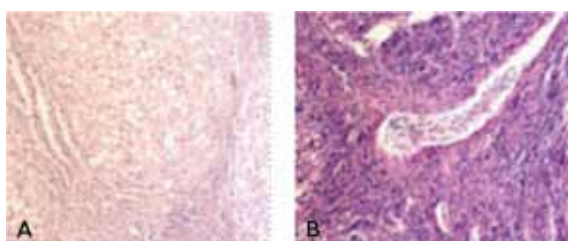


Fig. 4. Liver Parenchyma in patients with hepatitis c in HIV-infected. Pseudodolka liver — a, b) cirrhosis. Coloring g/e. Mikrofoto. HCS. $\times 200$

barriers may be macrophages during phagocytosis of transferrin, aggressively destructive to endothelium release into the blood stream. Due to the fact that ruined hemoglobin enters the blood, as in the unassociated state very toxic, begins a massive cell death due to ischemia/anoxic and intoxication. Hypoxia and anoksija, in turn, lead to a decrease in energy processes

of cellular apparatus, apoptosis, necrosis of hepatocytes, loss and development of cirrhosis of the liver and other organs of carcinogenesis.

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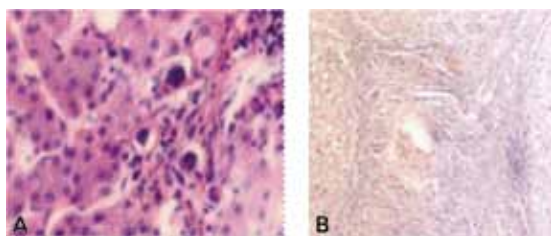


Fig. 5. Liver Parenchyma in patients with hepatitis c in HIV-infected. Pseudodolka liver — a) calf Councilman; b) cirrhosis and necrosis of the liver parenchyma. There is no central Vienna. Apoptosis. Coloring g/e. Mikrofoto. HCS. a) $\times 200$; b) $\times 400$

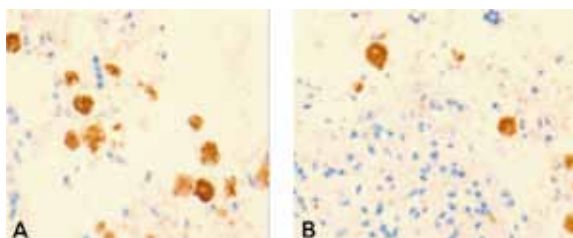


Fig. 6. Macrophages with transferrin in the lumen of blood vessels of the liver with hepatitis HIV-infection. Mikrofoto. Coloring g/e. SW. $\times 400$

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VASCULAR RESPONSES TO THE SUBCUTANEOUS INJECTION OF GOLD NANOPARTICLES

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ABSTRACT — The study presents the results of a study of the inhibitory role of gold nanoparticles, administered subcutaneously to mice line CBA. The migration paths of gold nanoparticles after subcutaneous injection have been studied, and the mechanisms of their influence on the tissue surrounding the injection site of nanoparticles have been examined. After subcutaneous injection, gold nanoparticles have been found to undergo phagocytosis by macrophages, some of which migrate to lymph node lymphoid follicles, and some enter the lumen of blood vessels, where nanoparticles exit the macrophage cytoplasm and enter the bloodstream. It has been established that as a result of the toxic effect of macrophages loaded with nanoparticles, the endothelium of the vessels growing into the tumor is destroyed. It was concluded that inhibition of angiogenesis and death of blood vessels in the tissues after the introduction of nanoparticles occurs in two ways. The first is not associated with direct inhibition of endothelial growth factor (VEGF), but with the deactivation of macrophages that produce VEGF, the molecules of which stimulate the formation of endothelium in growing blood vessels; and the second mechanism is implemented through the direct death of the endothelium during the migration of the macrophage through the vessel wall.

KEYWORDS — gold nanoparticles, toxicokinetics, mechanism of migration of nanoparticles of gold when a skin.

There is an assumption that gold nanoparticles can be used in oncology for treating tumors. [4] After the introduction of gold nanoparticles and exposure to infrared rays, there is a local death of cancer cells, but there is no data on the generalized effect and side effects of gold nanoparticles on experimental animals and humans, which dictates the need for research in this direction.

Gold nanoparticles with a number of unique characteristics (optical properties, strength, high surface area) are mainly used for diagnostic purposes [1, 8]. Gold nanoparticles can serve to amplify the signal from cancer cells in diagnosing a tumor by binding nanoparticles with antibodies to tumor cells [9]. Wang et al (2011) used gold nanoparticles to increase the sensitivity of cancer cells to drugs [15]. An electrochemical approach based on partial replacement of electrodes with gold nanoparticles has recently been used for tagless detection of a cancer-embryonic antigen.

The attachment of oligonucleotide sequences complementary to the target DNA molecule to the surface of gold nanoparticles for the colorimetric detection of DNA is a relatively new diagnostic technique, presenting an alternative to fluorescent and radioimmune methods [7]. This technique can also be used for the detection of extremely low (atom-molar) concentrations of protein in biological media. Thus, this technique was applied to measure the concentration of β -amyloid fragments (the putative marker of Alzheimer's disease) present in the cerebrospinal fluid in negligible amounts [6].

At the present stage, it has been established that gold nanoparticles are capable of destroying blood vessels of a cancerous tumor; on the basis of this, it has been suggested that the mechanism of vascular damage is associated with inhibition of endothelial growth factor (VEGF) [14, 10, 3].

It is known that gold preparations exhibit an antibacterial effect, for example, against *Helicobacter pylori*, toxoplasma, and also exhibit antifungal activity. At the same time they give a pronounced side effect.

Many cancer cells have a protein all over their surface, known as epidermal growth factor receptor (EGFR), while healthy cells usually do not express this protein so strongly. Conjugation (or binding) of gold nanoparticles with anti-EGFR antibodies, commonly called anti-EGFR, allowed the researchers to bind the nanoparticles to the cancer cells themselves. Therefore, the properties of NPG are studied as radio modifiers for use as targets for tumor damage. Also currently, work is underway to create complexes of gold nanoparticles and antibiotics for the destruction of antibiotic-resistant microorganisms [12, 18]. Further improvement of diagnostic approaches based on the use of gold nanoparticles is associated with the devel-

opment of methods for functionalizing the surface of these nanoparticles using carbohydrates and increasing the sensitivity of nanosensors based on gold nanoparticles with the *profiling* of their diagnostic capabilities.

Despite numerous studies on the possibility of using gold nanoparticles in the development of new antibiotics, their use is not yet possible due to the presence of side effects and the lack of data on their generalized effect on not only humans, but also experimental animals [5, 13, 2, 17]. The limited use of nanoparticles is due to the fact that gold compounds are toxic, accumulate in the kidneys, liver, spleen and hypothalamus, which can lead to organic diseases and dermatitis, stomatitis and thrombocytopenia [16, 11].

Therefore, the urgency of the need to study the toxicokinetics of gold nanoparticles on the material of experimental animals for further extrapolation to the human body is rapidly increasing.

MATERIAL AND METHODS

The study was carried out on 35 male CBA mice. Group 1 intact controls (n=5) were kept together with other groups under similar conditions (temperature, humidity, day/night, and nutrition). Control group 2 (n=5) mice were subcutaneously injected with 0.5 ml isotonic saline. Experimental group 3 (n=25) mice were subcutaneously injected with 0.5 ml gold NP suspension (50% dilution in isotonic saline). Sequentially, after 1, 2, 3, 4, 5 days, the rats were killed, soft tissues of the proximal third of the posterior thigh were isolated, including lymphoid tissue of the inguinal region, and then paraffin blocks were made using the classical method. The resulting sections were dewaxed, and then stained with standard hematoxylin-eosin. An illustrative material was obtained using an Olympus Bx51 microscope with a digital camera CDx25, and then analyzed using original Olympus morphometric computer programs.

Gold nanoparticles in a colloidal solution had sizes of 10–20 nm and were obtained at the Institute of Chemistry of the Far Eastern Branch of the Russian Academy of Sciences (Vladivostok).

RESULTS

No morphological changes were found in the tissues of mice from both control groups: typical structure of the connective tissue, vascular walls, muscle tissue, skin, and inguinal lymph nodes of the hip were found during all periods of the study.

The material obtained on the first day of the experiment from rats that received subcutaneous injections of gold nanoparticles made it possible to establish the effects of pronounced perivascular leukocyte infiltration around the wall of blood vessels near

the contamination of nanoparticles in the tissue. On the second, third and all subsequent days of the experiment, blood vessels of different caliber are detected, in which hypertrophy and death of endotheliocytes, destruction of the basement membrane are identified. The cytoplasm of endotheliocytes bulges into the lumen of the endothelium, and on the side of the vessel adjacent to the zone of introduction of nanoparticles. On the 1st day, gold nanoparticles are identified to a greater degree in the free state, and then the surrounding white blood cells contaminate them gradually. The number of nanoparticles in the cytoplasm of macrophages from single ones in the first–second day after injections increases by the 3rd day until the cytoplasm is full of nanoparticles. On the 3rd day, both free nanoparticles and contaminated and filled the entire cytoplasm of leukocytes are identified.

We noted that macrophages release lysosomes, as well as leukocyte migration in the direction of blood vessels, into the surrounding tissues which the nanoparticles were introduced. At 4–5 days, the main mass of macrophages is identified only near the wall of blood vessels. Also in the vessels, the death of a part of macrophages is observed with the release of gold nanoparticles into the blood. The second way to exit nanoparticles in the lumen of blood vessels is degranulation.

We noted that a part of macrophages loaded with gold nanoparticles migrates to T-dependent zones of lymphoid follicles, as we think, for the antigen presentation of nanoparticles and the activation of the T-lymphocyte pool in the direction of blast transformation of immune cell differenon for the implementation of cellular immune responses.

Thus, the dynamics of the migration of gold nanoparticles, introduced subcutaneously to rats, has the following algorithm:

The 1st day after the administration is accompanied by phagocytosis of gold nanoparticles in the interstitial tissue, as we assume, by two types of macrophages: monocytic and T-lymphocytic. Monocytic phagocytes carry out the delivery of gold nanoparticles into the lumen of blood vessels, releasing them and partially releasing them into the blood due to the death and rupture of the cell membrane; T lymphocytic cells deliver gold nanoparticles to the lymphoid tissue of rat lymph nodes for antigen presentation and induction of blast transformation of the effector cells of transplantation immunity.

On the second day, the number of phagocytosed nanoparticles in macrophages increases, the number of phagocytes increases, which migrate in the direction of the blood vessels. The endothelium of the vascular wall is hypertrophied. Moreover, hypertrophy does

not develop over the entire surface of the inner wall of blood vessels, but only in the zone adjacent to the site of introduction of gold nanoparticles, the result of hypertrophy is the death of endotheliocytes. On days 2 and 3, migration of macrophages in 2 directions is identified: to the blood vessels and in the direction to the lymphoid tissue to the periphery of the lymphoid follicle to T-dependent zones for antigen presentation. On the 4th day, macrophages migrating into the vessel lumen are determined, the cytoplasm of which is filled with gold nanoparticles. We have noted that there are two mechanisms for the removal of gold nanoparticles into the vessel lumen: one group of macrophages releases gold nanoparticles as a result of degranulation, the second due to death.

The obtained data on the dynamics of the migration of gold nanoparticles are important for the development of diagnostic and therapeutic measures. It is necessary to implement diagnostic and therapeutic measures in treating tumors on the first day after local subcutaneous administration of gold nanoparticles, since on the second day most of them undergo phagocytosis and migrate in different directions from the site of administration, therefore, the effectiveness of therapeutic measures in the later periods will be reduced.

Thus, we obtained data confirming the ability of effector cells of the phagocytic link loaded with gold nanoparticles to destroy the vascular wall, leading to an increase in its permeability due to the death of the endothelium. We suggest that the mechanism for reducing the growth factor of the endothelium and the absence of angiogenesis in the tumor is associated with the deactivation of macrophages that produce VEGF due to the phagocytosis of a large number of nanoparticles.

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THE EFFECT OF PIR-9 COMPOUND ON MARKERS OF APOPTOSIS IN EXPERIMENTAL FOCAL CEREBRAL ISCHEMIA IN RATS

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ABSTRACT — A study to assess the effect of a new pyrimidine derivative (PIR-9 at a dose of 50 mg/kg) on apoptosis markers in experimental focal cerebral ischemia of the rat brain. It has been confirmed that the investigated compound PIR-9 contributes to a decrease in the concentration of TNF α by 34,36% ($p < 0,05$) as compared to that in rats treated with a reference drug Cavinton (3,2 mg/kg) and has an effect comparable in effect to Gliatilin (60 mg/kg). The concentration of AIF in rats that received compound PIR-9 was 29,99% ($p < 0,05$) less than the group of negative control rats.

INTRODUCTION

It is known that cerebral ischemia triggers apoptosis — regulated neuronal death, the mechanisms of action of which are currently well studied [1]. Tumor necrosis factor — a pro-inflammatory cytokine that activates the extrinsic (caspase-dependent) pathways of apoptosis, AIF-a protein that triggers the mitochondrial (caspase-independent) pathways of apoptosis, blocking the main proapoptotic pathways, can be promoted by cerebroprotection [2, 3]. A potential cerebroprotective activity of pyrimidine derivatives has been confirmed earlier [4], therefore the problem of the effect of these compounds on apoptosis markers is of great interest.

Objective

To study the effect of PIR-9 compound on markers of apoptosis in experimental focal cerebral ischemia in rats.

MATERIALS AND METHODS

The study was conducted in accordance with the "Guidelines for Preclinical Trials of Drug Products" ed. by A.N. Mironov (a 2012 edition.) [5]. The experiment was performed on 30 male Wistar rats $m = 220 - 240$ g, divided into 5 groups ($n = 6$). Rats were kept on a standard vivarium diet, with a natural

succession of light and darkness. The first group was represented by falsely operated rats (FO), the second one — by negative control animals (NC). The both groups received an intraperitoneal suspension of Tween-80 in purified water. The third and fourth groups received reference drugs: Cavinton (3,2 mg/kg) and Gliatilin (60 mg/kg), respectively [6, 7]. The fifth group received the investigational pyrimidine derivative PIR-9 (50 mg/kg) [8]. The second and subsequent groups modeled focal cerebral ischemia, by occlusion of the left middle cerebral artery (under chloral hydrate anesthesia, 350 mg/kg) [9, 10]. All objects were injected intraperitoneally immediately after the surgery and then once daily for three days. The concentration of tumor necrosis factor (TNF α) and apoptosis-inducing factor (AIF) was determined by enzyme-linked immunosorbent assay in brain homogenate using a Tecan Infinite F50 microplate reader. All findings were processed by means of variation statistics methods using the STATISTICA 6.0 software. The normality of distribution was assessed by the Shapiro-Wilk test. In the case of a normal distribution of the data, a parametric t-test was applied. In the case of abnormal distribution of the data, the statistical processing was performed using the Mann-Whitney U-test. The difference was considered significant at the significance level of more than 95% ($p < 0,05$).

RESULTS AND DISCUSSION

The concentration of TNF α in falsely operated animals was $19,62 \pm 0,51$ pg/ml (Fig. 1), while in rats with focal cerebral ischemia not subjected to pharmacotherapy, this indicator reached $67,13 \pm 1,70$ pg/ml, which, in turn, exceeded the value of the FO group by 3,42 times ($p < 0,05$). In the group of rats that were injected with cavinton, the level of TNF α was significantly reduced by 45,11% ($p < 0,05$), compared with intraperitoneal administration of gliatilin, the identical value was 57,47% ($p < 0,05$) less in the negative control animals group. At the same time, statistically significant differences in this indicator between groups of rats treated with Cavinton and Gliatilin were noted. A tendency to a

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decrease in the concentration of tumor necrosis factor was also observed during the administration of the experimental compound PIR-9. The concentration of TNF α in the group of animals treated with PIR-9 was $24,19 \pm 1,22$ pg/ml, which is 63,97% ($p < 0,05$) and 34,36% ($p < 0,05$) was less values of rats not subject to therapy and treated with Cavinton, respectively.

In the group of FO rats, the AIF content was $4,08 \pm 0,24$ ng/ml. Occlusion of the left middle cerebral artery contributed to an increase in AIF concentration by 1,98 times ($p < 0,05$) (Fig. 2) in comparison with sham-operated animals and, as a result, activated AIF-mediated cell death [3]. Intraperitoneal administration of the comparing drugs Cavinton and Gliatilin led to a decrease in the concentration of the factor inducing apoptosis in relatively untreated animals by 35,19% ($p < 0,05$) and 38,41% ($p < 0,05$). A similar change was noted with the introduction of the experimental substance, for example, in individuals that were injected with compound PIR-9, the AIF concentration was 29,99% ($p < 0,05$) less relative to the group of untreated animals.

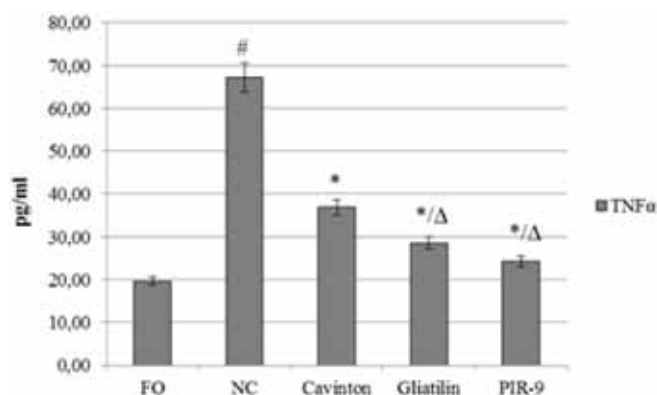


Fig. 1. Assessment of the effect of PIR-9 compound and the reference drugs on the concentration of tumor necrosis factor under conditions of focal cerebral ischemia in rats

Note: FO — false-operated rats; NC — negative control rats; Cavinton — a group rats treated with Cavinton; Gliatilin — a group of rats receiving Gliatilin; PIR-9 — a group of rats treated with PIR-9; # — statistically significant as compared to the FO rats ($p < 0,05$); * — statistically significant as compared to the NC rats ($p < 0,05$); Δ — statistically significant as compared to rats treated with Cavinton ($p < 0,05$).

CONCLUSION

In the experimentally simulated cerebrovascular insufficiency, a pyrimidine derivative (known under laboratory code PIR-9) reduced the concentration of apoptosis markers (TNF α and AIF) in animals, it is also essential that the effect was not inferior in its power to the comparison drug Gliatilin and superior to Cavinton.

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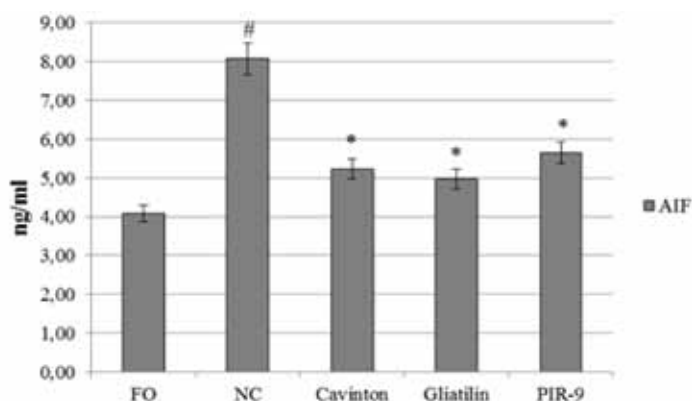


Fig. 2. Assessment of the effect of PIR-9 compound and the reference drugs on the concentration of apoptosis-inducing factor under conditions of focal cerebral ischemia in rats

Note: FO — false-operated rats; NC — negative control rats; Cavinton — a group rats treated with Cavinton; Gliatilin — a group of rats receiving Gliatilin; PIR-9 — a group of rats treated with PIR-9; # — statistically significant as compared to the FO rats ($p < 0,05$); * — statistically significant as compared to the NC rats ($p < 0,05$).

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INFEKTIONSKONTROLLE MITTELS GC-IMS UND EINSATZ VON WUNDPUDER (KLINOPTILOLITH) BEI CHRONISCHEN INFIZIERTEN WUNDEN

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ABSTRACT — In a clinical setting a standardized regime was used on 33 patients with chronic or acute wounds to detect and treat a wound infection. A GC-IMS was used as a new method for Infection Diagnostics. Wound size, germ colonization and clinical staging were documented on three examination dates in a distance from one week. For treatment of the wounds a novel wound powder Toxaprevent skin® ("Klinoptilolith") was used. Systematic trends were noticeable compared to the initial findings, so that an antimicrobial effect of the treatment can be assumed.

Due to the variability of germ infestation and the small number of patients assigned, a statistically significant statement is not to be made.

The results of microbiological studies using a classic wound smear and the MCC-IMS technique show that the latter has a distinct advantage over traditional microbiology. This methodology allows for immediate germ assignment and can be repeated as often as necessary. An advantage of germ identification using IMS may be that the method only responds to clinically relevant germ growth, while traditional studies from the smear can also be positive for randomly present ambient germs. The possibility of immediate germ assignment makes promptly specific therapy possible.

A prerequisite for a clinical application would be validation on large groups in order to define the germ-specific fingerprints even in the case of mixed infections.

Based on the study results so far, it can be concluded that the Toxaprevent Skin powder® has a positive therapeutic effect on wound healing, has good local tolerability and has a low side effect profile.

In order to find out further therapeutic effects principles of the Toxaprevent skin Powder®, further clinical application studies under outpatient conditions would be recommended, with the need to review local and systemic examination parameters (e.g. local Wound assessment, germ spectrum, systemic inflammatory parameters, immunology, oxygen partial pressure, proteins, muscle enzymes).

EINFÜHRUNG

Es ist bekannt, dass es in Deutschland ca. 2,7 Millionen Wundpatienten gibt, von denen ca. 800.000 an chronischen Wunden leiden. Die Patienten leiden oft an starken Schmerzen, ziehen sich aus dem öffentlichen Leben zurück und müssen oft längere Zeit behan-

delt werden. Weiter sind viele dieser Patienten multimorbide und leiden an chronischen Erkrankungen wie Niereninsuffizienz, Herzinsuffizienz, allgemeinen Durchblutungsstörungen und sind nur unzureichend mobil. Da diese Erkrankungen ursächlich chronische Wunden und Wundheilungsstörungen bedingen, sollte auch der Wundbehandlung eine größere Bedeutung beigemessen werden [7].

Aus den Leitlinien der Wundbehandlung ist abzuleiten, dass die Behandlung der chronischen Wunden sehr uneinheitlich erfolgt, so dass Aussagen über Kontinuität des Heilungsverlaufes nur bedingt getroffen werden können [3]. Deshalb sind weitere klinische Untersuchungen bzw. Studien wünschenswert. Ein weiteres Problem der Wundbehandlung besteht darin, dass die betroffenen Patienten bei stationären Aufenthalten entsprechend der Aufnahmediagnose oder ihrer Grunderkrankung behandelt werden und gemäß DRG meist nach wenigen Tagen wieder in das häusliche Milieu entlassen werden, ggf. auch in Pflegeeinrichtungen. Die Wundbehandlung wird stationär zwar fortgeführt, aber bei kurzem Aufenthalt ist der Wundheilungsprozess weder in der Effektivität noch im Erfolg beurteilbar [1; 2].

Ein großes Problem ist die Besiedelung chronischer Wunden mit nicht selten resistenten Keimen.

Die vorgestellte Studie sollte in einem klinischen Setting diesen Fragen nachgehen:

Es ist aus der Literatur und eigenen Voruntersuchungen bekannt, dass in der Ausatemluft, Geruch von Kot, Headspace über Bakterienkulturen, spezifische volatile Krankheitsmarker (VOC) und Metaboliten von Medikamenten und Stoffwechselprozessen gefunden werden [6; 8]. Es handelt sich dabei um kurz- und mittel langkettige Kohlenwasserstoffe bis hin zu Hormonen und körpereigenen Mediatorstoffen.

Dieselben oder ähnliche Biomarker wurden auch in der Headspace von Gewebeproben, Körpermaterial, Urin, Sekreten, Kot oder auch Kulturen von Bakterien gefunden bzw. werden vermutet [5].

Es ist weiter bekannt, dass Klinoptilolith die Heilung von infizierten Wunden und Verbrennungsverletzungen beschleunigen können und auch einen

positiven Einfluss bzw. hemmende Wirkung auf mögliche Superinfektionen haben [4].

Das Grundprinzip von diesen Klinoptilolithen besteht in der Aufnahme und Speicherung von Wundsekret und einer damit verbundenen Entgiftung der Wunde, Abbindung von Entzündungsstoffen.

Speziell bei Bakterienkulturen bzw. Wachstum von Bakterien gibt es sichere Hinweise auf spezifische Marker von Bakterienwuchs. In einer Studie der BecherConsult konnte bereits gezeigt werden, dass langsam wachsende atypische Mykobakterien in der Headspace von Kulturen, aber auch im Kot und der Ausatemluft identifiziert werden können.

Weitere Voruntersuchungen konnten zeigen, dass mit der verwendeten IMS-Technologie auch volatile Marker von MRSA, MSSA, E. Coli, Pseudomonas aeruginosa aus der Headspace von Kulturen nachweisbar sind [6; 8].

Bisherige aus der Literatur bekannte Untersuchungen basieren zumeist auf Methoden der Gaschromatographie, Massenspektrometrie. Diese Verfahren sind nicht für eine Anwendung als Point of Care Analyse adaptierbar, da die Geräte bezüglich technischen Aufwands und Bedienung nur im analytischen Labor sinnvoll betrieben werden können. Die Kosten-Nutzen Abschätzung dieser Methoden lässt keine Routineanwendung erwarten.

Mit der Verfügbarkeit von kleinen und im Verhältnis preiswerten Ionenbeweglichkeitsspektrometern besteht die Chance, solche Geräte vor Ort für eine Atemanalyse/Gasanalyse einzusetzen und somit die Keimdiagnostik sowie Verlaufskontrollen zu beschleunigen und sofort verfügbar zu machen. Die kombinierte Anwendung von etabliertem Wundmanagement, innovativer Diagnostik und Therapie war Gegenstand der Studie.

Eine gleichartig angelegte Studie ist aus der Literatur nicht bekannt.

METHODEN

Die in der Studie verwendeten Methoden:

1. Kriterien der Wundbeurteilung
2. IMS-Technologie
3. Froximun® Wundpuder
4. Klinische Wundpflege

Zu 1. Kriterien der Wundbeurteilung

In der Literatur werden einheitlich sowohl in den Reviews als auch Leitlinien Angaben zur Art der Wunde, Wunddauer und Wundlokalisierung empfohlen. Angaben zur Wunddauer sind relativ einfach in valider und reliabler Form als Zeitangaben zu erheben.

Zur Lokalisation der Wunde existieren standardisierte anatomische Begrifflichkeiten. Häufig werden

jedoch auch mit Hilfe von vorgegebenen Skizzen von Körperrumrissen entsprechende Markierungen zur Wundlokalisierung angebracht. Ebenfalls kann per Foto die Wundlokalisierung dokumentiert werden.

Dimensionen der Wundgröße

Die Wundgröße kann durch die Parameter Form, Länge, Breite, Umfang, Tiefe, Volumen, Fläche und Unterminierung/Tunnel beschrieben werden. Prinzipiell lassen sich diese Kriterien nur schwer voneinander trennen, da sie häufig mit den gleichen Verfahren erhoben werden und sich zum Teil auf Basis von Teilkriterien berechnen lassen (z.B. Fläche).

In der Studie wurde zu jedem Termin eine Fotodokumentation der Wunde erstellt. Die Wundfläche wurde dann bei gleicher Auflösung vergleichend zwischen den Terminen berechnet.

Exsudat, Geruch, Wundränder, Wundumgebung, Mazeration

Die typischen Bewertungen der Wunden wurden in einem Score tabellarisch erfasst.

Schmerzen

Ein Schmerzscores von 1–10 wurde bei jeder Visite vom Patienten angegeben.

Infektion

Für Nachweis bzw. Ausschluss einer Wundinfektion wurde bei Einschluss ein Wundabstrich für die bakteriologische Untersuchung durchgeführt.

Zu 2. IMS-Technologie (MCC-IMS)

Der kulturelle Nachweis eines bakteriellen Befalls ist nach wie vor die einzig beweisende Methode zur Infektionsdiagnostik. Andere Verfahren, wie PCR, können bei schon abgestorbenen Keimen oder nur geringem klinisch nicht relevanten Befall falsch positiv anzeigen und bedürfen oft der kulturellen Bestätigung.

Die traditionellen Methoden der Infektionsdiagnostik, Bakterienkultur oder PCR, sind langwierig oder teuer. Zum anderen ist gerade die PCR nicht beweisend für eine floride Infektion und bedarf vielfach der kulturellen Bestätigung. Diese Methoden stehen und fallen mit der Beschaffung einer relevanten, die gesuchten Keime enthaltenden, Probe.

Deshalb wird nach neuen, preiswerten und schnellen Verfahren zur Infektionsdiagnostik gesucht. Die Ionenbeweglichkeitsspektrometrie (IMS), die kombiniert werden kann mit unterschiedlichen Detektoren oder Vorsäulen zur chromatographischen Trennung, ist eine preiswerte und gleich empfindliche Methode. Es könnten sich hier also neue Möglichkeiten einer Infektionsdiagnostik ergeben.

Es ist aus der Literatur und eigenen Voruntersuchungen bekannt, dass in der Ausatemluft, Geruch

von Kot, Headspace über Bakterienkulturen, spezifische volatile Krankheitsmarker und Metaboliten von Medikamenten und Stoffwechselprozessen gefunden werden (VOC). Es handelt sich dabei um kurz- und mittel langkettige Kohlenwasserstoffe bis hin zu Hormonen und körpereigenen Mediatorstoffen.

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Weitere Untersuchungen konnten zeigen, dass mit der verwendeten IMS-Technologie auch volatile Marker von MRSA, MSSA, E. Coli, Pseudomonas aeruginosa aus Headspace von Kulturen nachweisbar sind.

Bisherige Untersuchungen in der Literatur dazu basieren zumeist auf Methoden der Gaschromatographie, Massenspektrometrie. Diese Verfahren sind nicht für eine Anwendung als Point of Care Analyse adaptiert, da die Geräte bezüglich technischen Aufwands und Bedienung nur im analytischen Labor sinnvoll betrieben werden können. Die Kosten-Nutzen Abschätzung dieser Methode lässt auch in der Zukunft keine Routineanwendung erwarten.

Bei vorliegender klinischer Studie wurden bei den Patienten im Rahmen der üblichen Untersuchung beim Verbandswechsel eine Absaugung einer Luftprobe aus dem Headspace über der Hautläsion/dem Ulcus oder der frischen OP-Narbe vorgenommen. Dazu wurde ein Einweg-Absaugschlauch darüber bzw. unter dem gelüfteten Verband positioniert und nach 1-2 Minuten Äquilibrierzeit die Probe genommen. Die Probe wird ohne eine weitere Probenaufbereitung mit dem IMS- Gerät vor Ort analysiert.

Zu 3. Froximun®Toxaprevent® Skin Hautpuder

Froximun®Toxaprevent® Skin Hautpuder bindet auf rein selektiv physikalischem Wege, durch Ionenaustausch toxische Stoffe, die der Dermis zugeführt werden (z.B. bei Insektenstich) bzw. die sich bei Verletzungen an der verletzten Dermis bilden (z.B. Histamin). Der Hautpuder hat nur einen sehr geringen Invasivitätsgrad. Es beschleunigt die Blutstillung an der verletzten Haut, lindert das Schmerzempfinden, legt sich wie ein Schutzschild auf die Wunde und bindet Exsudate. Es verhindert damit, neben der Bindung von Giftstoffen, Schwermetallen und Exsudaten, das weitere Eindringen von Mikroorganismen. Durch die Aufnahme von überschüssigem Histamin direkt an bzw. auf der Wundoberfläche kommt es zur Linderung von Entzündungen und zur Beschleunigung der Wundheilung. Bakterien die für ihren Stoffwechsel biogene Amine benötigen, werden somit eingedämmt und an einer unkontrollierten Ausbreitung gehindert.

Die Anwendungsindikationen sind: Schürf- und Schnittwunden, wunde Hautstellen, wunde Babypos, offene Beine oder Dekubitus, frische Brandwunden, blutende Verletzungen, Herpeserkrankungen, wie Herpes simplex und Herpes zoster sowie Akne und Hautunreinheiten.

Zu 4. Durchführung /klinische Methoden

Die Studie erfolgte mit einem Votum der Ethikkommission der Ärztekammer Sachsen in Dresden/Germany. In der klinischen Anwendungsstudie wurden insgesamt 33 Patienten mit chronischen und akuten Wunden einbezogen. Für alle eingeschlossenen Patienten liegt eine Einverständniserklärung vor.

28 Patienten erhielten neben der standardisierten Wundbehandlung zusätzlich täglich Froximun® Toxaprevent® Skin Hautpuder.

Der Studienablauf laut Prüfplan umfasste drei Untersuchungen im Abstand von etwa 1 Woche.

Die standardisierte Wundbehandlung beinhaltete:

- täglicher Verbandswechsel
- Wundspülung (Kochsalz, Octisept)
- Saugkompressen
- Intra Site Gel
- Jelonet
- Druckentlastung

Bei 5 Patienten mit kleinen Schürfwunden erfolgte die lokale Behandlung nur mit dem Hautpuder Toxaprevent Skin®. Die Untersuchungen erfolgten nach festgelegten Studienprotokoll.

Folgende Parameter wurden ausgewertet:

Wundbeurteilung

- Lokalisation der Wunde
- Bestehende Risikofaktoren an Hand von Grundkrankheiten (Diabetes mellitus, Chronische Niereninsuffizienz, Chron. Herzinsuffizienz)
- Infiziert (bei allen Wunden wurde ein Wundabstrich zur bakteriologischen Untersuchung vorgenommen)

- chronisch/akut
- Schmerzen (Schmerzskala 1–10)

Wundbeschreibung

- Rötung
- Teilverlust oder Verlust der Haut
- Verlust von Haut und Gewebe
- vermutete tiefe Wunde
- tiefe nicht einschätzbare Wunde

Wundverlauf im Beobachtungszeitraum

- positiv + 1
- negativ – 0

— keine Änderung 0,5

Zeichen der Wundinfektion

- Rötung
- Schwellung
- Schmerzen
- Exsudation

Verträglichkeit -Toxaprevent

Skin

- Brennen
- Juckreiz
- unangenehm
- gut verträglich

Eindruck Wundschwester

(subjektiv)

- positiv
- negativ
- indifferent

Wundgeruch (MCC-IMS)

Wundabstrich (Mikrobiologie)

Wundfläche (Berechnung der Wundfläche an Hand der Fotodokumentation mittels „ImageJ-Software“)

ERGEBNISSE

In die Studie konnten 33 Patienten beiderlei Geschlechts eingeschlossen werden.

Um systematische Fehler bezüglich des Auftretens von Krankenhauskeimen, Verschleppen von Keimen, saisonale Effekte oder subjektive Effekte durch das Personal wurde die Rekrutierung über einen Zeitraum von 10 Monaten durchgeführt.

In Tabelle 1 sind die Patienten mit der Charakterisierung der Wunde und den Begleitdiagnosen aufgeführt.

Die Mehrheit der Wunden war im Bereich der unteren Extremitäten lokalisiert, gefolgt von Gesäß und Rückenbereich und generalisiertem Hautbereich. 21 von 33 Wunden wurden als klinisch infektiös eingeordnet.

Bei den 33 Patienten waren 17 Diabetiker (Diabetes mellitus Typ II), 22 medikamentös eingestellte Hypertoniker und 15 Patienten mit

Tab. 1. Patienten

Lfd Nr.	Geschl	Diagnose	Nebendiagn	Inf ?
1	m	Großzäh Phlegmone	Dm, Hyperton	n
2	w	Gesäß-Gangrän	Dm Hyp	j
3	m	Gangrän re Unterchenkel	Dm, Hyp	j
4	m	Gangrän li Ferse	Dm, Hyp, cNI,	j
5	w	Humerusfraktur re	keine	n
6	w	Carotis-OP li	Hyp	n
7	w	Dekubitus Trochanter re	keine	j
8	m	Gangrän Rektum	Dm, Hyp	j
9	m	Allergie Bläschen am ganzen Körper	Dm, cNI	n
10	m	Fersenulcus bds	Dm	j
11	w	Femurfraktur li.,	Dm, Hyp, cNI	n
12	m	Schürfwunde re US	Hyp, Chron N,	n
13	m	Gangrän li Fuß, Zehamput	Dm, resp.Infekt	j
14	w	Ulcus cruris, Erysipel,	Dm, Hyp, cNI,	n
15	m	Gangrän re Fuß, Zehamput	Dm, Hyp,	j
16	m	Dekubitus re Gesäß	Dm, Hyp, cNI	j
17	m	Fußphlegmone re,	Dm, Hyp, cNI	j
18	w	Stauungsdermatitis	Dm, Chr N,	n
19	m	SHF re, Ulcus Knöchel	Dm, Hyp, cNI	j
20	m	Erysipel linker US,	Dm, Hyp,	j
21	w	Dekubitus Rücken,	Dm, Hyp, cNI	j
22	m	Fußphlegmone li.	Hyp, cNI	j
23	w	Dekubitus sakral,	Hyp, cNI	j
24	m	OP-Wunde, OS re.	keine	j
25	w	OP-Wunde sakral,	chron H,	n
26	w	OP-Wunde li OS	Hyp, cNI	n
27	m	OP-Wunde abdominal	keine	j
28	m	OP-Wunde Abdomen,	keine	n
29	w	Femurfraktur re	Hyp	j
30	w	Dekubitus	Hyp, cNI	j
31	w	Decubitus	keine	n
32	w	Erysipel, Ulcera am Gesäß	Hyp	j
33	w	Ulcus cruris li.	Dm, Hyp	j

Abkürzungen: Dm: Diabetes mellitus, Hyp.: Hypertonie; chron. N = cNI: chronische Niereninsuffizienz n: nicht infiziert; j: infiziert; Schmerz: Skala von 1 – 10

einer chronischen Nierenerkrankung auffällig. Die subjektiven Schmerzangaben schwankten zwischen 2 und 8 (Schmerzskala 1–10), der Durchschnittswert lag bei 5,2, wobei die Hälfte der Wunden als „chronisch“ eingeordnet wurden.

Tab. 2. Zusammenfassung der Wundbeschreibung

Hautdefekt	33
Verlust an Haut	31
Verlust an Gewebe	27
Tiefe Wunde	13,5
Tiefe Wunde/nicht einsehbar	11

Der Wundverlauf wurde subjektiv durch die Wundschwester beurteilt. Es war allerdings bei den teilweise relativ großen Wunden in einer ca. 14-tägigen Verlaufskontrolle kaum mit signifikant relevanten

Veränderungen zu rechnen. Aus diesem Grunde ist es jedoch bemerkenswert, dass der Wundverlauf 17x positiv beurteilt wurde und lediglich 4x nur negativ.

Bei der Beurteilung der Wundinfektionszeichen wurden seitens der Wundschwester folgende Angaben gemacht:

Tab. 3. Zusammenfassende Beurteilung durch die Wundschwester

Rötung	30
Schwellung	27
Schmerz (bei Wundmanipulation, z.B. Verbinden, Spülen)	24
Exsudat (eitrig)	6

Verträglichkeit von Toxaprevent – Skin Hautpuder®

Die Wirkungsweise des Toxaprevent-Skin Hautpuders liegt in der Blutstillung an der verletzten Haut, Linderung des Schmerzempfindens und Exsudatbindung. Bei der lokalen Aufbringung auf die Wunden wurden folgende Verträglichkeiten /bzw. Unverträglichkeiten abgefragt:

Tab. 4. Verträglichkeit/Nebenwirkungen von Toxaprevent –Skin® Hautpuder

Brennen	7
Juckreiz	0
allgemein unangenehm	3
gut verträglich	24

Die Beurteilung des Patienten 29–33, die ausschließlich mit Toxaprevent-Skin Hautpuder behandelt wurden, zeigte, dass die Verträglichkeit sich im Vergleich zu den anderen Patienten nicht unterschied. Auch der Anteil von „Brennen“ war nicht höher. Der Eindruck der Wundschwester war 4x positiv und 1x indifferent. Statistisch relevante Aussagen wären in einer weiteren ambulanten Studie sicherlich zu erheben.

Die Beurteilung der Wundschwester hinsichtlich des Eindruckes des Toxaprevent-Skin Hautpuders bei der Wundbehandlung ist von besonderer Bedeutung, da täglich Wundvisiten durchgeführt wurden. Dadurch konnte die Gesamtbeurteilung des Wundverlaufes und deren Einflussfaktoren objektiviert werden.

Tab. 5. Gesamtbeurteilung durch die Wundschwester

Positiv	21 x
Indifferent	11 x
Negativ	0 x (1x keine Bewertung)

2 ERGEBNISSE IMS

Für die Auffindung spezifischer Unterschiede im VOC Spektrum der Luft über der Wunde wurden zunächst alle Patienten ohne Nachweis einer Wundinfektion zusammengefasst (Gruppe 2) und alle Patienten mit einer Wundinfektion unabhängig vom gefundenen Keim (Gruppe 1) und gegeneinander getestet. Dabei wurden 225 verschiedene Cluster von VOCs unterschieden, die Unterschiede zwischen Gruppe 1 und 2 waren im T-Test bei 22 Clustern signifikant ($p < 0,05$).

In Tabelle 6 wurden die beiden Gruppen nach den ersten 5 Clustermerkmalen verglichen, ob zur Gruppe 1 oder Gruppe 2 zugehörig. Basis war dazu der bakterielle Befund einer Wundinfektion.

ERGEBNISSE KEIMBEFALL

Es zeigte sich, dass die kulturellen Keimnachweise vom Wundsabstrich bis zu 5 verschiedene Keime innerhalb der Studientermine erbrachten. Das steht in einem Mißverhältnis zu der Trennung der Wundinfektionen an Hand der IMS-Messungen und der damit erstellten Einordnung von Wunden ohne und mit nachgewiesenem kulturellem Keimnachweis (siehe Tabelle 6). Dort wurde bei 12 Patienten die Zuordnung nicht sicher erbracht. Bei diesen Fehlzuordnungen war 6-mal *Staphylococcus aureus* (unspezifisch) beteiligt, zweimal *Candida*.

Die Frage bleibt, ob die in der Kultur vom Wundabstrich gefundenen Keime relevant für die Wundinfektion, oder nur ubiquitär vorkommende Keime der normalen Hautbesiedelung sind. Dieser Verdacht wurde in einigen Befunden aus dem bakteriologischen Labor gestellt. Weiter konnte bei der letztlich noch geringen Fallzahl nicht sicher geklärt werden, ob bei Zusammenfassen aller Patienten ohne bakteriologisch nachgewiesener Wundinfektion tatsächlich im Einzelfall immer generelle Unterschiede im VOC-Spektrum bestehen, die Infektion von Non-Infektion unterscheiden.

Es muss auch beachtet werden, dass die Umgebungsluft bei allen Messungen mit beteiligt war. Um das weiter aufzuklären, wurden danach einzelne Keime gegen die andere getestet (ab Tabelle 9)

AUSWERTUNG DER MESSUNGEN DES WUNDGERUCHES MITTELS GC-IMS

Zu jedem Zeitpunkt des Verbandwechsels und der fachgerechten Versorgung der Wunde wurde mittels eines unter den Verband geschobenen Ansaugschlauches (Heidelberger Verlängerung, mittels Luer-Lock am Gerät-Probeneingang angeschlossen, eine Luftprobe über der Wunde abgesaugt und gemessen.

Die Auswertung erfolgte für eine Retentionszeit von bis zu 150 sec mit einer eingestellten Clustergrösse

Tab. 6. Zuordnung der Patienten nach IMS-Befund zum parallel gegebenen bakteriologischen Befund (1 – Infektion pos.; 2: Keine bakteriologisch nachgewiesene Wundinfektion) Database Ergebnisse: Clustergrösse 5–5; sign-Level 0,05 (Rauschverhalten)

Patient	m/w	1 = Inf = ohne Inf	2 T1	T2	T3	Befund It- Abstrich Infiziert	
St.-Nr.							
1	m	2		2	2	2	
2	w	1		2	2	1	
3	m	1				1	
4	m	2				1	falsch neg
5	w	2		2		2	
6	w	2				2	
7	w	1		2		1	
8	m	2		2	2	1	falsch neg
9	m	2		2	2	2	
10	m	2		2	1	1	falsch neg
11	w	2		2	1	2	
12	m	2		2	2	2	
13	m	2		2	2	1	falsch neg
14	w	2		2	2	2	
15	m	1		2	1	1	
16	m	2		1	2	1	
17	m	2		2	2	1	falsch neg
18	w	2		2	2	2	
19	m	2		1	2	1	
20	m	2		2	2	1	
21	w	1		2	2	1	
22	m	2		2	2	1	falsch neg
23	w	2				1	falsch neg
24	m	1				1	
25	w	2				2	
26	w	1				2	
27	m	2				1	falsch neg
28	m	2				2	
29	w	2		2		1	falsch neg
30	w	2		2		1	falsch neg
31	w	2		2		2	
32	w	2		2		1	falsch neg
33	w	2		2		1	falsch neg

Tab. 7. Nachgewiesene Keime in den Wundabstrichen, korreliert zu den Studienterminen

Nachgewiesener Keimbefall in den Abstrichen

Patient	m/w	T1	T2	T3
Stud.-Nr.				
1	m	7 ++	neg	neg
2	w	18 +++, 21 +	18 ++	14 ++
3	m	1 +++		
4	m	7 +,		13 +++
5	w	ohne Bakteriennachweis		
6	w	ohne Bakteriennachweis		
7	w	19 ++		
8	m	11 MRSA +	12 ++, 11 (MRSA) +	MRGN neg, 8 +, 6 (+)
9	m	ohne Bakteriennachweis		
10	m	21 +++, 8 +	24 ++,	1 +++, 21 ++, 8 +
11	w	steril, Erys +++++		16 +++
12	m	steril		
13	m	7 +++, 20 ++	7 +++	7 ++, 20 ++
14	w	7 +,		steril
15	m	7 +++, 14 +++ vor Beginn	9 (+)	
16	m	11 (MRSA) +++++		7 ++
17	m	1 +++++, 6 +++++ R	6 +++++ R	1 +, 6 +++++ vorw S
18	w	ohne Bakteriennachweis		
19	m	6 +++ sens		
20	m	9 ++		17 +++
21	w	9 (+)	9 (+)	
22	m	1 +++++ 2++++ 3++ R	5 ++ R	4 (+) 5 (+-)
23	w	7 (+)		
24	m	7 +	nd	nd
25	w	ohne Bakteriennachweis	nd	nd
26	w	ohne Bakteriennachweis	nd	nd
27	m	8 ++ sens, Leukos +++	nd	nd
28	m	ohne Bakteriennachweis	nd	nd
29	w	22 ++, 1 ++	22 ++	nd
30	w	7 ++, 8 +++++	7 +++, 8 ++, 6 +++	nd
31	w	steril	steril	nd
32	w	1 +++, 21 +++	1 ++, 21 +	nd
33	w	16 +++++, 7 +++	7 +++	nd

von 5 zu 3 und Driftzeiteinstellung von 20 bis 100% der relativen Driftzeit. Im Retentionszeitbereich über 150 sec konnte man auf eine Analyse verzichten, da hier keine signifikanten Peaks auftraten.

Es wurde weiter entsprechend den anderweitig nachgewiesenen Keimbefall der Wunden eine Gruppierung der Messungen nach den Keimanalysen vorgenommen, Das war insofern schwierig, da bei einzelnen Probanden bis zu 5 verschiedene Keime kulturell nachgewiesen wurden.

Alle Keime mit mehr als 2 betroffenen Fällen wurden gruppiert und in der Auswertung gegeneinander und gegen die Patientengruppe ohne nachgewiesenen Keimbefall der Wunde getestet.

Da es nicht möglich ist, aus dem bakteriologischen Befund mit Anzüchtung von Keimen aus dem Abstrich den eigentlich federführenden Keim des Wundbefalls zu differenzieren, wurde versucht, ggf. Patientenproben mit nachgewiesener Mehrfachinfektion nacheinander mehreren Gruppen zuzuordnen,

Tab. 8. Legende zur Zuordnung der Keime in IMS-Differenzierung bzw. in Tab. 9

Keim	Subspec	Abstrich	Patient							
Enterococcus	Faecalis		22	17	3	10	29	32		
Pantoea agglomerans			22							
Leclercia Adecarboxyiata			22							
Stenotrophomonas	maltophilia		22							
Staphylococcus	pseudointermedius		22							
Pseudomonas aeruginosa			19	17	8	30				
Staphylococcus	aureus		23	8	15	14	13	4	30	33
Candida	albicans		27	8	10	30				
Staphylococcus	Kogulase neg.		21	(15)						
Korynebacterium	amycolatum		11							
MRSA			8	16						
Klebsiella	oxytoca		8							
Klebsiella	pneumoniae		4							
Streptococcus	agalactiae		15							
Proteus	vulgaris		14	10						
Corynebacterium	species		13	33						
Staphylococcus	epidermidis		13							
Escherischia Coli			2							
Enterobacter	cloaceae		7							
Serratia	marcescens		13							
Proteus	mirabilis		10	32						
Staphylococcus	simulans		20							
ohne Bakterienachweis im Abstrich			12	1	5	6	9	11	12	
ohne Bakterienachweis im Abstrich			18	25	26	28	31			
Streptococcus Group G			10							

Tab. 9. Zuordnung der Patienten zu den im Wundabstrich nachgewiesenen Keimen (mit Mehrfachnennungen)

Gruppe	Keim	Lfd. Nr. des Patienten
1	Sonstige pos. Keimnachweise	2, 7, 11,
2	Ohne Nachweis eines Befundes	1, 5, 6, 9, 11, 12, 18, 25, 26, 28, 31
3	MRSA	8, 16
4	Sonstige Staph. aureus	4, 8, 13, 14, 15, 22, 23, 30, 33
5	Pseudomonas aeruginosa	8, 17, 19, 30
6	Proteus	10, 32
7	Candida albicans	8, 10, 27
8	Enterococcus	3, 10, 17, 22, 29, 31

um ggf. durch gefundene höhere Trennschärfe den federführenden Keim zu identifizieren. Die Auswertung bleibt auf Grund der geringen Fallzahlen überwiegend deskriptiv.

Bei der Analyse wurden in einigen Fällen die Termin T1, T2 und T3 der Patienten zusammengefasst, um die für eine statistische Auswertung ausreichende Fallzahl zu erzeugen. Nachfolgend konnte gezeigt werden, dass es aber auch zwischen T1, T2 und T3 signifikante Änderungen bei einigen Patienten gab.

ERGEBNISSE DER IMS UNTERSUCHUNGEN AUF KEIMSPEZIFISCHE VOC

An den drei Beispielclustern konnte gezeigt werden, dass es möglich war, spezielle Cluster zu identifizieren, die ggf. geeignet sind, einen bestimmten Keim im Einzelfall sicher zu erkennen.

Bei mehreren „Leave one out“ Versuchen konnte im Einzelfall gezeigt werden, dass bei den o.g. Auswertungen auch einzelne herausgezogene Messungen

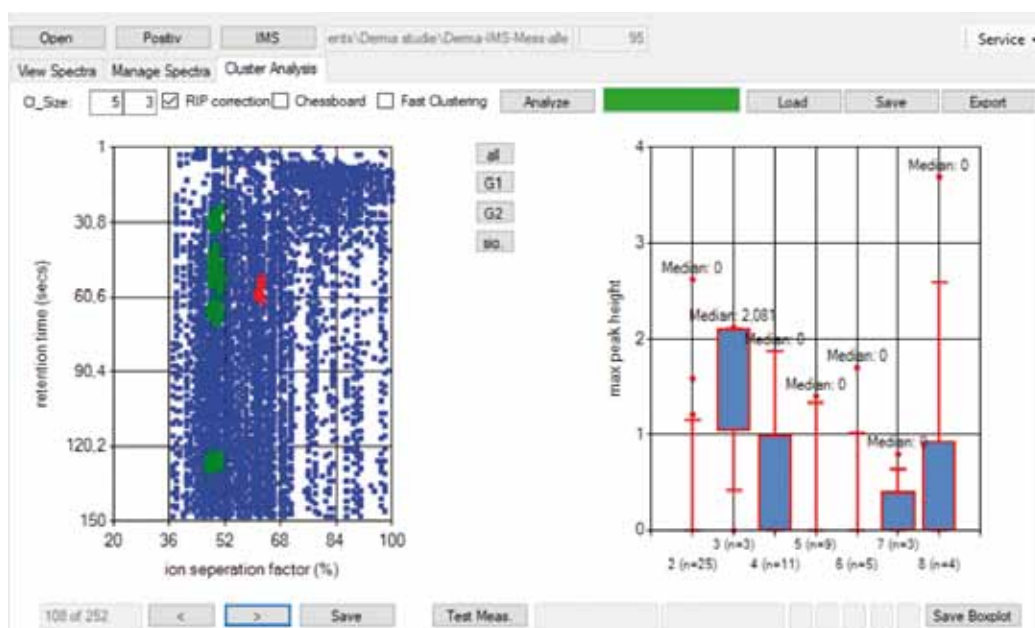


Abb. 1. Spektralanalyse 1

Cluster für MRSA-Verdacht

Linke Seite: Heatmap der identifizierten Peaks

Rechte Seite: Beispielcluster (rot in Heatmap) mit signifikantem Unterschied ($p < 0,05$) zwischen den Gruppen:

2: Patienten ohne Nachweis einer Infektion der Wunde

3: MRSA; 4: Staph aureus, n.n.b.; 5: Pseudomonas aeruginosa; 6: Proteus; 7: Candida; 8: Enterococcus

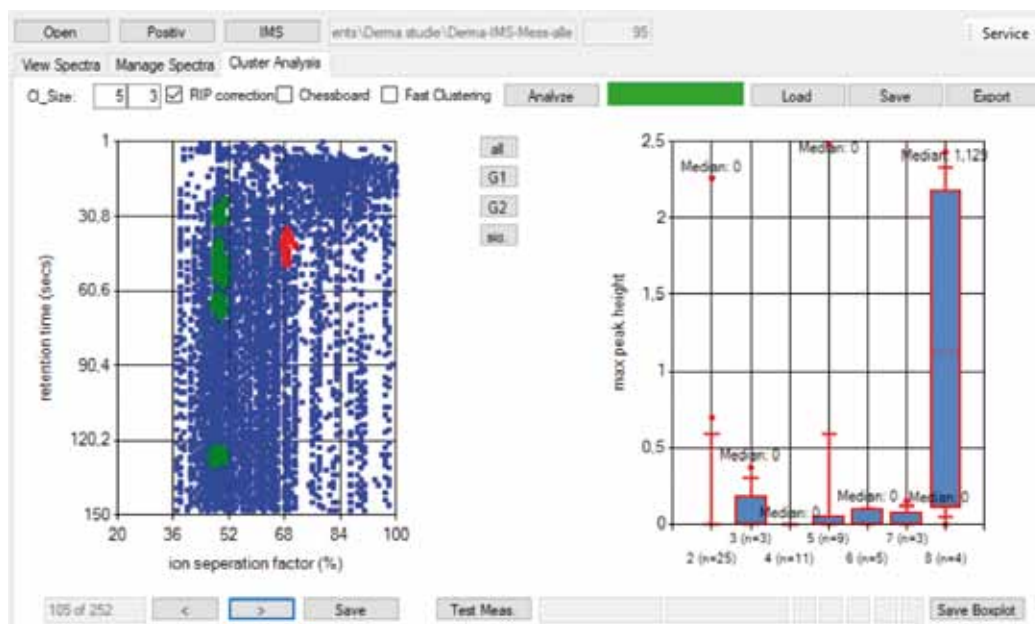


Abb. 2. Spektralanalyse 2

Cluster für Enterococcus Verdacht

Linke Seite: Heatmap der identifizierten Peaks

Rechte Seite: Beispielcluster (rot in Heatmap) mit signifikantem Unterschied ($p < 0,05$) zwischen den Gruppen:

2: Patienten ohne Nachweis einer Infektion der Wunde

3: MRSA; 4: Staph aureus, n.n.b.; 5: Pseudomonas aeruginosa; 6: Proteus; 7: Candida; 8: Enterococcus

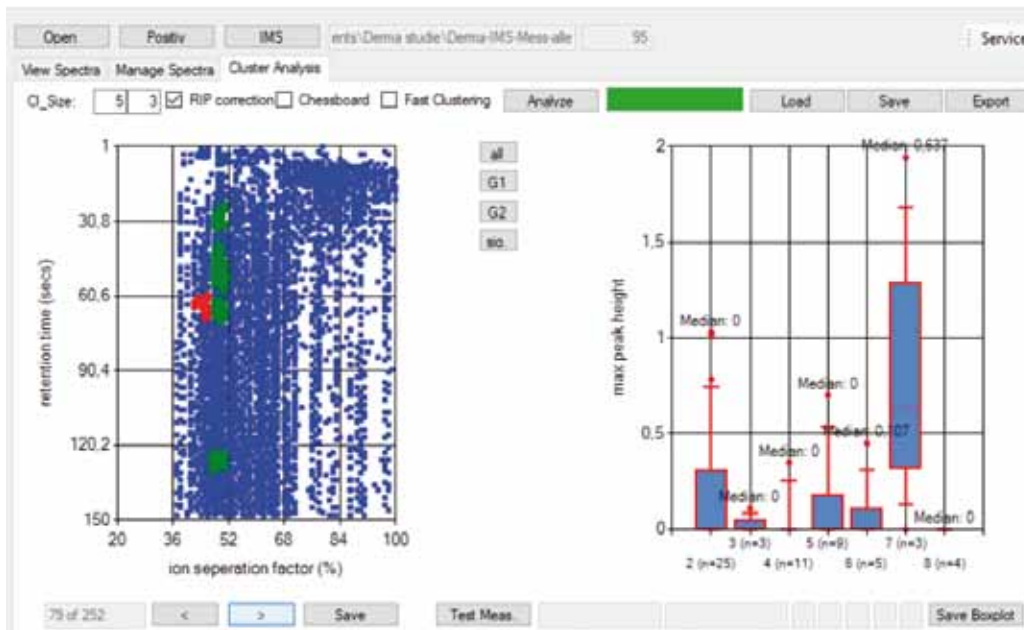


Abb. 3. Spektralanalyse 3 Cluster für *Candida* Verdacht
 Linke Seite: Heatmap der identifizierten Peaks
 Rechte Seite: Beispielcluster (rot in Heatmap) mit signifikantem Unterschied ($p < 0,05$) zwischen den Gruppen:
 2: Patienten ohne Nachweis einer Infektion der Wunde
 3: MRSA; 4: *Staph aureus*, n.n.b.; 5: *Pseudomonas aeruginosa*; 6: *Proteus*; 7: *Candida*; 8: *Enterococcus*

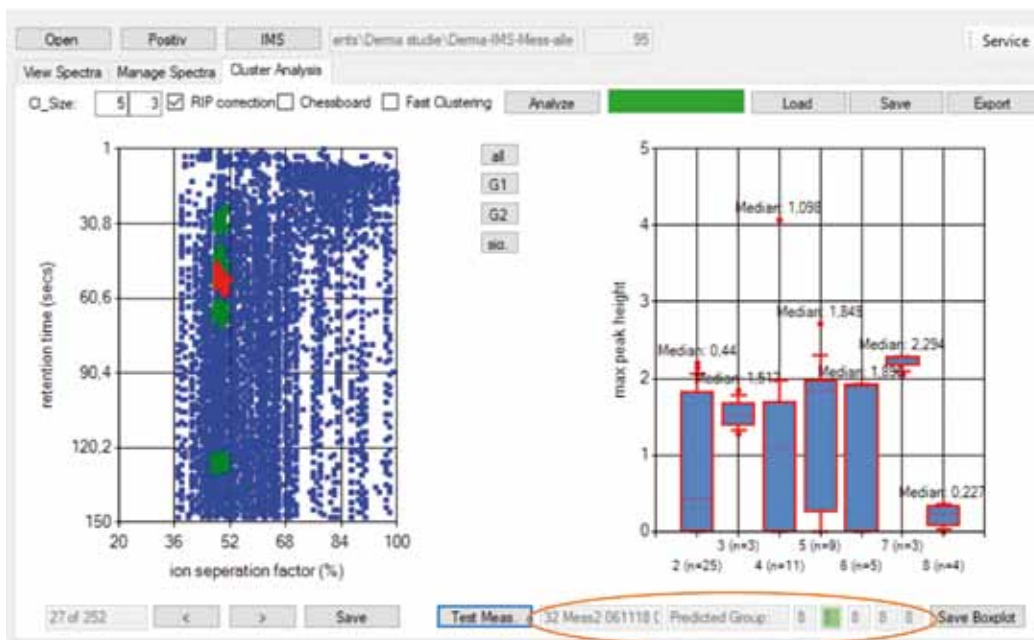


Abb. 4: Pat. 32 – richtige Zuordnung zu *Enterococcus* nach den ersten 5 signifikanten Clustern (rot bzw. grün markiert in der Heatmap).

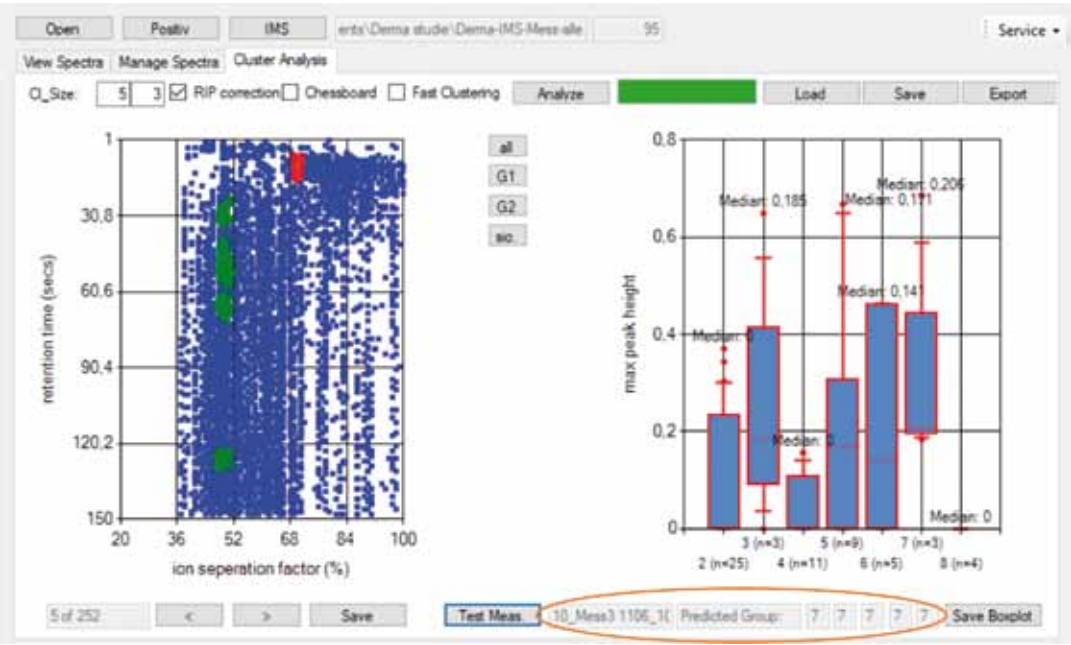


Abb. 5: Patient 10 richtige Zuordnung zu *Candida albicans* nach den ersten 5 signifikanten Clustern (rot bzw. grün markiert in der Heatmap).

wieder richtig in ihre Gruppe zu geordnet wurden (Kreuzvalidierung). Für diese Zuordnung wurden jeweils die ersten 5 signifikanten Cluster verwendet. Im Weiteren wurde versucht, die Analyse für die Differenzierung von jeweils zwei Gruppen zu verbessern. Dazu wurde auch der Verlauf zwischen T1 und T3 betrachtet (siehe Abb. 6):

Im Vergleich der Spektralanalyse zwischen Patienten ohne bakteriologischem Nachweis von Keimbefall im Verlauf (T1; T2; T3; respektive 21, 22, 23) mit Patienten mit nachgewiesenem MRSA (31; 32; 33) zeigten sich signifikante Unterschied in den Clustern (im Heatmap grün bzw. rot markiert)

Cluster 82 fehlt weitgehend bei den Kontrollen ohne Nachweis einer Infektion, während es bei MRSA auftritt, vermindert bei T2 und T3. Solche Cluster können einen Ansatz bieten, auch den Verlauf der Infektion während Therapie zu kontrollieren.

Im direkten Vergleich zwischen 2 Gruppen zeigt sich eine bessere Trennschärfe. Das gibt die Möglichkeit, mittels spezieller Anpassung der Auswertesoftware in einem Stufentest einzuführen, bei dem unbekannte Messungen gegen die vorhandene Grundgesamtheit der Messungen und bei Verdacht auf Infektion einzeln auf jeden bekannten Keim getestet werden.

Insgesamt sind diese Ergebnisse als vorläufig zu betrachten, da die Fallzahlen zu gering sind, um eine sichere statistische Aussage zu erlauben.

Im Trend zeigt es sich aber, dass die Methode bei entsprechender Erprobung bei größeren Fallzahlen in der Lage ist, eine sofortige Aussage zu einer möglichen Wundinfektion zu bekommen, insbesondere im Hinblick darauf, dass auch bei Anzüchtung aus dem Wundabstrich nicht immer die gefundenen Keime auf ihre tatsächliche Relevanz im Wundgebiet zu beurteilen sind.

Das sollte Gegenstand weiterer Studien oder eines Feldversuches sein.

2 WUNDFLÄCHE

Die Auswertung der Entwicklung der Wund-

Tab. 10. Darstellung der nach der Fotodokumentation geschätzten Wundfläche in Prozent der Fläche zum Termin 1 (sortiert nach Infektion — non-Infektion) Mittelwerte u d Standardabweichung

	m/w	Bemerkung	T1	T2	T3
MW	13/8	infiziert	100	104	93
MW	4/8	nicht infiziert	100	82	90
SD				71	27
SD				27	38

fläche erfolgte mittels elektronischer Vermessung der Wundfotos. Dabei wurden die Angaben in mm2 sowie in der prozentualen Änderung zum Erstbe-

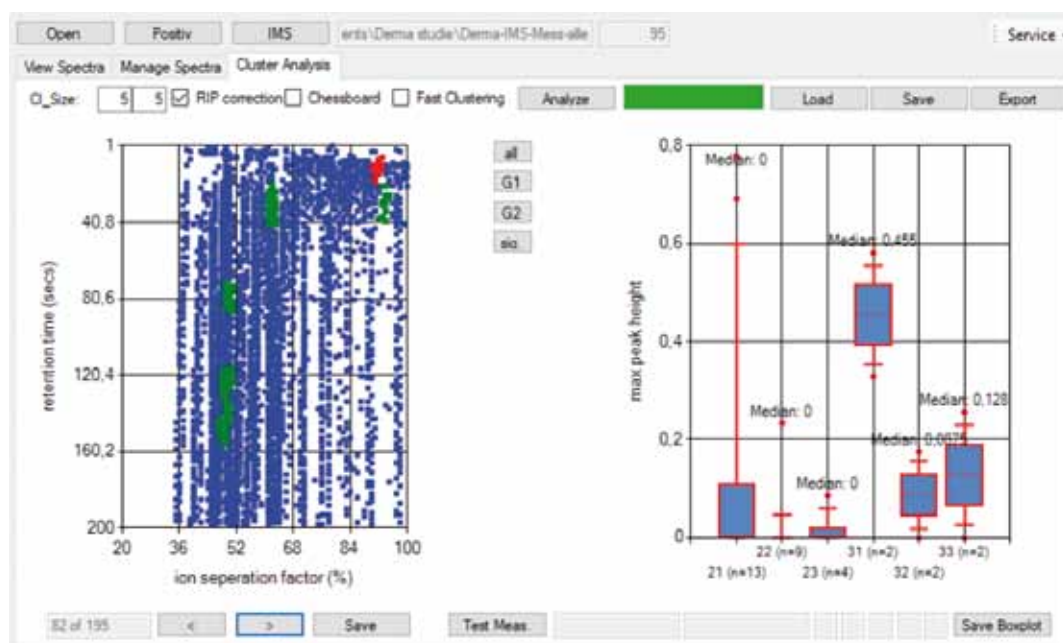


Abb. 6. Darstellung des Verlaufs von T1 über T2 nach T3 bei nichtinfizierten Patienten (21; 22; 23) bzw. bei MRSA (31, 32; 33) für ein Beispielcluster 82.

fund gemacht. Bei 11 Patienten gelang die Auswertung nicht, bei 11 Patienten war eine deutliche Verkleinerung der Wundfläche sichtbar, bei ebenfalls 11 Patienten eine Vergrößerung. Aufgrund der relativ kurzen Beobachtungszeit von maximal 14 Tagen sind diese Ergebnisse nur als orientierende Aussagen zu bewerten.

Eine Beurteilung der Wundheilung als Funktion der verbleibenden Wundfläche bedarf einer längerfristigen Beobachtung in einer Studie.

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AGONISTIC AUTOANTIBODIES, A RISK FACTOR IN PATIENTS WITH TYPE 2 DIABETES

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ABSTRACT — In addition to insulin intolerance, patients with type 2 diabetes suffer from hypertension, renal insufficiency, retinopathy, wound healing disorders, coronary heart disease, heart attacks, strokes, and amputations. In addition to metabolic syndrome, many patients have pathological changes in macro- and microcirculation. One of the causes might be agonistic autoantibodies (agAAB), an immunological component. This specialized group of autoantibodies activates the G protein-coupled receptors similar to the way natural agonists do and triggers receptor-specific reactions in the cell (1). The pathological potential of agAAB has been described in numerous publications. The pathological processes triggered by agAAB for the β -1-adrenoceptors (AR), AT1 AR, and α 1 AR (2,3,4,5) have been particularly well researched. Animal experiments provided valuable insights into the causality of receptor-specific autoantibodies for the development of diseases and disease-relevant symptoms. These autoantibodies can only be removed with specific antagonists at the receptor or by plasmapheresis or immunoadsorption. The agAAB do not respond to immunosuppression as classical autoantibodies do. Patients in whom agAAB was removed by extracorporeal treatment benefited from it. In patients with dilated cardiomyopathy, cardiac output improved (6,7); those with Alzheimer's disease (8) achieved stabilization of cognition. In subjects with Thromboangiitis obliterans (9), further amputations were able to be avoided after removal of the autoantibodies, and in patients with inadequate control of hypertension through pharmacological means, blood pressure was considerably reduced (10). In only a few cases did agAAB reappear. These positive treatment results for various diseases formed the basis for screening diabetics with respect to the prevalence of agonistic autoantibodies.

INTRODUCTION

There are currently 425 million people worldwide who have been diagnosed with type 2 diabetes. A further 179 million people already have this disease, but are not yet aware of it. The WHO assumes that by 2045, a total of 700 million people worldwide will be suffering from type 2 diabetes and associated health impairments. In Germany alone, the number of new cases is 442,000 people annually, or more than 1,000 people per day. Untreated, this disease has dramatic consequences. Macro- and microangiopathies have been diagnosed in patients, which lead to terminal organ damage if left untreated. Diabetics more

frequently suffer a heart attack or stroke. They suffer more often from congestive heart failure and dementia than non-diabetics. The risk of myocardial infarction in post-menopausal women is six times higher among diabetics than for non-diabetics (Table 1). The risk of developing dementia by diabetics is twice as high as for people without diabetes [11, 12, 13].

The number of amputations in Germany is 40,000 patients per year, 2000 patients go blind, and 30–40% of diabetics experience kidney damage. Some of them require dialysis. Nephropathy is promoted by poorly regulated glucose levels and by blood pressure levels above 120–130/70–80 mm Hg. The treatment costs for patients with type 2 diabetes are enormous. The pharmaceutical industry expects its sales of medications for diabetics will increase by 50% between 2016 and 2022. In order to counteract a further increase in cases of disease and the considerable associated costs, possible additional causes that influence the genesis of this disease must be sought. One possible additional risk factor might be agonistic autoantibodies that act against various G-protein-coupled receptors [14]. AgAAB against the β -1 AR, β -2 AR, endothelin receptor, angiotensin II type-1 receptor, and α -1 AR were detected in sera of 150 diabetics. It was found that within the first five years following diagnosis of diabetes type 2, 48% of the test subjects had at least one agonistic autoantibody, five years later the prevalence was 66%, and after more than 20 years the number increased to 68%. Agonistic autoantibodies against the α -1 receptor were dominant in all the patient groups studied. Their prevalence increased from 69.6% to 81.8% for both positively detected subjects.

Agonistic autoantibodies acting against α -1 AR have considerable pathological potential. Binding of agAAB to the α -1 AR leads to activation of the receptor, similar to the action of physiological agonists. The increase of intracellular Ca^{2+} transient means acute elevation of intracellular Ca^{2+} , hypertrophic remodeling due to this increased intracellular Ca^{2+} , phosphorylation of cardiac regulatory proteins and other phosphorylation of target proteins (i.e. the 15-kDa) protein phospholemman — a cardiac regulator of $\text{Na}^+/\text{Ca}^{2+}$ exchanger and Na^+/K^+ ATPase), activation of protein kinase C, and proliferation of vascular smooth muscle

Table 1.

	Infarct	CHD	Apoplexy	CHF	Atrial fibrillation	Cancer
Diabetics	9.0	15.8	6,4	6.9	8.8	10.5
Non-diabetics	4.3	7.9	3,9	3.3	5.6	9.9

cells. It also leads to hyperplasia, to triggering of various pathological mechanisms by activation of the receptor, causes a reduction of the vessel lumen in the vessels, and the increase in calcium transient decreases the calcium concentration in the mitochondria and endoplasmic reticulum [15, 16, 17, 18].

METHODS/MATERIAL

An ELISA test developed in-house was used for the detection of agonistic autoantibodies. Autoantibody analysis was performed using peptides corresponding to the first and/or second extracellular loops of the following GPCR: α -1 AR, endothelin A, angiotensin II type-1 AR, β -1 AR, β -2 AR and protease-activated receptor (PAR) 1/2. Peptides were coupled to pre-blocked streptavidin-coated 96-well plates (Perbio Science, Bonn, Germany). Patient serum was added in a 1:100 dilution and incubated for 60 min. A horseradish peroxidase conjugated anti-human IgG antibody was used as the detection antibody (Rockland Biomol GmbH, Hamburg, Germany). Antibody binding was detected by the 1-Step Ultra TMB ELISA (Perbio Science, Bonn, Germany). The absorbance was measured at 450 nm against 650 nm with a SLT Spectra multiplate reader (TECAN, Crailsheim, Germany)

OUTCOMES

3 patient groups of 50 subjects each were examined:

Group 1: diabetes duration 0–5 years, prevalence 48%

Group 2: diabetes duration 6–10 years, prevalence 66%

Group 3: subjects / cardiovascular complications prevalence 46% (heart attack/stroke/stents),

In Group 3, the largest group (n= 31) had a stent.

Of these patients, 14 had an agAAB against the α -1AR.

Of the 18 subjects with myocardial infarction, 8 had a positive result with respect to α -1 AR.

In subjects testing positive for agAABs, the distribution of the various agAABs is shown in Table 2.

It was notable that 66% of the test persons in Group 1 and 76% in Group 2 had systolic blood pressure values above 130 mm Hg several antihypertensive medication revenue. Diastolic blood pressure was over 80mm Hg in 72% of patients. These blood pressure levels promote the development of diabetic nephropathy. As kidney damage progresses, the structure of the filtering domains is increasingly destroyed, creating actual holes in the renal corpuscles [19, 20].

In an animal experiment with male Wistar rats (10–13 weeks of age; 280–350g) we were able to show the effect of agonistic agAAB on the kidneys of the animals. Two experimental cohorts 10 rats each were allocated at random. One cohort of animals (PEP) was immunized by subcutaneous injection of 300 μ g α -1-AR peptide coupled to BSA and emulsified in incomplete Freund's adjuvant at 0, 2 and 4 weeks. Then the injections were repeated monthly for 8 month. The respective control animals (C-PEP) were subcutaneously injected with BSA. Blood aliquots were taken from anesthetized animals by retro-orbital sampling. The obtained sera were analyzed for the presence of α -1AR antibodies by ELISA techniques. The rates we obtain from Charles River Laboratories, Sulzfeld, Germany.

In rats positive for agAAB against α -1 AR (Fig.1B), we were able to observe a change in kidney tissue after 8 months with immunohistochemistry with CD31 in contrast to the control animals (Fig.1A). The animals also developed holes in the glomerular filter without suffering from diabetes. As a result, ever larger quantities of protein are lost.

An animal experiment by a Chinese research group has shown that the holes in the kidney in diabetic rats are first formed by agAAB against the α 1-AR [21].

Table 2.

Receptor	α 1 AR	β -2 AR	β -1 AR	AT-1	ETA
Group 1	69.6%	56%	52%	39%	39%
Group 2	81.8 %	75.8%	63.6%	21%	42%
Group 3	60,8%	52,1%	43.5%	17%	17%

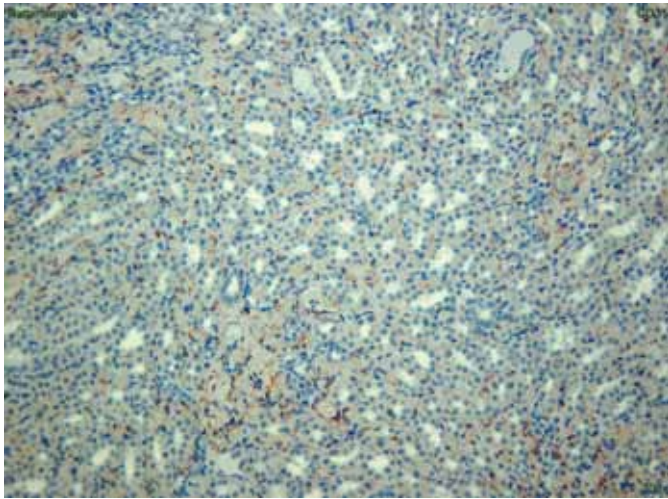


Fig. 1A. Control animal untreated 8 months old without diabetes

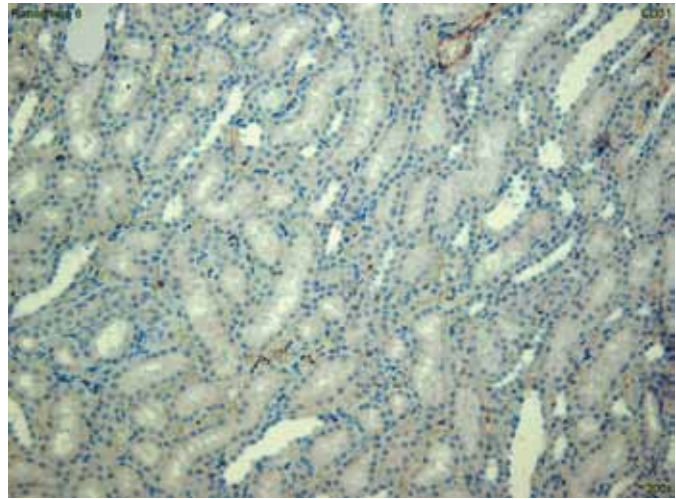


Fig. 1B. Changes after eight months in a 1-AR positive animal without diabetes

CONCLUSIONS

Agonistically acting autoantibodies represent an additional risk factor for patients with diabetes type 2 due to the pathological mechanisms triggered by them. The activation of the α -1 adrenergic receptor by agAAB activates calcium homeostasis. An increase of cytosolic Ca^{2+} represents a threatening development for the cell and leads to irreversible damage to it — up to and including cell death — if not buffered and eliminated. Free and protein-bound Ca^{2+} ions trigger intracellular signaling cascades, such as the activation of calcium-dependent cell death proteases (calpains), and thus act as secondary messengers for the cytotoxicity that occurs. This cell loss leads to, among other things, a change in the morphology of the renal cell tissue with the consequence of reduced filtration capacity in the kidney. The resulting renal insufficiency leads to compulsory dialysis in many patients.

Protein kinase C (PKC) requires cellular calcium for its correct functioning. Calcium activates hypertrophic remodeling, i.e. the vascular wall thickens inwards (18). Due to the long duration of the agAAB binding to the receptor, activations take place over a long period of time (7–21 days). As a result, normal cell state is not attained and therefore the pathological parameters are expanded. Protein kinase C plays a central role in signal transduction (10). Its activity is controlled by hormones and neurotransmitters whose signals are transmitted via secondary messengers. Calcium is required for the functioning of PKC. Calcium is released from the endoplasmic reticulum and/or from the mitochondria. ATP and proteins serve as substrates. Permanent receptor activation

leads to overload of the cell with calcium. PKC is important for the regulation of cellular growth. Malfunction can be involved in triggering cancer and in the development of late complications in diabetes. Short-term changes in the intracellular concentration of cytosolic calcium concentrations can be compensated for by control mechanisms. However, if there is a pronounced change in equilibrium or if transport processes are chronically disturbed (for example by the reduction of the Ca^{2+} -ATPase or by perturbed Na^{+} - Ca^{2+} exchange), the cell becomes overloaded with calcium ions and cytosolic calcium concentration increases chronically [14]. This leads to activation of messenger systems such as calmodulin and protein kinase C. These changes lead to chronic changes in the cell or even to cell death. The permanent activation of the signal cascades leads to pathological cell changes, as the cell no longer returns to its normal resting state. $\text{Na}^{+}/\text{K}^{+}$ ATPase [16] regulates the transport of Na^{+} from the cell and the transport of K^{+} into the cell. ATP is hydrolyzed to ADP. Dysregulation or lack of neuronal $\text{Na}^{+}/\text{K}^{+}$ -ATPase can lead to neuronal dysfunction and behavioral abnormalities. Moreover, neurodegeneration can be triggered.

In all the subject groups studied, it was conspicuous that autoantibodies against the β -2 AR were often the most frequently detectable after autoantibodies against α -1 AR. AgAAB against β -2 AR also activate this receptor in a non-physiological manner. β -2 AR activation couples to the adenylate cyclase system, leading to increased cAMP formation and activation of protein kinase cascades that influence numerous processes such as glycogenolysis, cellular calcium flows,

immune responses, storage and learning processes, as well as gene expression. AgAAB against β -2 AR may therefore cause dysregulation of the adenylate cyclase / cyclic AMP system and may lead to abnormalities in energy metabolism and neuronal function, for example. As shown by Ni et al., the activation of β 2 AR by the selective agonist clenbuterol stimulates γ -secretase and increases the production of amyloid β 40 and β 42 [22]. It must be assumed that agAAB also has that effect against the β -2 AR and, like an agonist, triggers amyloid β production by stimulating the receptor. This activation of the signal cascades as described might be a possible cause for diabetics developing dementia more frequently than people without diabetes [23, 24, 25]. Autoantibodies against the endothelin-A receptor also act like natural agonists and are thus involved in increased vasoconstriction. Only autoantibodies against the ETA receptor were sought in the present prevalence study. Angiotensin II causes vasoconstriction in blood vessels and an increased release of aldosterone in the adrenal cortex.

The processes described, triggered due to activation of adrenoceptors by agAAB as well, and considerable prevalence of agAABs in patients with diabetes type 2, should be given greater attention in the treatment of diabetics in future. It is possible that a number of secondary diseases could be greatly reduced or avoided by early pharmacological intervention or by immunoadsorption. Prerequisite for treatment is the diagnosis of agAAB.

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CONFLICT OF INTEREST STATEMENT

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Animal experiments were carried out in accordance with the guidelines provided and approved by the animal welfare department of the Landesamt für Gesundheit und Soziales Berlin (Berlin State Office of Health and Social Affairs, Permit Number: G0197/10).

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IMMUNOLOGICAL AND VIROLOGICAL EFFECTS OF THE TREATMENT OF ACUTE HIV INFECTION WITH THE USE OF DRUGS NIKAVIR AND TENOFOVIR

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KEYWORDS — nicavir, tenofovir, acute stage of HIV infection.

MATERIALS AND METHODS

23 patients were treated with the acute stage of HIV infection for 8–48 weeks. All patients received antiretroviral therapy with the inclusion of 2 NRTIs and 1 NNRTIs. The first group of 11 people received a regimen with Nikavir, the second — of 12 people — with Tenofovir, in combination with Lamivudine and Efavirenz in standard doses.

RESULTS AND ITS DISCUSSION

In all patients, an acute stage of HIV infection was established on the basis of clinical manifestations, DNA and RNA detection by PCR. The final diagnosis was obtained in an immune blot reaction [1, 2]. To assess the effectiveness of early antiretroviral therapy, lymphocyte CD4 levels, HIV viral load before treatment were monitored, and then 12–24–36–48 weeks later.

Identified ways of transmission of HIV infection: sexual transmission in 10 patients of groups 1 and 2, parenteral — in 1 and 2 people, respectively. Secondary infections — herpes and candidiasis [3] were detected.

All patients started therapy until the final laboratory confirmation of the disease.

The estimated baseline level of HIV VN RNA was, on average, 2 times higher in patients of the first group (109660 versus 56436). In the group receiving ART Nikavir, the rate of viral load reduction was significantly higher (287081 times) than in the group receiving therapy with Tenofovir (2915 times). In patients in the VN RNA study group, HIV was suppressed from 24 weeks of therapy, in the comparison group, only after 36 weeks.

The number of CD4 lymphocytes in patients of the first group increased by 479 cells / μ l (from 391 to 870), while in patients of the second group it remained at the same level (574–540).

CONCLUSION

Early diagnosis of HIV infection has positive epidemiological and clinical significance. At the same time, a persistent reduction in viral load in combination with a stable number of CD4 lymphocytes of more than 500 cells / μ l suggests that both ART regimens are effective and recommend their use for the treatment of the acute stage of HIV infection.

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RISK FACTORS FOR DEVELOPING DIASTOLIC DYSFUNCTION IN NONALCOHOLIC STEATOHEPATITIS

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INTRODUCTION

In the last 20 years, nonalcoholic fatty liver disease (NAFLD) has become the leading cause of chronic liver disease worldwide, primarily as a result of the epidemic of metabolic syndrome. NAFLD is strongly associated with insulin resistance, glucose intolerance, and dyslipidemia and is currently regarded as the liver manifestation of the metabolic syndrome. Mortality in NAFLD is associated with cardiovascular disease, not with liver failure. Nonalcoholic steatohepatitis (NASH) is a type of NAFLD. NASH suggest about inflammation in liver cell damage.

OBJECTIVE

To assess the risk factors in nonalcoholic steatohepatitis, which can lead to the development of diastolic dysfunction.

RESEARCH DESIGN AND METHODS

In cohort study, we enrolled 140 patients with nonalcoholic steatohepatitis (NASH) in results of metabolic syndrome. All patient was non-alcoholic and without any concomitant heart disease. All patients undergone biochemical blood testing, ultrasonography and echocardiography. NASH was diagnosed by ultrasonography and biochemical blood analysis. All patients were excluded for viral hepatitis (B, C, D).

RESULTS

According to our echocardiography data we found occurrence of diastolic dysfunction in NASH is 60%. Diastolic dysfunction was more often in male than female. Patient with grade 3 diastolic dysfunction was symptomatic in terms of dyspnea, palpitation and intolerance to moderate to heavy physical activity. HOMA-IR index was raised in 96% patients with NASH. In presence diastolic dysfunction in NASH observed that high level of the HOMA-IR

(6.06 ± 0.7 , $p < 0.05$), fasting glucose (6.30 ± 1.91 mmol/l, $p < 0.05$), ALT (43.61 ± 0.422 u/l, $p < 0.05$), Alkaline phosphatase (143.59 ± 2.848 u/l, $p < 0.001$), Gamma-glutamyl transferase (82.22 ± 1.178 u/l, $p < 0.05$) cholesterol (5.99 ± 1.324 mmol/l, $p < 0.05$), triglyceride (2.91 ± 0.258 mmol/l, $p < 0.05$), LDL (1.68 ± 0.492 mmol/l, $p < 0.05$) compare to patients without presence of diastolic dysfunction in NASH. In patient with NASH had high level of uric acid. In presence of diastolic dysfunction in NASH 56.90% of patients had high level of uric acid (male 427.60 ± 12.344 mmol/l, $p < 0.05$, female 365.43 ± 10.344 mmol/l, $p < 0.05$) compare those patients without diastolic dysfunction in NASH.

CONCLUSIONS

Our study data showed that high level of HOMA-IR, LFT (ALT, alkaline phosphatase, gamma-glutamyl transferase), dyslipidemia, uric acid are associated with diastolic dysfunction in NASH. Probably these factors lead to development of cardiovascular disease in NASH.

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THE EFFECT OF ASSOCIATED CHRONIC OBSTRUCTIVE PULMONARY DISEASE ON THE INDICATORS OF PRECURSOR OF TYPE B NATRIURETIC PEPTIDE AND PROADRENOMEDULLIN AMONG PATIENTS WITH ISCHEMIC CARDIOMYOPATHY

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ABSTRACT — The study showed that a statistically significant increase of NT-proBNP levels (779,36 [473; 2193] pg/ml) and MR-proADM (1,72 [1,56; 1,98] nmol/l) relative to the control values (69.90 [48.96; 91.00] pg / ml and 0,49 [0,18; 0,58] nmol/l, respectively) is common for the patients with ischemic cardiomyopathy. The presence of concomitant chronic obstructive pulmonary disease among the patients is associated with more pronounced increase in the level of NT-proBNP (872,37 [510; 2355] pg/ml) and MR-proADM (1,97 [1,75; 2,19] nmol/l) compared with a group of patients with isolated ischemic cardiomyopathy. This can be considered as one of the compensation links for this comorbid combination.

KEYWORDS — ischemic cardiomyopathy, chronic obstructive pulmonary disease, proadrenomedullin, precursor of type B natriuretic peptide, chronic heart failure (CHF).

The study of the features of pathogenetic mechanisms, clinical picture, diagnosis and treatment of various somatic diseases when they are combined remains one of the urgent problems of medicine. To a large extent, this refers to coronary heart disease and chronic obstructive pulmonary disease (COPD), which is currently defined as comorbid [1, 2]. They are the leading chronic diseases among patients of older age groups and occupy leading position among the causes of incapacity, disability and premature death [3, 4].

The aim of the study

Is to evaluate the effect of concomitant chronic obstructive pulmonary disease on the precursor levels of

type B natriuretic peptide and proadrenomedullin among patients with ischemic cardiomyopathy.

MATERIALS AND METHODS

A one-time (transverse) observational study included 172 men who, in accordance with the purpose of the study, were divided into two groups: 130 patients with ischemic cardiomyopathy (ICMP) and 42 patients with ICMP and chronic obstructive pulmonary disease (ICMP + COPD). Exclusion criteria from the study: age over 65 years, acute and malignant diseases, mental disorders. The control group consisted of 30 somatically healthy men, the average age was 52.76 [40; 59]. Clinical characteristics of patients are presented in Table 1.

Chronic ischemic heart disease diagnosis: ICMP was made on the basis of clinical recommendations "Diagnosis and treatment of chronic coronary heart disease" by the Ministry of Health of the Russian Federation (2013) and formulated according to the International Classification of Diseases (X revision) [5]. The COPD diagnosis was made according to the recommendations provided by the "Global strategy for the diagnosis, treatment and prevention of chronic obstructive pulmonary disease" program (GOLD, 2018) [6].

To determine the level of proadrenomedullin (MR-proADM) in serum samples, the test system "BRANMSMR-proADM KRYPTOR" (Germany), the level of the precursor of the natriuretic peptide type B (NT-proBNP) - test system "BiomedicNT-proBNP" (Austria) was used.

The study was done in accordance to the standards of good clinical practice (GoodClinicalPractice) and the principles of the Declaration of Helsinki and was approved by the Regional Independent Ethics Committee (protocol № 11 dated November 6, 2014). All patients received complete information about the study and gave informed consent to voluntary participation in it.

Table 1. Clinical characteristics of patients in groups

Indicator	ICMP n = 130	ICMP + COPD n = 42
Age, years	55,57 [43; 63]	54,81 [41; 63]
Body mass index, kg/m ²	31,65 [22,96; 45,92]	31,3 [28,04; 49,73]
The duration of symptoms of coronary artery disease, years	4,98 [2; 13]	5,14 [3; 12]
Duration of CHF symptoms, years	2,84 [1; 6]	2,76 [1; 5]
Functional class CHF (NYHA)		
2, n (%)	21 (16%)	6 (14%)
3, n (%)	88 (68%)	28 (67%)
4, n (%)	21 (16%)	8 (19%)
6-minute walk test, m	169 [38; 368]	158 [41; 349]
Scale of assessment of the clinical condition, points	9,19 [4; 15]	9,46 [5; 14]
The duration of arterial hypertension in history, years	14,17 [3; 25]	13,34 [2; 25]
Systolic blood pressure, mm hg. art.	98,51 [80; 130]	95,38 [80; 125]
Diastolic blood pressure, mm hg. art.	65,83 [60; 80]	67,28 [60; 80]
Smoking at the time of the study, n (%) / history of smoking, n (%)	82 (63%) / 8 (6%)	37 (88%) / 5 (12%)
Smoking Man Index (pack/year)	24,35 [12; 32]	36,46 [22; 48] p* < 0,001

Note: p* — statistically significant differences in the group of patients with ICMP.

Statistical data processing was done using the program "Statistica 12.0" (StatSoft, Inc., USA). The values of the median (Me) and percentiles (5% and 95%) were calculated for each studied indicator. Statistically significant differences between the studied parameters were considered at $p < 0,05$.

RESULTS

As shown in table 2, the data in the studied groups, the indicators of the levels of NT-proBNP and MR-proADM were statistically significantly higher than in the control group. At the same time they were statistically significantly higher in the ICMP + COPD group than in the group with isolated ICMP.

cardiomyocytes in response to an increase in left ventricular wall tension, an increase in ventricular volume and pressure, and a complex of its physiological effects aimed at reducing the hemodynamic load on the myocardium. COPD among the patients with ICMP apparently contributes to increased hypoxemia, oxidative stress and cytokine imbalance, which has an additional negative impact on the state of cardiomyocytes among the patients with ICMP. In addition, COPD leads to more pronounced structural changes in the heart (hypertrophy and dilatation of the right heart, development of pulmonary hypertension), which increases the mechanical stretching of cardiomyocytes and increases the expression of NT-proBNP [7, 8, 9].

Table 2. NT-proBNP and MR-proADM levels in the studied groups

Indicator	Control	ICMP n = 130	ICMP + COPD n = 42
NT-proBNP, pg/ml	69,90 [48,96; 91,00]	779,36 [473; 2193] p1 < 0,001	872,37 [510; 2355] p1 < 0,001, p2 = 0,042
MR-proADM, nmol/l	0,49 [0,18; 0,58]	1,72 [1,56; 1,98] p1 < 0,001	1,97 [1,75; 2,19] p1 < 0,001, p2 = 0,046

p1 — the level of statistical significance of differences with the control group.

p2 — the level of statistical significance of differences with the group of patients with ICMP.

The detected high levels of NT-proBNP in the ICMP group are explained by pronounced structural and functional dysfunction of the left ventricle with ICMP, since this peptide is known to be secreted by

The revealed change in the MR-proADM level with ICMP is consistent with the data of other researchers, indicating its increase in various forms of IHD. Hypoxia and cytokine release are indicated as a

possible reason for this increase, which cause increased secretion of MR-proADM by vascular cells as a compensatory agent involved in neoangiogenesis, which suppresses collagen synthesis and has antioxidant, inotropic effects and increases myocardial contractility. The presence of ICMP among the patients with COPD increases hypoxia and hypoxemia, which leads to increased stimulation of the production of MR-proADM. In addition considering the antibacterial, bronchodilatory and immunoregulatory effects of MR-proADM, it can be assumed that changes in the respiratory tract with COPD are also an additional stimulus for its development [10, 11, 12].

CONCLUSION

Patients with ICMP are characterized by increased levels of NT-proBNP and MR-proADM relative to control values. The presence of concomitant COPD is associated with more pronounced increase in the level of NT-proBNP and MR-proADM, compared with the group of patients with isolated ICMP, which can be considered as one of the compensation links for this comorbid combination.

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THE STATE OF THE MYOCARDIUM, THE VASCULAR WALL AND THE SEVERITY OF ANXIETY-DEPRESSIVE DISORDERS IN PATIENTS WITH MYOCARDIAL INFARCTION AND ATRIAL FIBRILLATION

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ABSTRACT — In patients with myocardial infarction with atrial fibrillation, the relationship between vascular wall parameters, structural and functional changes in the myocardium, and the severity of emotional disorders were clarified. 138 inpatients of the cardiology department were closely monitored. It turned out that patients with myocardial infarction and a constant form of atrial fibrillation, unlike patients with paroxysmal form, show significant structural changes in the myocardium, endothelial dysfunction with a reduction in wall elasticity, which must be considered during therapeutic and preventive, rehabilitation measures.

KEYWORDS — myocardial infarction, atrial fibrillation, vascular wall stiffness, anxiety and depressive disorders.

INTRODUCTION

Atrial fibrillation is a frequent complication of acute myocardial infarction [12], significantly aggravates the patient's condition, leads to deterioration of hemodynamic parameters and the appearance of recurrent myocardial ischemia [3,4,7]. Currently, a large amount of data on the causes, electrophysiological mechanisms and hemodynamic consequences of the development of atrial fibrillation in myocardial infarction has been accumulated [13]. However, a number of issues related to this arrhythmia appear to be insufficiently studied. These include the structure of anxiety-depressive disorders, the state of the elastotonic properties of the vascular wall, endothelial function and cardiac remodeling in patients with myocardial infarction with various forms of atrial fibrillation, which requires detailed study.

Objective

To evaluate parameters of the contour analysis of the pulse wave and endothelium function, as well as structural and functional changes in the myocardium and the severity of emotional disorders in patients with myocardial infarction in various forms of atrial fibrillation.

MATERIALS AND METHODS

138 patients were examined (63 men, 75 women) who were hospitalized in the cardiology department of the City Clinical Hospital No. 7 with a diagnosis of myocardial infarction with atrial fibrillation. Depending on the form of atrial fibrillation, the patients were divided into 2 groups: the 1st was 83 (60.1%) patients with paroxysmal form, the 2nd group was 55 (39.9%) with the permanent form. The survey was conducted in the first three days of hospital stay.

Conducted: general clinical examination, localization of myocardial infarction, its frequency rate (primary, repeated) [4,7,12], complications (acute left ventricular failure according to Killip, 1967) [10] were studied. All patients were determined plasma lipid spectrum (total cholesterol, low density, high density lipoproteins, triglycerides; mmol/l) while taking lipid-lowering drugs (atorvastatin 40–80 mg/day) [9]. An echocardiographic study was performed on a Vivid I apparatus (GE Healthcare UK) with an assessment of the following parameters: ejection fraction (EF%), end diastolic size of the left ventricle (CRLD; mm), end diastolic volume of the left ventricle (CEDI; ml), posterior wall thickness of the left ventricle (TSS-LZH; mm), thickness of the interventricular septum (TMZHP; mm), size of the left atrium (LP; mm), right atrium (PP; mm), right ventricle (RV; mm), systolic pressure in the pulmonary artery (SDLA; mm rt.art.) [6]. The rigidity of the vascular wall was studied by the photoplethysmographic method (apparatus Angioscan-1) in the morning in a quiet darkened room, strictly on an empty stomach; before the procedure, the patients did not smoke or drink tea or coffee. Immediately before the procedure, the patient was at least 10 minutes at rest. The test was carried out in a sitting position with fixed hands. The procedure for performing a contour analysis was carried out in several stages:

1. Measurement of blood pressure by the standard oscillometric method using a certified device;
2. Entering the patient's data (level of blood pres-

- sure, height, weight, date of birth) into the AngioScan computer program;
3. Installation of the optical sensor on the end phalanx of the index finger of the right hand;
 4. Registration and automatic evaluation of pulse waves.

Based on the contour analysis of the photoplethysmogram [1], the following were evaluated: pulse rate (PE; beats/min), stiffness index (SI — Stiffness index; m/s), reflection index (RI — Reflection Index; %), amplitude occlusion index (IRA; %), increase index (Alp — Augmentation index; %), increase index normalized for pulse rate (CP = 75) (Alp 75 — Augmentation index @ HR = 75), age index (AGI — Aging Index), vascular age (VA — Vascular Aging; years), duration of systole (ED — Ejection Duration; m/s), pulse wave duration (PD — Pulse Duration; m/s), central systolic pressure (Spa — Systolic Pressure — Aortic — prognosis, mm Hg), type of pulse wave (A, B, C). To assess the endothelial function, a test was performed with reactive hyperemia with the calculation of the occlusion index by amplitude (IOA; used units) and phase shift (MF; ms) between the channels. The occlusion of the brachial artery was carried out for 5 minutes by inflating the standard cuff of the tonometer to a pressure of 50 mm Hg, exceeding the systolic pressure with simultaneous recording of the signal. After 5 minutes, the pressure in the cuff was quickly dropped to zero and the signal was recorded for 3 minutes.

To assess the severity of anxiety/depression, a scale of anxiety and depression HADS [14] was used, which includes 14 questions: part 1 contains 7 questions of anxiety; Part 2 — 7 questions of depression. Each answer corresponds to a certain number of points. By the sum of points, the result was evaluated: 0–7 points — the absence of reliably expressed symptoms of anxiety and depression, 8–10 points — subclinical anxiety/depression, 11 points and above — clinically expressed anxiety/depression. For the analysis and evaluation of the obtained data, standard methods of descriptive statistics were used: the calculation of average values and standard deviation ($M \pm \sigma$) for the normal distribution. Student's t-test was used to compare groups (for quantitative variables). The level of statistical significance was taken as $p < 0.05$. For statistical processing of the results obtained, Statistica version 10 was used.

RESULTS

Among patients of the 1st group (age — 71.9 ± 8.9 years), anterior myocardial infarction was recorded in 33 (39.7%), lower — in 20 (24.3%),

repeated anterior — in 15 (18, 0%), repeated lower — in 15 (18.0%) patients. In patients of the 2nd group (age — 73.7 ± 9.0 years), anterior myocardial infarction occurred in 25 (45.4%) people, lower myocardial infarction — in 17 (30.9%), repeated anterior — in 11 (20.0%) people, repeated lower — in 2 (3.6%). As can be seen from the data presented in Table 1, in patients with paroxysmal atrial fibrillation, I and II prevail, less frequently, III and IV, the functional class of acute heart failure, whereas in patients with permanent atrial fibrillation, frequency II and III increased, while I and IV functional class.

As can be seen from the data presented in Table 2, patients with a constant form of atrial fibrillation compared with the paroxysmal form, there was a statistically significant increase in LP, PP, SDLA, there was also a tendency to an increase in indicators of LVEDD, CLLT, TLSS, LV, which indicates about significant structural changes in the myocardium in patients with permanent atrial fibrillation, which are combined with signs of severe heart failure.

According to Table 3, patients with myocardial infarction with a constant form of atrial fibrillation, compared with the paroxysmal form, have a significant increase in PD, decrease in RI, as well as a tendency to increase in AGI, SI, decrease in ED, which indicates the effectiveness of elastic vascular walls in large resistive arteries. The high tone of the thin muscular arteries, in patients with paroxysmal atrial fibrillation, is an additional risk factor for heart muscle damage. In the studied groups, an increase in the frequency of the pulse waves of type A and B was noted, the type of curve C tended to decrease, which characterizes the decrease in the elasticity of the vascular wall. However, in individuals with a permanent form, these types of waves were encountered more frequently than in individuals with a paroxysmal form, which indicates a significant increase in the afterload of the left ventricular myocardium and a violation of its diastolic relaxation.

When assessing endothelial function in patients of the 2nd group, compared with patients of the 1st group, there was a statistically significant decrease in the SF, as well as a tendency to decrease in IRA, which indicates significant endothelial dysfunction in the large muscle arteries. In patients of the 1st group, there was a direct correlation of the average force between the parameters of CEDI and RI ($r = +0.536$), Alp and Spa ($r = +0.523$), VA and Spa ($r = +0.588$), the inverse correlation link of a weak force between EF and RI ($r = -0.492$) and the average force between TMZHP and RI ($r = -0.624$); in patients of the 2nd group, the direct correlation of the average force between the IOA and TLSVFL ($r = +0.517$), SI and TLSAFL ($r = +0.520$), SI and TMD ($r = +0.530$), Spa and FV ($r = +0.543$), SI

Table 1. The frequency of the functional class of heart failure by Killip in patients with myocardial infarction

Monitoring group	Killip Functional Heart Failure Class			
	I	II	III	IV
1 st n=83	57 (68,6%)	11 (13,2%)	8 (9,6%)	7 (8,4%)
2 nd n=55	31 (56,3%)	11 (20,0%)	9 (16,3%)	4 (7,2%)

Table 2. Indicators of echocardiography in patients with myocardial infarction with atrial fibrillation

Indicator	Atrial fibrillation		
	Paroxysmal (n=83)	Permanent (n=55)	p <
EF, %	42,1 ± 10,9	41,6 ± 10,6	-
CRLLD, mm	47,8 ± 4,9	49,1 ± 7,6	-
CEDI, ml	97,7 ± 34,0	107,9 ± 43,2	-
TSSLZH, mm	12,8 ± 2,9	14,3 ± 2,4	-
TMZHP, mm	14,1 ± 2,8	14,3 ± 2,4	-
LP, mm	4,2 ± 0,5	4,6 ± 0,6	0,001
PP, mm	3,9 ± 0,5	4,2 ± 0,5	0,001
RV, mm	2,8 ± 0,4	3,09 ± 0,4	-
SDLA, mm Hg.	38,9 ± 13,1	41,1 ± 8,6	0,05

Statistical significance is indicated between patients with paroxysmal and persistent AF ($p < 0.05-0.001$)

Table 3. Indicators of contour analysis of pulse wave and endothelium function in patients with myocardial infarction with atrial fibrillation

Indicator	Atrial fibrillation		
	Paroxysmal (n=83)	Permanent (n=55)	p <
PD, beats/min	541 ± 9,4	600,9 ± 16,2	0,05
AGI	0,8 ± 0,2	1,1 ± 0,4	-
RI, %	32,2 ± 1,7	21,2 ± 2,3	0,05
Spa, mm Hg.	112,6 ± 4,1	112,5 ± 4,8	-
Alp, %	8,8 ± 1,3	8,5 ± 1,9	-
SI, m/s	7,8 ± 2,0	8,7 ± 1,8	-
ED, %	45,2 ± 1,0	40,4 ± 7,9	-
IOA; used.units.	1,4 ± 0,7	1,15 ± 0,6	-
MF; ms	- 3,7 ± 0,9	- 12,2 ± 2,6	0,05
Curve type A, %	72,1 ± 4,2	78,4 ± 5,0	-
Curve type B, %	19,2 ± 3,6	15,1 ± 3,4	-
Curve type C, %	8,6 ± 3,3	6,4 ± 2,8	-

Statistical significance is indicated between the patient and the paroxysmal and permanent form of AF ($p < 0.05$).

and RI ($r=+0.569$), AIp 75 and SI ($r=+0.706$), AIp 75 and RI ($r=+0.712$).

When studying anxiety disorders in patients with myocardial infarction with atrial fibrillation, it was found that in patients with paroxysmal and persistent atrial fibrillation, no statically significant changes were detected. As can be seen in Fig. 1, patients with myocardial infarction with a paroxysmal form of atrial fibrillation in most cases lacked anxiety, then subclinical and less often clinically expressed anxiety was recorded. In patients with myocardial infarction with a constant form of atrial fibrillation, in contrast to those with paroxysmal form, the frequency of subclinical and clinically severe anxiety increased. In the 1st group, among individuals with no anxiety, the level on the HADS scale was 3.59 ± 2.0 points, with subclinical anxiety — 8.9 ± 0.8 points, with clinically severe anxiety — 12.0 ± 0.1 points; in patients of the 2nd group, respectively, 3.6 ± 1.8 ; 8.8 ± 0.7 ; 12.0 ± 0.9 points.

When studying depressive disorders (Fig. 2), among patients in the 1st group, the frequency of subclinical and clinically severe depression was higher than in the 2nd group. In the first group among individuals with no depression on the HADS scale, its level was 4.2 ± 1.8 points, with subclinical depression — 8.8 ± 0.7 points, with clinically severe depression — 12.5 ± 0.5 points; in group 2, respectively, 3.7 ± 2.0 ; 8.5 ± 0.7 ; 13.0 ± 0.1 points.

CONCLUSION

In patients with myocardial infarction with a permanent form of atrial fibrillation, in contrast to patients with paroxysmal form, there are significant structural changes in the myocardium, endothelial dysfunction with a decrease in the elasticity of the arterial vascular wall. In the case of paroxysmal atrial fibrillation, emotional stress is characterized by the predominance of depressive disorders, and in permanent form, alarming, which must be taken into account when carrying out treatment-and-prophylactic, rehabilitation measures and solving expert issues.

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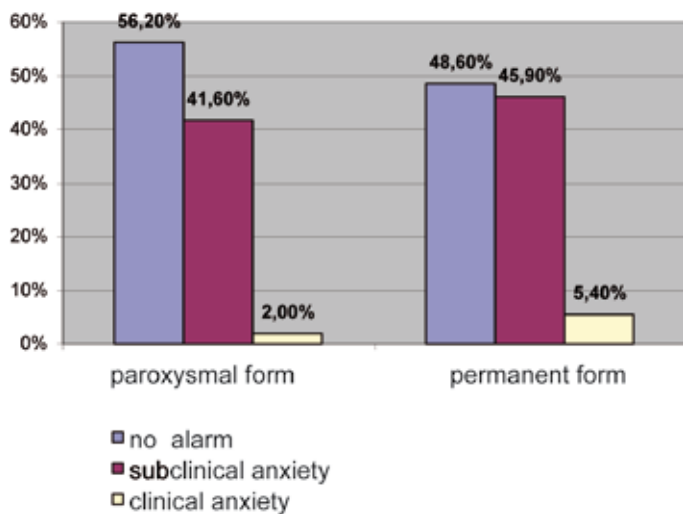


Fig. 1. Structure of anxiety disorders in patients with myocardial infarction with atrial fibrillation

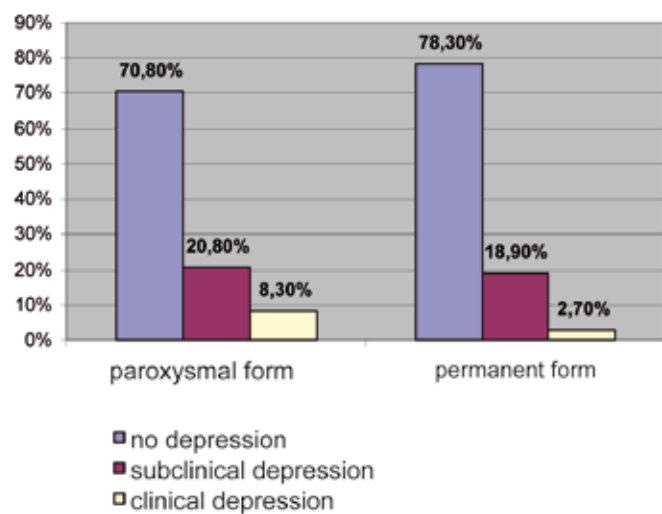


Fig. 2. The structure of depressive disorders in patients with myocardial infarction with atrial fibrillation

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APPLICATION OF VARIABLE VACUUM IN CARDIOSURGERY WITH COMPLICATIONS

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RELEVANCE

In the conditions of progress of modern medicine in the field of surgery, antibacterial therapy and preventive practices, postoperative sternomediastinal infections still remain a pressing public health problem. They have a significant impact on the survival rate, duration of hospitalization and the economic burden of treating cardiac patients. The problem of postoperative complications in cardiac surgery is very relevant at present, given the increase in the number of geriatric patients, patients with overweight and diabetes [1, 2].

Median sternotomy, as a surgical approach, has several disadvantages, one of which is the risk of developing infectious complications in the field of surgical intervention. They proceed with the formation of a superficial or deep wound infection, diastasis and fragmentation of the sternum, destabilization of the bone skeleton of the chest [3, 4, 5].

The frequency of mediastinitis after cardiac surgery, as a rule, varies from 1% to 4% [3]. The failure of the stitches and the infection of the sternotomy wound is a terrible complication, with high mortality rates, which are in the risk group from 14 to 75% [6]. The development of PSM is associated with a significant decrease in long-term survival [7, 8]. Risnes and colleagues showed that patients undergoing PSM have a 59% greater risk of death within a 10-year period after surgery compared to patients who did not tolerate this complication. [9]. The authors attribute this to the fact that the chronic inflammatory process associated with mediastinitis can negatively affect the long-term patency of the shunts and thus lead to a decrease in survival [10].

The cost of treatment of patients with PSM is on average 2–3 times higher than the treatment of similar patients without this complication [1].

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PURPOSE OF THE STUDY

Assess the effect of different vacuum drainage regimes and open reference methods on the healing of infected wounds and long-term results.

MATERIAL AND METHODS

Group 1 included patients using variable vacuum drainage, group 2 using continuous vacuum drainage, group 3 using the open reference method. Specialists involved in the analysis and interpretation of the histological component of the study were not provided with any information about the patients belonging to individual study groups, in order to reduce the likelihood of systematic statistical errors in the study and maximum objectification in the interpretation of histological data.

The study was conducted in accordance with the requirements of the Ministry of Healthcare of the Russian Federation No. 82 dated April 29, 1994 and according to the nomenclature of clinical laboratory research of the Ministry of Health of the Russian Federation (order No. 64 of February 21, 2000) taking into account the provisions of the Helsinki Declaration (2013). On the basis of prospective, controlled comparative studies, monitoring of morphological changes in the conditions of regeneration of an infected sternotomy wound was conducted in accordance with the principles of evidence-based medicine. Clinical and classical morphological research methods were used in monitoring reparative processes in patients with postoperative sternomediastinitis, followed by statistical analysis of the data obtained.

To solve questions about the possible mechanisms of reparative regeneration under the conditions of an open method of treatment, using constant and variable vacuum using morphological methods of research, we obtained an objective assessment of regeneration in damaged tissues. For a comparative assessment, tissue sampling for research was performed on the day of PSM detection and every 4 days after detection and initiation of PSM treatment, during the surgical rehabilitation of post-motone wounds, according to indications, in the volume of tissues not more than 1 mm³.

Table 1. The distribution of patients by postoperative treatment methods

Group number	Postoperative methods treatment	Number of patients
1	Variable vacuum discharges	13
2	Permanent vacuum discharges	14
3	Open reference method	30
Total:		57

THE RESULTS OF THE STUDY

In our studies, in all observation groups, in cuts made from biopsy samples of the wound surface area, CD differentiation cells CD68, CD163, CD34 were identified. Macrophages, which begin to migrate into the wound from the vessels together with granulocytes, have a more significant effect on the following stages of healing, but they reach the maximum level only by the 3rd day, decreasing after 6–7 days.

The physiological role and influence of macrophages are associated not only with their function of wound cleansing (by phagocytosis of erythrocytes, decaying leukocytes, fat cells and fibrin), but also with the secretion of specific substances that enhance fibroblast proliferation. Collagen fibers in any wounds are one of the main parts of wound detritus. They remain for a long time after the breakdown of the cells of the preexisting tissue, undergoing swelling, fibrillation, partial destruction and loss of fuchsinophilia. Collagen resorption is mainly a function of macrophages. However, they are not capable, like fibroblasts, to phagocytosis of collagen fibrils. The latter are subjected to fragmentation, destruction, granular disintegration and lysis in the immediate vicinity of macrophages, under the action of collagenolytic enzymes secreted by the cell, and then was phagocytosed. The most interesting are patients with type 2 diabetes mellitus, since they have active neo-vascularization in neuro-sensory structures and reduced angiogenesis and impaired trophism of tissues from other sites. Considering the role of the macrophage pool, which induces angiogenesis and participates in the phagocytosis of necrotic tissues, the effect on collagenogenesis in the healing process, we have obtained data on the localization and quantitative characteristics of cells expressing CD163.

In patients treated with variable vacuum drainage, identification of CD163 was detected in greater numbers than in patients in other observation groups.

In our studies, it was noted that the proliferative activity of structures in the zone of a regenerating postoperative wound correlates with the processes of angiogenesis and an increase in the number of macrophages. These indicators were dependent on the method of treatment and the most adequate ratios of indicators to successfully accelerate regeneration were observed in patients treated with variable vacuum drainage. We noted that in patients with diabetes,

angiogenesis is compounded (less than CD163 and capillary density), less than endothelium growth factor, lower than CD34.

Analysis of the clinical manifestations in the postoperative period showed that the creation of negative pressure in the wound has a pronounced complex positive effect on the course of the disease: edema decreases, local blood circulation improves, bacterial load decreases, healing accelerates. Vacuum therapy improves throughout all stages of the wound process: reduces local edema, as a result — helps to enhance local blood circulation, reduces the level of microbial contamination of the wound, causes deformation of the wound bed and a decrease in the wound cavity, leading to accelerated wound healing. Also, vacuum therapy reduces the severity of wound exudation, helping to maintain a moist wound environment necessary for normal wound healing. All these effects contribute to an increase in the intensity of cell proliferation, enhance the synthesis in the wound of the main substance of connective tissue and proteins. The advantages of VAC therapy are that vacuum therapy by improving the quality of granulation tissue increases the chances of success in closing the wound with local tissues. The imposition of a vacuum-dressing on the wound allows you to remove excess wound exudate, stimulates angiogenesis.

The direct effect of vacuum on the wound bed leads to a local decrease in the partial pressure of oxygen in the wound; however, this, like in diabetes mellitus, stimulates the formation of new vessels and further improvement of the quality of granulation tissue in the wound. This ultimately results in increased tissue oxygenation, which is especially important for patients with concomitant CD.

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THE USE OF PHYSICAL THERAPY FOR KNEE INJURIES IN CHILDREN

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Various injuries of the knee account for 5 to 25% of all injuries of the musculoskeletal system in children and are among the most *expensive* injuries, which often require surgery and intensive rehabilitation [1, 2]. Currently, physical factors are widely used in the medical rehabilitation of children with the knee injury, including after arthroscopic operations in the early rehabilitation period [3–5].

However, evidence-based recommendations for medical rehabilitation of children with post-traumatic non-specific pain in the knee joint in children in the absence of intra-articular lesions seem not effective enough due to changes in functional status of a limb in regard to musculoskeletal system as a whole.

Clinical observations and comparative studies of the effectiveness of the integrated application of pulsed low-frequency electrostatic field and physical therapy exercises were performed in 40 children with post-traumatic stress pain syndrome aged 6–18 years.

Complex application of pulsed low-frequency electrostatic field and physical therapy helped to improve the general state of the middle of the course. These sensory-analogue scale showed a significant decrease of the intensity of pain by the end of treatment (from 4.27 ± 0.05 to 1.12 ± 0.13 points, $p < 0.05$).

Under the influence of combined use of pulsed low frequency electrostatic field and physiotherapy mentioned tone and muscle strength recovery, eliminating the stiffness of the knee joint, reducing the severity of muscle wasting femur as hip circumference reduction volume deficit of 1.7.

Results of dynamic knee ultrasound recorded leveling inflammatory changes, signs of synovitis knee joints under the influence of combined use of pulsed low frequency electrostatic field and physical therapy. The dynamics of average scoring echographic changes in the joint ranged from 3.8 ± 0.71 to 0.3 ± 0.21 score, $p < 0.05$.

Investigation of capillary blood flow by laser Doppler flowmetry enabled to establish a favorable

level of tissue perfusion dynamics in children in a normalizing microcirculation indicator as in congestive stagnant-type microcirculation: from 18.6 ± 1.14 to 13.6 ± 0.74 pf.unit., and in the spastic type: from 5.6 ± 0.56 to 8.4 ± 1.12 pf.unit. The frequency registration microcirculation type increased by 3.3 times while reducing the frequency of adverse registration types microcirculation: hyperemic-stagnant 2.5 times, spastic — 2 times.

These infrared thermography showed significant decrease in thermoasymmetry periarticular damaged tissue joints and symmetrical with 1.8 ± 0.04 °C to 0.3 °C ± 0.02 ($p < 0.05$) after a course of action of physical factors that correlate with by laser Doppler flowmetry.

Comprehensive assessment of therapeutic efficacy on combined use of pulsed low frequency electrostatic field and physical therapy in children with post-traumatic pain syndrome was 95.0%

Thus, a new technology for medical rehabilitation has been developed and scientifically substantiated on children with post-traumatic pain syndrome. Its use was positively confirmed against a background of dynamic control over post-traumatic inflammation with the help of non-invasive diagnostic techniques.

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RESULTS IN THE TREATMENT OF SACRAL CHORDOMA

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INTRODUCTION

Chordoma — a malignant, slowly growing tumor that develops from chord residues, is localized mainly in the lumbo sacral junction. It occurs in 2,5–4% of cases of all primary malignant bone neoplasms [2]. Men get sick 1,5–2 times more often than women [1]. Clinically manifested dysfunction of the pelvic organs: intestines, bladder, impaired sensitivity and paresis of the lower extremities. Often the tumor is determined by rectal examination [5]. Differential diagnosis of sacral chordoma, most often carried out with chondrosarcoma and metastatic lesion [3, 4]. Treatment of chordoma is usually combined, which includes: surgery and radiation therapy.

MATERIALS AND METHODS

61 patients were treated with chordoma sacrum. The first group consisted of 35 patients who underwent only surgical treatment in the volume of the sacral resection at the S3 level, of which radical ablative surgery was performed in 26 patients, and non-radical non-ablative — 9. The second group consisted of 26 patients who underwent combined treatment. In the preoperative period, all 26 patients underwent radiation therapy on the sacral tumor at a total focal dose (TFD) of 20 grays. In the postoperative period, 6 patients with non-elastic and 4 patients with non-radical surgery were given radiation therapy in TFD 40 gray.

RESULTS

As a result of the surgical treatment of 35 patients of the first group, 6 (17%) patients died in the early postoperative period due to various complications (acute cardiovascular insufficiency, pulmonary embolism, urosepsis, pelvioperitonitis). Therefore, long-term results were evaluated in 29 patients. Recurrences of chordoma were observed in 25 (86,2%), metastases mostly in the lungs in 12 (34,3%) patients. Three-year survival was $45,3 \pm 1,8\%$, five-year — $37,7 \pm 2,3\%$. In the second group of 26 patients who received the combined treatment, 2 patients died in the postopera-

tive period, so long-term results were evaluated in 24 patients. Recurrences of chordoma were observed in 9 (37,5%) patients. Three-year survival in the second group was $90,0 \pm 0,8\%$, five-year — $76,1 \pm 1,1\%$.

DISCUSSION

In the surgical treatment of sacral chordoma, the lethality of patients is usually due to tumor recurrences with local complications and progression of the disease with distant metastases.

CONCLUSIONS

Taking into account the results obtained, it can be said that the combined method of treatment is more effective in treating patients with chordoma of the sacrum, since the number of tumor recurrences has decreased and the survival rate of patients has increased.

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ACTIVE SURGICAL TREATMENT OPTIMIZATION OF SEVERE BURNS

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RELEVANCE

The results in treatment and recovery of severe burns are directly dependent on how soon the lost skin is restored. In this regard, the healing of burn wounds remains the most important general biological, medical and social problem [5]. There are no comprehensive data on the regeneration processes, not only in the burn wound itself, but also in the transplant [8]. Assessment of the condition of a burn wound, its readiness for autodermoplasty, the prediction of the success of surgical treatment are still subjective, depend on the experience and professionalism of the attending physician [2, 7]. In this regard, it is important to develop objective morphological criteria to optimize the surgical treatment of burn wounds. Therefore, it is necessary to have objective information about the depth of the burn lesion, about the possibilities of the regenerative potential of cellular elements in the affected area [1, 6]. The issues of reparative processes and angiogenesis in the engrafted autodermal graft also remain poorly understood and are the subject of heated debate. The problem of accelerating the regeneration processes in a burn wound, suppressing wound infection, improving the results of autodermoplasty remains unsolved [3]. Despite the fact that in recent years the arsenal of means and methods used for thermal injury has significantly expanded, the results of treatment are not always satisfactory [4]. The costs of treatment of burn patients remain significant, resulting in difficulties with the long stay of patients in the hospital. This dictates the need for both the improvement of active surgical treatment of severely burned and the search for a morphological rationale for the optimal timing of necrotomy and autodermo-

plasty, which can ensure the fastest possible healing of burn wounds.

PURPOSE OF THE STUDY

Optimization of surgical treatment of patients with burn injuries based on the study of patterns of reparative regeneration of the morphological structures of the skin in the area of thermal damage.

MATERIAL AND METHODS

The study was conducted in accordance with the requirements of the Ministry of Healthcare of the Russian Federation No. 82 dated April 29, 1994 and according to the nomenclature of clinical laboratory research of the Ministry of Health of the Russian Federation (order No. 64 of February 21, 2013) taking into account the provisions of the Helsinki Declaration (2013). The work is based on studies of 196 patients aged 18 to 60 years with thermal burns who were treated in the Primorsky Burn Department of the Far Eastern Regional Medical Center of the Federal Medical and Biological Agency of Russia from 2004 to 2016. Inclusion criteria were the presence of burns of the IIIA–IIIB degree with an area from 10 to 20% of the body surface, the Frank index of 30–60 units. Exclusion criteria were the presence of a large area of superficial burns of I and II degrees, as well as deep ones of IV degree. To study the dynamics of morphological changes in all patients after receiving written voluntary consent, biopsy material was taken from burn wounds under local anesthesia and anesthesia. The study design was approved by the FEFU Biomedicine School of Ethics. The size of biopsy specimens was 2–3 mm³. It was immunohistochemical identification of immunocompetent cells (Langerhans cells, macrophages, CD4, CD8). All patients received standardized treatment: infusion, antibacterial therapy, drugs to prevent acute stress ulcers of the upper gastrointestinal tract, DIC syndrome.

THE RESULTS OF THE STUDY

The dynamics of morphological changes in burn wounds was studied in two groups of operated patients, autodermal transplantation of which was performed in the first 7–14 days and at a later time.

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We found that in the early days after a burn injury in the pathological focus in the 1–2 day there is a slight increase in the number of blood vessels in the loose to fibrous connective tissue with diffuse inflammatory infiltration, mainly lymphocytic, which is subject to the epidermis or wound surface. At the same time in the study of the proliferative activity of the epidermis and other skin structures, it was found that in the basal layers only a few cells have a high regenerative potential, and the Ki-67 gene is absent in the spinous layer. A mild regenerative potential is observed in the wall of hair follicles and sebaceous glands, in proliferating cells of the dermis. In the endothelium of the blood vessels, the low activity of the Ki-67 gene is also determined. By 3–4 days the regenerative potential of the skin increases. Epithelial cells with the inclusion of the Ki67 gene were found on the border of living and dead tissue. The fourth, fifth and sixth days are characterized by the fact that the number of proliferating cells in all skin structures increases, reaching a maximum on the 7th day and in the basal layers of the epidermis, where activity is manifested both in the basal and thorny layers, in the endothelium of blood vessels, and in the epithelial cells of the sweat glands. A quantitative analysis of the density of the capillary network of the skin showed that the density of capillaries increases from 7–8 days, then is approximately at the same level up to 9–14 days; at a later date, there is some decrease in this indicator. Engraftment of free skin autografts is divided into several stages: the formation of an adhesive or intermediate layer; degenerative processes; vascularization; regenerative processes.

When studying transplanted skin with the help of vital dyes, the bilateral conductivity of the *spine*, or intermediate, layer that develops between the flap and the bed is found. The skin flap is initially powered by soaking its intercellular gaps with tissue fluid. 8 hours after transplantation, leukocytes enter the graft, and after two days fibroblasts. We have found that with full engraftment of the graft, the amount of CD8+ increases less than 2 times to 5–7 days and by 14–15 days remains slightly elevated from the initial level. With full lysis of the graft, their content is tripled and remains high for 18–21 days. In the study of CD4+, it was found that in the case of complete engraftment of the autodermal graft, their number slightly increases by 5–7 days, remains at the same level up to 14 days, and then quickly returns to its original level. With full lysis, the number of these cells remains elevated for a long time, but this indicator is not reliable. In the group of patients who had complete or partial lysis of the autodermal graft, it was noted that the number of Langerhans cells increased from 2–3 days after autodermoplasty and reached a maximum at 7–8 days.

However, in contrast to the group where the complete engraftment of the skin flap occurred, their content remained high for 14–15 days after autodermoplasty. Only on the 20–21st day their number decreased to 15 in sight. In these same patients, the content of macrophages also increased, starting from 7–8 days, and reached maximum values also by 14–15 days, which indicates a pronounced antigenic stimulation and the development of immune responses in a burn wound.

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EXPERIENCE IN THE TREATMENT OF CONGENITAL SYNDACTYLY IN THE TVER REGIONAL CHILDREN'S HOSPITAL

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Syndactyly is a congenital malformation, consisting in the fusion of two or more fingers, accompanied by a cosmetic defect and dysfunction of the limb. According to various authors, syndactyly accounts for more than 50% of all congenital anomalies of the hand. The frequency of occurrence is 1: 2000–1: 4000. Treatment of congenital syndactyly is most effective in the first two years of life [1,2].

Syndactyly is classified according to the degree of fusion to total and subtotal (Fig. 1, 2); by type of adhesion on soft tissue and bone forms; as the affected fingers are simple and complex. Depending on this, one or another method of correction of this defect can be chosen.

15 children with congenital syndactyly aged 1 to 15 years were operated in the trauma-orthopedic department of the Tver Children's Regional Clinical Hospital from 2016 to 2018 (8 male and 7 female). It was performed 19 operations on the separation of the fingers with the recreating the web space. 11 surgical interventions were performed on the total form of syndactyly (2 of them had bone fusion); 8 operations on the subtotal form.

In 18 cases, the operation was performed using local tissues; in one case, a free skin flap taken from the front surface of the forearm was used. In the treatment of an incomplete form of syndactyly, we used the procedure described by Yamashita et al. [3]. (Fig. 3).

In the case of the complete form of syndactyly, we used various treatment methods described by Juan Liu et al. [4] (Fig. 4), Feng Ni et al. [5] (Fig 5), and P. Samson, B. Salazard [1].

Skin sutures were removed for 14–21 days. We did not observe complications in the form of necrosis of the skin graft or inflammation of wounds. In all cases, a good functional result was obtained.



Fig. 1. Simple subtotal form of syndactyly

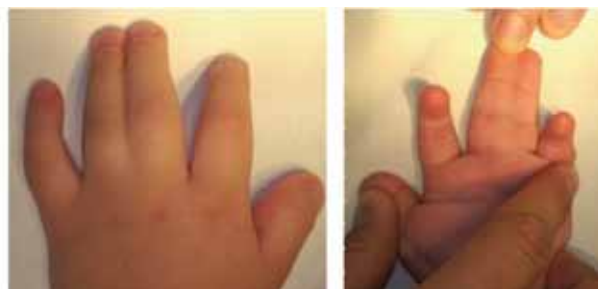


Fig. 2. Simple total form of syndactyly



Fig. 3. Using V-Y flap for release of subtotal congenital syndactyly



Fig. 4. Using dorsal plane-shaped advancement flap for the reconstruction of web space



Fig. 5. Using hourglass dorsal advancement flap for the reconstruction of web space



Fig. 6. Using squaredorsal advancement flap for the reconstruction of web space

CONCLUSION

Syndactyly is a complex defect of the hand, which requires a differentiated approach in the choice of surgical correction methods. The most effective are operations that allow the formation of web spaces without using skin grafts. Given this, the task of the orthopedic surgeon is to select the optimal technique that will be the least traumatic and more cosmetically beneficial.

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A NEW METHOD FOR SURGICAL TREATMENT OF CYSTS LOCATED IN THE HEAD OF THE PANCREAS

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ABSTRACT — Over the past two decades, the number of patients with cystic formations of the pancreas has increased significantly. Especially the most productive part of the population aged 35–50 years suffers from this disease. The question of the choice of optimal and rational treatment policy is still an actual problem of modern surgery. The problem of choosing the most radical and at the same time the organ-preserving technique, helping to improve the immediate and long-term results, the quality of life and social and labor rehabilitation, has not lost its relevance, and the studies carried out in this area are currently important.

KEYWORDS — cyst of the pancreas, internal drainage, pancreatocystogastrostomy.

INTRODUCTION

Among experts there is no consensus in matters of surgical tactics for pancreatic cysts [2]. The range of surgical interventions performed for pancreatic cysts is quite wide: external drainage of cysts, enucleation of a cyst, various in volume resections of the pancreas together with a cyst (radical operations), the formation of internal fistulae between the cyst wall and various sections of the gastrointestinal tract.

Internal drainage of pancreatic cysts is most prevalent. The frequency of its use reaches from 30 to 60% [4, 5, 6].

Indications for internal drainage of pancreatic cysts are [2, 6, 7]:

1. The presence of single-chamber pancreatic cysts formed with the capsule communicating with the ductal system of the pancreas
2. Cysts of retention
3. The location of pseudocysts in the head of the pancreas
4. Cystic expansion of the main pancreatic duct.

Performing internal drainage is especially advisable when pancreatic cysts are located in the head of the pancreas, since [4]:

1. radical operations are technically difficult to perform, due to the trauma of the pancreas
2. external drainage in most cases is complicated by long-existing external pancreatic and purulent fistulas in 15–30% of patients, and the rapid closure of the puncture channel, followed by recurrent cyst formation in 20–60% of patients

The final decision on the formation of a specific type of cysto-digestive anastomosis is made during surgery and depends on many factors including the nature, location, size, number of cysts, degree of maturity, the condition of the wall and characteristics of the contents of the cyst, as well as the condition of the ductal system of the gland.

The main methods of internal drainage are:

1. Cystojejunostomy;
2. Cystogastrostomy;
3. Cystoduodenostomy

Most often, surgeons use cystojejunostomy. Along with the obvious advantages of this method it has disadvantages:

1. Effect of tension of organs stitched together due to short mesentery of the small intestine;
2. Disorders of digestion, malabsorption due to the penetration of pancreatic juice through the anastomosis below the duodenal junction;
3. Adhesive process in the abdominal cavity;
4. Tight fusion of the cyst with the posterior wall of the stomach.

In addition, enterokinases released into the lumen of the small intestine, cause activation of trypsinogen, leading to the destructive action of the anastomosis zone, causing its failure. When applying the longitudinal pancreato-cysto-jejuno-anastomosis, postoperative complications developed in 20% of cases [6].

Cystoduodenostomy is the rarest variant of internal drainage of pancreatic cysts. Its application is shown in cases when the cyst is located in the head of the pancreas and performing a transventricular operation is difficult for some reason. But at the same time, cystoduodenostomy has drawbacks: significant technical complexity; danger of injury to the pancrea-

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roduodenal vessels and intrapancreatic choledochus. According to C. Frey, when cysto-duodeno-anastomosis was applied, the outcome was fatal in 40% of patients, and 20% of those operated on had chronic pancreatitis. [3].

Currently, endoscopic drainage is widely used in the treatment of patients with pancreatic cysts [5, 7]. This also includes an endoscopic imposition of cystogastro-anastomoses and cystoentero-anastomoses, as well as transpapillary stenting of the pancreatic duct [11]. The disadvantages of these types of operations are: the difficulty of hemostasis in the area of the anastomosis, the impossibility of a thorough revision of the cavity of pseudocyst [10]. The most frequent of them are suppuration of the contents of the cyst as a result of reflux of the contents of the stomach and duodenum, bleeding from the puncture site and fistula in the process of performing transmural access and stenosis of the anastomosis. In addition, when performing transluminal drainage without the use of visualization tools, a perforation of the hollow organ of the abdominal cavity, bleeding from large vessels is possible [9]. Recurrence rate can reach 25% [9]. In transpapillary drainage, inflammatory changes in the parenchyma and in the main pancreatic duct are the most common complications (35%) [7, 1]. Less common complications: occlusion of the stent, bleeding, perforation, the addition of infectious complications and migration of the stent. Moreover, the frequency of migration of the stent is 3–15% [1].

Cystogastrostomy is technically the most simple, fairly safe and appropriate intervention for cysts of the pancreatic head [6]. At the same time:

1. penetration of food masses into the cyst cavity leads to the development of pancreatitis;
2. long-term stagnation of food masses in the cavity of the cyst leads to the development of suppurative processes;
3. powerful peristaltic waves of the stomach can lead to the eruption of the sutures and subsequently to the failure of the sutures.

The desire to reduce the number of common and local postoperative complications forced us to look for new methods of surgical treatment of patients with chronic pancreatitis with pancreatic cysts.

The purpose of the research was to develop a new method of surgical treatment of cysts of the pancreatic head using the pyloric antrum part of the stomach.

MATERIALS AND METHODS

In the experiment on 12 mongrel dogs, we developed a new method of surgical treatment of cysts of the pancreatic head. A patent of the Russian

Federation No. 2571711 dated November 25, 2015 was obtained for the developed method [8]. The experiments were performed in the laboratory of Astrakhan State Medical University in accordance with the International Recommendations for Biomedical Research using Laboratory Animals (Strasbourg, 1986).

To monitor the degree of inflammatory response and the depth of the pancreatic secretory function in experimental before the operation and at 1-4, 7, 14 day and 1, 3 and 6 months after the operation, serum amylase and blood glucose concentrations were evaluated using an IDEXX VetTest 8008 biochemical analyzer.

The statistic work-out of data was carried out on a personal computer using specialized program Statistica 6.0 for Windows-XP. The following parameters were calculated: M - arithmetic mean, m - standard error of the mean, p-level of statistical significance, σ - standard deviation. Significant differences between the mean values were estimated using Student's t-test with a confidence coefficient $p < 0.05$

RESULTS AND DISCUSSION

The developed method consists in the following. Under general anesthesia, after median laparotomy, some 5 cm from the pylorus, both along the greater curvature and minor curvature, after mobilization of areas of the stomach over 3 cm in the proximal direction, the pyloric part of the stomach was dissected (Fig. 1). Then, through the gaping hole of the pyloric stomach, puncture of the cyst of the pancreatic head was performed, the back wall of the pyloric and anterior wall of the cyst of the pancreas was dissected over 3 cm. The contents of the cyst were removed, an endoscopic revision of the cyst was performed. Having achieved thorough hemostasis, then we sutured the formed "front lip" of the future fistula between the posterior wall of the pyloric department and the anterior wall of the cyst with a continuous suture with absorbable material (vicryl) (Fig. 2). After that, the pyloric orifice was sutured tightly with a single-row suture using an atraumatic thread (Fig. 3). The continuity of the gastrointestinal tract was restored by imposing an anastomosis between the stomach and the jejunum on the type of end to side (Fig. 4).

The proposed method of pancreatocystogastrostomy includes:

1. Isolation of the fistula zone from food masses, which is the prevention of the development of pancreatitis and suppurative processes;
2. Obstacle of activation of trypsinogen due to the weakly acidic environment of the pyloric department, which is the prevention of the development of insolvency of fistula sutures and secondary bleeding;

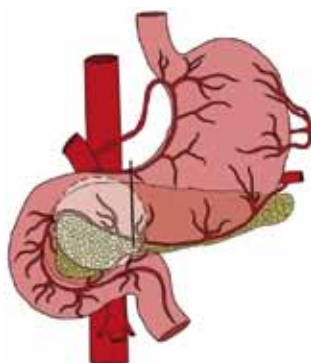


Fig. 1.

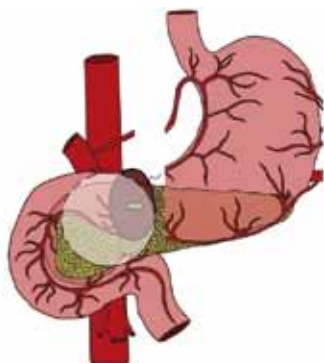


Fig. 2.

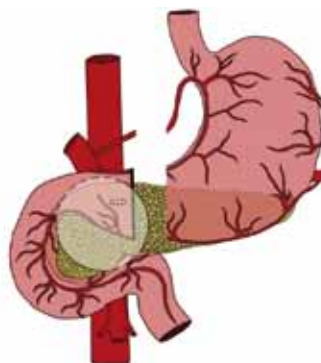


Fig. 3.

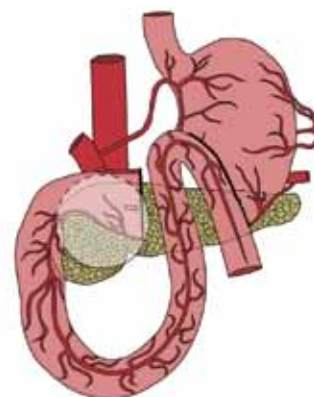


Fig. 4.

3. The lack of powerful peristaltic waves of the pyloric part of the stomach, preventing tension of the anastomotic zone, which is a prevention of insolvency of fistula sutures;
4. The lack of the effect of the tension of the organs due to the proximity of the pyloric part of the stomach to the pancreas, which is the prevention of the failure of the anastomotic sutures.

The results of dynamic monitoring of serum amylase and blood glucose concentrations in operated animals are presented in table 1.

— 1412 ± 10.2 (units/l); blood glucose — 9.4 ± 0.24 (mmol/l), and by the 3rd month all indicators almost reach baseline values.

CONCLUSIONS

Summarizing the data obtained during the experiments, we found that the draining operation of pancreatocystogastrostomy using the pyloric antrum of the stomach is technically feasible and does not lead to any functional impairment of the general condition of the animals, except for the first 3–4 days after

Table 1. The average values of blood amylase and blood glucose before and after pancreatocystogastrostomy.

Research date	Number of cases	Blood amylase (units / l)				Blood glucose (mmol / l)			
		M	$\pm m$	$\pm \sigma$	P>	M	$\pm m$	$\pm \sigma$	P>
Before surgery	12	648	1,5	2,4	0,01	4,8	0,04	0,22	0,01
1 day	12	1828	2,4	10,6	0,04	13,4	0,03	0,18	0,01
2 day	12	1796	2,3	8,8	0,04	13,1	0,03	0,16	0,01
3 day	12	1748	2,3	8,2	0,04	12,9	0,02	0,17	0,01
4 day	12	1622	2,2	9,2	0,03	12,7	0,08	0,36	0,01
7 day	12	1412	2,4	10,2	0,04	9,4	0,07	0,24	0,01
14 day	12	864	2,2	8,2	0,02	7,9	0,04	0,15	0,01
1 month	9	746	2,3	8,7	0,03	7,8	0,05	0,15	0,01
3 months	6	686	1,7	1,9	0,01	6,85	0,04	0,1	0,01
6 months	3	658	1,8	1,9	0,01	5,2	0,04	0,12	0,01

As a result of biochemical analysis, it was found that on the first day after surgery an increase in amylase occurs from 648 ± 2.4 (units/l) to 1828 ± 10.6 (units/l), that is, 2.9 times, and glucose blood from 4.8 ± 0.22 (mmol/l) to 13.4 ± 0.18 (mmol/l), that is, 2.8 times. Starting from the 7th day after the operation, these indicators show a steady decline (blood amylase

operation. Good results made it possible to apply this method in the clinic in 5 patients. Operated patients were examined after 5 years. All patients recovered. No complaints. Patients do not have a deficiency of body weight, they have retained the ability to work. This method can be applied in clinical practice.

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COMPLICATIONS AFTER ARTHROPLASTY FOR BONE TUMORS

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INTRODUCTION

The incidence of bone tumors is 0.5–2% per 100 thousand population. Arthroplasty is the main type of organ-sparing surgery in patients with bone tumors in 90% of cases. But at the same time, the effectiveness of arthroplasty is caused by complications that lead to repeated operations, including re-prosthetics. Revision endoprosthetics in primary oncologic endoprosthetics is about 30% [1], and the risk of re-grafting in five years is 12–32%, in 10 years — 25–61% [2]. The literature reports that the main complications after arthroplasty are: infectious complications, aseptic instability of the endoprosthesis, a fracture of the endoprosthesis design, wear of the plastic parts of the endoprosthesis [3, 4, 5, 6]. Thus, complications after joint arthroplasty is a significant problem that leads to dysfunction and sometimes loss of limb, significantly worsen the quality of life of patients who underwent joint arthroplasty for long tubular bone tumors.

MATERIALS AND METHODS

In the clinical departments of the State Institution “Institute of Traumatology and Orthopedics of the National Academy of Medical Sciences of Ukraine” for the period from 2009 to 2019, 167 operations were performed for bone tumors in the volume of segmental bone resection followed by arthroplasty or re-prosthetics of the joints and bone segments. 110 patients received implantation of domestic oncologic endoprostheses, 57 patients received implantation of foreign modular endoprostheses. Morphologically, the following types of tumors were observed: giant cell tumor of the bone, osteogenic sarcoma, chondrosarcoma, fibrosarcoma and metastatic tumors. Replacement of the knee joint was performed in 95 patients, shoulder — 22, hip — 20, ulnar — 9, ankle — 6, diaphysis of the femur — 5, diaphysis of the tibia — 4, diaphysis of the humerus — 4, diaphysis of the radial bone — 1, hip and knee (megaprosthesis) — 1. During endoprosthesis replacement, the basic principles of oncological surgery radicalism and ablative surgery were

observed. Removal of the tumor was performed in one block with excision of the biopsy site with covering the endoprosthesis with surrounding muscles. For fixation of muscles, polymer tubes Mutars (Germany) were used, which increased tropism to soft tissues, which contributed to the rapid restoration of the natural muscle attachment point. Cement implant fixation was used for endoprosthetics. Pathological fractures were observed in 43 patients before surgery, 25 patients underwent various orthopedic surgeries before endoprosthetics, 74 patients underwent chemotherapy before surgery, 30 patients underwent radiation therapy before surgery, which played an important role in the occurrence of postoperative complications. In all cases, endoprosthetics were used to measure the volume of the resected bone segment. The length of the resected bone segment, the duration of anesthesia and blood loss during the operation were taken into account, which also influenced the development of postoperative complications. The functional result of the operated limb was calculated on the MSTS scale. The quality of life of patients was determined by points according to the EORTC QLQ-30 questionnaire. Patient survival was determined by the Kaplan-Meier method.

RESULTS

After primary oncologic endoprosthetics, 51 (30,5%) patients experienced complications in different postoperative periods, 37 (22,2%) of them underwent re-endoprosthetics. The most frequent complications after arthroplasty were the following: infectious — 24 cases, aseptic loosening of the endoprosthesis leg — 21, fracture of the endoprosthesis design — 5, wear of the polyethylene parts of the endoprosthesis — 1. Recurrences of the tumor were observed in 13 (7,8%) patients. The functional outcome of the limb (on the MSTS scale) after hip joint arthroplasty was 80%, femur diaphysis 94%, knee joint 84% of the tibial diaphysis 92%, ankle joint 70%, shoulder joint 70%, diaphysis of the humerus — 96%, of the elbow joint — 78%, diaphysis of the radial bone — 90%, hip and knee (megaprosthesis) — 72%. The quality of life of patients after arthroplasty has increased from 40–50 to 75–80 points. The total three-year survival of patients was 82,2±0,14%, the five-year one — 65,8±0,26%.

CONCLUSIONS

The main complication factors after arthroplasty in patients with bone tumors were the following: previous surgery, previous chemotherapy or radiation therapy, tumor localization, tumor volume removed, length of resected bone fragment relative to bone length, duration of surgery, and amount of blood loss during surgery, implant design and implant installation technique.

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OPTIMIZATION OF SURGICAL TREATMENT IN DENTAL IMPLANTATION IN DIFFICULT ANATOMICAL CONDITIONS WITH RECONSTRUCTIVE INTERVENTIONS

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INTRODUCTION

Dental implantation in dental surgery makes up from 8 to 36% of all types of treatment, and among cases requiring inpatient treatment — 10–57% [1]. The modern approach to the use of implantation in difficult anatomical conditions includes the implementation of measures aimed at creating optimal conditions associated with the restoration of bone tissue. In spite of the fact that today dental implantation is the most effective and high-tech method of prosthetics for lost or completely missing teeth in the shortest possible time and with maximum comfort for patients. Issues concerning the period of implantation, problems of rejection, determination of not only clinical, but also morphological criteria for signs of implantability of implants, as well as the possibilities of re-implantation after rejection of the implanted structure, are still not fully resolved. The appearance among the surgical methods of the methods of preparing the mouth for prosthetics and implantation has greatly reduced the severity of the problem with the fixation of the prostheses on the edentulous jaws. Results of surgical treatment for partial or complete anodontia are not always satisfactory. In some patients, due to the lack of load, the alveolar processes of the jaws atrophy, which makes implant placement impossible [8]. A number of researchers, in order to improve the fixation of prostheses, offer various ways to increase the alveolar part of the jaws: alveolar plastic with auto-bone, allogeneic, xenogenic and artificial materials. The initial volume suitable for successful implantation is achieved with the help of various types of bone plastics, which are selected subjectively, without relying on objective, pathogenetically substantiated criteria, as which you can use the state of the structures of local immune homeostasis

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in the implantation zone. A significant proportion of patients with surgical treatment and dental implantation should be carried out pathogenetically justified, taking into account the morphological indicators of readiness of the oral mucosa for surgical treatment. This will significantly reduce the time of treatment, hospital stay, improve the results of treatment, prevention of complications of dental implantation [3]. Implantation causes a state of secondary immunodeficiency, determined primarily at the organism level. Despite the fact that studies have been conducted that prove the impaired function of cellular and humoral immunity during implantation [9], at the present stage there are only a few studies on local factors of immune protection. Not only prevention of the development of purulent-necrotic tissue changes, but also the processes of epithelialization, angiogenesis, and the formation of intimate connections of the implant with the surrounding tissues depend on the activity of immunocompetent cells. These cells are regulators of regeneration processes [2]. However, studies on the comparative characteristics of the local immune status in implant placement are practically absent, and the available work has been performed mainly in experiments on animals [5, 7]. There are practically no data on the possibility of dental implantation and long-term results in patients with myeloma, with osteoporosis, on the background of oncological diseases, with endocrine pathology, as well as after extensive injuries of the facial skull. Therefore, the study of the activity and state of the ensembles of immunocompetent cells in the area of dental implantation is relevant and is among the main key problems of dentistry.

OBJECTIVE

To study the patterns of changes in the immune homeostasis of the oral mucosa in the dynamics of dental implantation in patients of different age groups under normal and pathological conditions in order to increase the effectiveness of treatment and prevention of complications.

METHODS

The material was obtained from patients of dental hospitals that were observed during the preparatory reorganization of the oral mucosa, during bone reconstructive measures before the implants were installed and during the implants installation with the subsequent observation of reparative regeneration processes. The study was carried out taking into account the provisions of the Helsinki Declaration (2013) and with the permission of the Ethics Committee of the Far Eastern Federal University. The material was obtained in accordance with the nomenclature of clinical laboratory studies of the Ministry of Health of the Russian Federation (Order No. 64 of February 21, 2000). Clinical material for the study was obtained on the basis of the FEFU medical center (Vladivostok) during 2012–2017. The study included patients diagnosed with myeloma, cancer, injuries of the maxillofacial area, ectodermal dysplasia. The patients underwent reconstructive operations with taking tissue fragments to be disposed of for this study. After surgery, patients continued to receive glucocorticoids to prevent further relapses. The study took into account the age of patients, gender, anatomical topography of damage to the facial part of the skull. The analysis of the material was carried out using classical morphological and immunohistochemical methods with the identification of diabetes positive cells of various differentiation. The material was embedded in paraffin or frozen in a cryostat for the preparation of sections. Filling in paraffin was carried out according to the classical method. The localization of CD4, CD8, CD34, CD68, CD163, CD203a, p53, p63 of the company DAKO for the illustration and subsequent comparative analysis of the dynamics of their number in different periods of dental implantation was detected. For labeling CD163, clone 10 D6, a class of immunoglobulins IgG1, was used. Unmasking of antigenic determinants was carried out in a glass container filled with a regenerating solution and creating the conditions of a water bath for 1 hour. Part of the preparations was treated with microwave radiation, which gives the best unmasking effect, within half an hour. A 10 mmol/l citrate buffer, pH 6.0 or DAKO TRS (Target retrieval solution, code No. S 1700) was used for the unmasking of antigens. The cooled preparations were washed in distilled water. Antibodies were used at a dilution of 1:50 and 1: 100. The brown color indicated a positive reaction.

RESULTS

The value of indicators of the content of effector immunocytes in the clinical and morphological reaction was proved when implantation was used in dental patients in normal conditions and with comorbidities.

The role of immunocompetent effector cells of the oral mucosa as an important prognostic criterion for the success of dental implantation is shown for the first time. Algorithms for choosing the terms of dental implantation are developed and proposed, which allow to exclude the occurrence of clinical manifestations of implant rejection, substantiating the prognostic efficiency of the use of dental implantation and prognosis in various states of local immune mucosal homeostasis in different age groups in normal conditions and with comorbidities. A tightly attached keratinized mucosa around endosseous dental implants is believed to be protective against peri-implant bone loss. According to Kaufmann R, Bassetti R, Mericske-Stern R, Enkling N. (2014). tension caused by buccal frena and mobile non keratinized mucosa is to avoid. This case report documents the optimization of peri-implant mucosal conditions in the upper and lower jaw. At the time of second stage surgery (re-entry) at submucosally osseointegrated dental implants an enlargement of keratinized mucosa and a thickening of soft tissue was obtained administrating a vestibuloplasty combined by a free gingival graft or a vestibuloplasty combined by an apically moved flap [4]. The clinical efficacy of using the developed algorithms when choosing the terms of implantation after the surgical treatment of dental patients on the basis of a survey of the state of the local immune homeostasis of the oral mucosa has been proven. For the first time, a medical tactics for the management of dental patients has been proposed, which allows preventing and eliminating the occurrence of clinical manifestations of complications of dental implantation against the background of various pathologies, taking into account the plasticity of the epithelial barriers of the oral mucosa. Materials of the thesis were the basis for the development of additions to the algorithms of examination of dental patients on the background of osteoporosis, multiple myeloma, oncological and endocrine pathology in need of dental implantation, which actually contributed to the improvement of the quality of surgical care and the efficiency of dentists and maxillofacial surgeons. Recommendations were developed for optimal and effective dental implantation in patients of different age groups, introduced into practical healthcare in the work of public and private dental clinics of Primorsky Krai and the city of Vladivostok. Despite the success of implantation, cases of rejection, the presence of patients with relative and absolute contraindications and risks when installing implants, the terms of using implants dictate not to stop there, but to improve the methods of surgical intervention, develop cellular technologies and strategies to improve osseointegration and reparative regeneration the development of implant coatings

using nanotechnology and osteoinductor coatings, as well as the search for overshennyh materials for replacement in autologous transplantation [6].

DISCUSSION

The existing framework of diagnostic measures does not fully meet the clinical needs of modern dentistry, since they give a conditional assessment of the processes occurring during osteointegration and osteosynthesis [2]. For the development of personal medical approaches and ideas about the processes occurring during reparative regeneration in the area of implant installation, an extension of the diagnostic resource is required. This will allow not only to predict the success and outcomes of implantation, but also to develop new strategies at the cellular and molecular levels [5]. To create all the conditions for normal reparative regeneration, in an optimal time sequence and with a certain spatial distribution of cells and signaling molecules involved in this particular healing process, it is necessary to have clear ideas about the mechanisms of reparative regeneration of periodontal structures [3].

With significant violations of tissue regeneration, the development of local distortions of local or systemic processes of cell regeneration, restriction of blood supply due to systemic shifts and major defects that occur, the use of implantable materials, membranes or biological agents is limited, and ideally their use should be accompanied by careful selection to promote the predictable and sufficient quantity and quality of regenerated tissue. According to P.A. Shajahan et al. (2018), the ability to quickly treat adentia becomes a real need [5]. The study of tissue reaction to the implant in the zone of reconstruction of the damaged periodontal and lost bone is the main area in which molecular mediators should be used and investigated [2]. Infectious antigens that produce biofilm microorganisms are one of the main causes of failed dental implants. It should be borne in mind that the survival of dental implants is an individual process [4]. The timing of osseointegration depends on the area in which the implantation was performed, as well as on the quality of the bone tissue [9]. In general, the implantation of dental implants lasts from three months in the lower jaw to six months in the upper [5]. The understanding of complex mechanical bone behavior and size-dependent properties ranging from a nano- to a macroscopic level are essential in the biomechanical optimization of implants. Shibata Y, Tanimoto Y, Maruyama N, Nagakura M. (2015) The requirements of regenerated tissue at the interface include high strength, fracture toughness related to ductility, and time-dependent energy dissipation and/

or elastic-plastic stress distribution. Moreover, a strong relationship between strain signals and peri-implant tissue turnover could be expected, so that ideal implant biomechanics may enable longevity via adaptive bone remodeling [5].

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THE DYNAMICS OF MICROLYMPHATIC FLOW IN TWO-STAGE SURGICAL TREATMENT OF PILONIDAL ABSCESS AND THE USE OF REGIONAL LYMPHATIC AND NO-THERAPY

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ABSTRACT — Comparative results of non-invasive laser Doppler flowmetry of micro-blood-flow and micro lymphatic flow in the tissues adjacent to the wound with two-stage surgical treatment of 29 patients with pilonidal abscesses are given. In the studied group of patients (15), regional lymphatic therapy (RLT) and NO-therapy were performed. In the comparison group (14), comparable by sex and age, the treatment was carried out by the traditional administration of similar antibiotics, immunomodulator and UHF-therapy. It was revealed that in the studied group, the micro-blood-flow and lymphatic flow normalized almost 2 days earlier due to regional lymphotropic antibiotic, immune and NO-therapy.

KEYWORDS — piloid abscess, micro lymphatic flow, lymphatic and NO-therapy.

INTRODUCTION

Restoration of hemodynamics in the microvasculature and lymphatic flow in the wound walls and adjacent tissues depend on the effectiveness of the drug therapy aimed at suppressing the activity of wound microflora and stimulating local immune protection [1,2].

Thanks to the creation of the LAKK device cluster (NPP “Lazma”, Russia), in particular “LAZMA MC”, it became possible to conduct laser Doppler flowmetry and explore the state of the microhemolymphocirculation [3, 4, 5]. Information on laser Doppler flowmetry in the application of regional lymphotropic antibiotic, immune and NO-therapy in the complex treatment of piloid abscesses is absent in both domestic and foreign scientific literature.

MATERIALS AND METHODS

Micro-blood-flow and micro lymphatic flow were studied in 15 male patients (mean age 22 ± 1.4 g) treated with regional lymphotropic administration of cefotaxime 1.0, diluted in 4 ml of a 0.5% lidocaine solution + 32 units of Lydazum and Imunofan (50 mg,

diluted in 4 ml of 0.9% sodium chloride solution) at 48 hour intervals. Every day, with a 5-minute exposure, the wound and the adjacent tissues were treated with a stream of exogenous nitric oxide (ENO) produced by the Plason device in the stimulator mode from a distance of 25 cm from the nozzle. In the comparison group (14 men), comparable by sex and age, the treatment was carried out by traditional administration of similar drugs and UHF-therapy. Installation of sensors for information retrieval was carried out in 1 cm from the upper angle, to the right and left of the postoperative wound in the middle part of it at different times: after the operation, after days 1, 3 and 6 from the start of treatment. Information retrieval was carried out in the supine position, at a room temperature of 25°C . Reference values were obtained from 9 healthy males aged 20 to 22 years. We studied M — the average flow in the microcirculatory bed, Q — an indicator affecting the constancy of particles in the lymphatic bed and L — coefficient of red blood cell dispersion in the probed tissue volume. Reference values of these indicators were obtained from 9 healthy males aged 20 to 22 years. The research results were compared with the clinical course of the wound process and were analyzed by methods of variation statistics using the Statistica 6.0 program. The research results are presented in the table 1.

In the comparison group, the indicators M, Q, Kv before the surgery scarcely differed from those ($p < 0.05$) of the main group and on the day 3 of postoperative treatment only approached the results obtained on the 6th day of treatment in the main group. Thus, the application of the developed algorithm for the complex treatment of piloid abscesses has a pathogenetically substantiated effect on the course of the wound process. RLT in combination with the processing of paravulnar tissues by the ENO stream produced by the “Plason” device in the “stimulator” mode, contributes to its earlier transition to the regeneration phase.

Thus, the application of the developed algorithm for the complex treatment of pilonidal abscesses has a

Table 1. Dynamics of indicators of the results of laser Doppler flowmetry of the micro-lymphocytic circulatory bed of postoperative wounds of the piloidal area in the studied group of patients (n — 15)

Wound area	Reference indicators	After surgery	Day 1	Day 3	Day 6
Microcirculation indicators					
Upper angle:	M	6,71±1,23	3,76±1,28	6,71±1,23*	9,76±1,22**
	Q	0,67±0,09	3,67±0,19	2,67±0,09*	1,61±0,09*
	Kv	9,64±2,1	49,62±4,1	39,64±2,1*	19,64±2,10*
Right edge:	M	8,7±1,25	3,76±1,28	10,56±1,20*	9,56±1,20*
	Q	0,69±0,10	4,61±0,17	3,68±0,19*	1,58±0,19*
	Kv	9,84±2,6	48,72±3,6	39,62±4,0*	19,62±3,1*
Left edge:	M	9,1±2,0	4,76±1,20	11,56±1,20*	10,56±1,20*
	Q	0,72±0,11	2,70±0,18	2,17±0,15*	2,01±0,15*
	Kv	9,95±2,5	48,62±4,22	38,62±4,11*	18,52±4,11*
Lymph flow Indicators					
Upper angle:	M	0,57±0,09	3,76±0,28	1,71±0,23*	1,06±0,20**
	Q	0,71±0,10	3,67±0,19	1,97±0,09*	1,28±0,18*
	Kv	10,12±2,7	49,62±4,1	39,64±2,1*	29,64±2,10*
Right edge:	M	0,78±0,12	0,16±1,28	1,66±1,20*	1,06±1,20*
	Q	0,79±0,02	3,64±0,18	1,98±0,08*	1,28±0,19*
	Kv	19,84±3,54	49,62±4,1	39,60±4,3*	29,62±3,1*
Left edge:	M	0,80±0,09	4,76±1,20	11,80±1,21*	10,56±1,20*
	Q	0,80±0,08	2,70±0,18	2,09±0,15*	2,07±0,15*
	Kv	20,01±2,96	48,62±4,22	38,60±4,11*	28,62±4,11*

* $p < 0,05$ from the start of treatment; ** $p < 0,01$ from the start of treatment

pathogenetically substantiated effect on the components of the course of the wound process. RLT in combination with the processing of paravulnar tissues with the ENO stream produced by the "Plason" device in the "stimulator" mode contributes to earlier stopping of the inflammation phase of the wound process.

The dynamics of the result indicators of laser Doppler flowmetry of the micro-blood-flow and lymphatic flow in the study group confirm a more rapid normalization of the micro-blood-flow in the paravulnar tissues and the lymphatic-stimulating effect of regional antibiotic, immuno- and NO-therapy, which ultimately improves the quality of complex treatment of abscesses in the pilonidal area.

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THE USE OF RADIATION THERAPY IN THE SYMPTOMATIC TREATMENT OF OSTEOARTHRITIS OF THE KNEE

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INTRODUCTION

Osteoarthritis affects over 20% of the world's population. The prevalence of osteoarthritis in patients over 35 years old reaches 50%, while in patients over 55 years old reaches 80% [1]. Deforming osteoarthritis is the cause of chronic pain in 45% of the population of economically developed countries of the world [4, 5]. In the treatment of osteoarthritis, non-steroidal anti-inflammatory drugs, aimed at relieving pain, and cartilage repair have become widespread [2, 3, 7]. Physiotherapy is often used to treat inflammatory changes in the joint. All of the above methods of treatment are included in modern standards for the treatment of osteoarthritis, but in some cases they are not effective enough, which leads to the search for alternative methods. The latter includes orthovoltage radiotherapy, which is prescribed in cases of ineffectiveness of standard treatments for osteoarthritis [6]. Orthovoltage radiotherapy is an effective treatment for osteoarthritis, pain reduction occurs in 65-90% of patients, and minimal doses of X-ray radiation used to treat osteoarthritis do not cause tissue damage [6].

MATERIALS AND METHODS

Treatment with orthovoltage radiotherapy was performed in 39 patients with deforming osteoarthritis of the knee joint. X-ray stage III was determined in 29 (74,4%) patients, and X-ray stage II — in 10 (25,6%). The course of orthovoltage roentgenotherapy was performed on a radiotherapy device "RUM-17". Irradiation at a voltage of 200 kV, a current of 10 mA, a layer of half attenuation of 1,7 Cu, a filter of 1,0 mm Cu and 1,0 cm Al and a focal length of 46 cm with an interval of 48 hours. Single doses were 0,50–1,0 Gray, total 5,0 Gray. The severity of pain in osteoarthritis of the knee joint was assessed according to the VAS scale (Visual Analog scale), in mm on a 100-mm scale (no pain — 0, maximum pain syndrome — 100), WOMAC scale (Western Ontario and McMaster rate arthrose index), mm and the Lequesne index (in points).

RESULTS

When assessing the effectiveness of orthovoltage radiotherapy, it was established that there is a decrease

in the level of pain syndrome measured on a VAS scale at rest, the WOMAC and the Lequesne index throughout the entire observation period. The level of VAS scale at rest and WOMAC did not exceed 20 mm 3 years after treatment, and after 5 years did not exceed 10 mm. There was also a decrease in the time of pain from 15 minutes to 3,5 minutes. The range of motion in the knee joint increased to 80% by the end of 3 years of observation. The values of the Lequesne index decreased from 14 to 5 points 3 years after treatment.

CONCLUSIONS

1. o-voltage low-dose radiotherapy is a clinically more effective, compared with the standard, treatment of osteoarthritis.

2. Long-lasting and more pronounced analgesic effect gives grounds to recommend orthovoltage radiotherapy as the method of choice in the treatment of osteoarthritis.

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ESTIMATION OF SURGICAL TREATMENT EFFICIENCY FOR YOUNG CHILDREN WITH HIP DYSPLASIA BASED ON X-RAY ANATOMICAL DATA

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INTRODUCTION

Hip joint (HJ) dysplasia is a set of pathological anatomical and functional anomalies, including poor development of the hip socket (HS), the proximal femur (PF), ligamentous apparatus failure, which is accompanied by a disturbed relationship of the joint parts [1–4]. Joint radiography in young children still remains the only reliable way for diagnosing and identifying the severity of dysplastic changes in the HJ [5, 6], which determines the treatment [7–10]. One of the major objectives for treating HJ dysplasia is the approximation of the joint bone structures relationships to the age norms.

Aim of study.

To propose an effective system for assessing the severity of HJ dysplastic changes in young children, which would help determine the treatment method, and comparing the joint radiological parameters prior to surgical treatment and in the early postoperative period.

Objects and methods of study.

The study was based on analyzing dysplastic HJ changes in 82 children (113 joints) aged 1–3, with a mean age of 2.3 ± 0.8 . All the patients were treated in the Child Trauma and Orthopedics Department of

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Research Institute for Traumatology, Orthopedics and Neurosurgery of Saratov State Medical University within the period of 2015–2018. The study was conducted upon receipt of the respective child's parents' due consent subject to Clause 32, Basics of Russian Legislation on Health Protection. The results of the study were compared with similar indicators for 32 children of the same age (mean age 2.4 ± 0.6 years) revealing no signs of HJ dysplasia. Apart from a set of examinations including clinical and electrophysiological methods, the children had 6 HJ angular parameters evaluated on radiographs following the degree of deviation from the age norm. We identified the following: Wiberg angle (WA), Sharp's angle (SA), acetabular angle (AA), cervical-diaphyseal angle (CDA), femoral neck anteversion angle (AtA), vertical correspondence angle (VCA), which were scored in points (from 0 to 3), identified the parameters severity (mild — from 2 to 7 points, moderate — from 7 to 13, severe — from 14 to 18 points) and determined the treatment [8].

Data format: $M \pm \sigma$. In order to evaluate the treatment results, Cohen's concept of effect size was employed, which was calculated following the formula:

$R = (\text{Mean score before surgery} - \text{Mean score after surgery}) / \text{Standard deviation before surgery}$ [11].

RESULTS

The normal (N) value for the AA in children aged 1–3 is $20^\circ - 25^\circ$; at an angle of $26^\circ - 30^\circ$ it is estimated at 1 point, at $31^\circ - 35^\circ$ — at 2, with an angle of $> 35^\circ$ — at 3 points; CDA ($130^\circ - 145^\circ$ — N, $146^\circ - 154^\circ$ — 1, $155^\circ - 160^\circ$ — 2, $> 160^\circ$ — 3 points); SA ($45^\circ - 49^\circ$ — N, $50^\circ - 55^\circ$ — 1, $56^\circ - 60^\circ$ — 2, $> 60^\circ$ — 3 points); WA ($30^\circ - 21^\circ$ — N, $20^\circ - 16^\circ$ — 1, $15^\circ - 11^\circ$ — 2, $< 11^\circ$ — 3 points), VCA ($> 75^\circ$ — N, $74^\circ - 70^\circ$ — 1, $69^\circ - 65^\circ$ — 2, $< 64^\circ$ — 3 points); AtA ($16^\circ - 34^\circ$ — N, $35^\circ - 45^\circ$ — 1, $46^\circ - 55^\circ$ — 2, $> 55^\circ$ — 3 points). 28 children (33 joints) were found to have mild dysplastic alterations, 31 (42 joints) — moderate, and another 23 (38 joints) — severe. In mild cases of dysplasia were recommended dynamic observation and, if necessary, conservative treatment and coxarthrosis prevention. For moderate cases, an intertrochanter osteotomy of the proximal femoral bone was used with calculated medioli-

zation; in severe cases, combined surgery on the proximal femoral bone with pelvic osteotomy was the treatment of choice. The mean values of the HJ angular parameters after the surgery approached the age norms. In patients with moderate dysplastic HJ changes, the average values of angular signs increased: WA — from 13.0° to 23.0° (by 43.5%); VCA — from 67.0° to 77.5° (by 13.6%); the other angles, on the contrary, decreased: SA — from 58.0° to 44.0° (by 21.2%), AA — from 33.0° to 21.5° (by 34.9%); CDA — from 157.0° to 135.5° (by 13.5%); AtA — from 51.0° to 23.5° (by 44.0%). The mean score sum in children with moderate dysplastic changes prior to the treatment was 11.7; the mean score was 1.95 ± 0.5 points, and the mean score in the group after surgery was 1.3 ± 0.2 points. The mean effect was 1.3, which can be defined as strong ($R = (1.95 - 1.3) / 0.5 = 1.3$).

The patients with prominent dysplastic changes had a decrease in the HJ values: SA — from 63.0° to 43.0° (by 31.7%); AA — from 40.0° to 20.5° (by 48.8%); CDA — from 162.0° to 135.0° (by 16.3%); AtA — from 62.0° to 23.0° (by 62.9%); WA had an increase from 8.0° to 24.0° (by 66.6%), VCA — from 62.0° to 78.5° (13.5%). The effect size in children with prominent HJ dysplasia was 0.87 (strong effect), the mean score of dysplastic signs based on radiographs before the surgery was 2.3 ± 0.7 points, after — 1.45 ± 0.2 points ($R = (2.3 - 1.45) / 0.7 = 1.2$).

CONCLUSION

Selecting an adequate method of surgical treatment, taking into account the degree of the HJ dysplasia allows obtaining positive results, while the HJ anatomical parameters get close to the age norm.

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THE ROLE OF OXIDATIVE STRESS IN THE PATHOGENESIS OF VASCULAR COMPLICATIONS IN CHILDREN WITH INSULINABLE SUGAR DIABETES

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ABSTRACT — The focus of this article is to evaluate lipid peroxidation, antioxidant protection and oxidative stress indicators based on the neutrophil granulocytes functional activity model in children with Type 1 Diabetes Mellitus (T1D). The studies have revealed that, in case of negative effects of reactive oxygen species, children with T1D had intensification in the lipoperoxidation and activation of the antioxidant defense system, including bidirectional changes in non-enzymatic mechanisms. Coordinated generation of reactive oxygen species and oxygen-dependent blood cell metabolism in children with compensated T1D is indicative of the oxidative stress second stage (resistance) development. Reduced production of reactive oxygen species, decrease in the phagocyte oxygen-dependent metabolism activation, incomplete phagocytosis mechanisms correlated with an increase in the pancreas affected area (destruction of insulin-producing β -cells) in children with decompensated T1D, points at the onset of the third stage (depletion) of oxidative stress. Metabolic disorders in children with T1D are determined by the intensity of the “respiratory explosion” of neutrophilic granulocytes in the Lipid peroxidation and antioxidant protection system.

KEYWORDS — type 1 diabetes mellitus, child population, chemiluminescence, neutrophil granulocytes, lipid peroxidation, antioxidant protection.

INTRODUCTION

Latest data indicates that prevalence of diabetes mellitus (DM) in the world increased during the last decade more than two-fold, reaching some 415 million patients by the end of 2015. According to the current estimation by the International Diabetes Federation, 642 million patients will be suffering from DM by 2040. These observations resulted in the UN Resolution on Diabetes 61/225 passed on 20.12.2006, and in 2011 — UN Political Declaration, addressed to national health systems, calling for the establishment of multidisciplinary strategy in the prevention and control of non-communicable diseases, where special attention is drawn to the problem of diabetes as one of the leading causes of disability and mortality [1,–9].

Like many other countries, Russian Federation experiences a sharp rise in the prevalence of DM. According to Russian Federal Diabetes Register, there are at least 4.35 million patients with DM in this country by the end of 2016 (3% of population) with 92% (4 million) — Type 2 DM, 6% (255 th) — Type 1 DM and 2% (75 th) — other types of DM. However, these results underestimate real quantity of patients, because they consider only registered cases. Results of Russian epidemiological study (NATION) confirmed that only 50% of Type 2 DM are diagnosed. So real prevalence of patients with DM in Russia is no less than 8–9 million patients (about 6% of population). This is a great long-term problem, because a lot of patients are not diagnosed, so they don't receive any treatment and have high risk of vascular complications [10–17].

According to the National register, 22,969 children and 8,758 adolescents with T1D had been identified in Russia by 2017. The prevalence of T1D as per 100,000 persons was 86.73 for the *child* category, and 203.29 for the category of *adolescents*, while the morbidity and mortality indices were 11.78 and 8.03, respectively and 0.05 and 0.10, respectively [18–20].

Severe consequences of the global pandemics of DM include its vascular complications: nephropathy, retinopathy, coronary, cerebral, coronary and peripheral vascular disease. These conditions are responsible for the majority of cases of diabetes-related disability and death [21–23].

Lipoperoxidative mechanisms play a significant role in the human body life activity. There is research data available proving that free radical reactions occurring at a low level of functional activity are universal modifiers for the structure and function of cell membranes, having a direct involvement in their recovery (renewal). There is evidence to prove a role played by free-radical oxidation reactions in microbial lysis and phagocytosis. The role of lipoperoxidative mechanisms in cell division and nerve impulse conduction has been established, too [24–27].

Free radicals are atoms, structural fragments of molecules or whole molecules, which have unpaired electrons in the external orbitals. Free radicals have an extremely high reactivity thus interacting with various molecules, causing their damage. Potentiation of lipid peroxidation contributes to a sharp (abrupt) increase in the level of free radical derivatives and exo-, endo-cellular superoxidant oxygen metabolites that have a direct toxic effect. A high level of functional activity in free-radical and peroxide reactions has been observed in case of many external (industrial pollution; hyperbaric oxygenation; hypoxia; vibration; exposure to electromagnetic fields, radioactive and ultraviolet radiation) and internal (low levels of antioxidants; stress; effect of synthetic drugs and xenobiotics; hypodynamia; aging; excessive consumption of fats and carbohydrates) factors affecting the human body. Peroxidation syndrome plays a significant role in the pathogenesis of malignant neoplasms, communicable diseases, atherosclerosis, heart attack, stroke, coronary heart disease, peptic ulcer and burn disease, bronchopulmonary pathology, adaptive overstrain syndrome, diabetes [28–32].

The results obtained by Russian and foreign researchers indicate that oxidative stress and activation of lipid peroxidation are the proven pathogenetic mechanisms of T1D. A significant increase of blood plasma glucose levels through glycation, glucose auto-oxidation, as well as polyol pathway intracellular activation, which potentiates the NADH/NAD⁺ ratio imbalance, contributes to free radicals excessive development and accumulation. The metabolic changes (hyperglycemia, dyslipidemia, insulin secretion change, reduced antioxidant reserve) observed in case of T1D trigger mechanisms activating the functional status of cell membranes, as well as mechanisms that activate lipid inflammation mediators, which control lipid peroxidation and antioxidant protection in the damaged area. The key condition for lipoperoxidation is the development of reactive oxygen species. Given that, an objective assessment of the oxidative stress intensity in T1D implies investigating the severity of the homeostatic imbalance, which is due to neu-

trophils oxygen consumption with the development of oxygen-dependent bactericidal activity that is required to eliminate the agents [33–40].

Systematizing the published research data, we can state that identifying the patterns of free-radical processes and the specific features within the functioning of various antioxidant protection components, as well as oxygen-dependent neutrophils metabolism in children with T1D, will allow specifying early diagnostic criteria for endocrine pathologies, also adding to scientific understanding of the change pattern in lipoperoxidation intensity at different stages of the disease compensation. Besides, the outcomes will increase the explanatory value of diagnostic and prognostic criteria in pediatric practice, also validating the approach of viewing the body as a whole integrated system, and thus contributing to a search for integrated solutions in making treatment and rehabilitation arrangements for endocrine diseases.

Aim of study

To assess the status of lipid peroxidation, antioxidant protection and oxidative stress indicators based on the functional activity model of neutrophilic blood granulocytes in children with T1D depending on the endocrinopathy compensation stage.

MATERIALS AND METHODS

Prior to carrying out the research involving children, a conclusion was obtained from the Committee on Bioethics as well as expressed voluntary consent from the parents (custodians). The results of the ethical review confirmed the research protocols compliance with national and international regulations — the World Medical Association Declaration of Helsinki, 1964 ETHICAL PRINCIPLES FOR MEDICAL RESEARCH INVOLVING HUMAN SUBJECTS, as amended by the WMA LXIV General Assembly (2013); Cl. 24 of the Russian Federation Constitution; Rules of Clinical Practice in the Russian Federation (Decree 266 issued by the Ministry of Healthcare of the Russian Federation on June 19, 2003); ethical standards by the Committee on Experiments, Standards for Clinical Trials (GOST R 52379-2005); Federal Law of the Russian Federation 323-FL ON THE PRINCIPLES OF THE PROTECTION OF CITIZENS' HEALTH IN THE RUSSIAN FEDERATION (of 11/21/2011).

Clinical and laboratory diagnostic studies involving 121 children in their second childhood period (boys — aged 8–12; girls — 8–11) were carried out after obtaining voluntary consent from the parents (guardians). All the patients were divided into two groups. The comparison group included 32 children

(Health Groups I and II; Veltischev, 1994). The diagnosis of healthy was given subject to the Pediatrician's conclusion. The main group (89 people) included children diagnosed with T1D who were undergoing treatment in the Endocrinology Departments, G. K. Filippovsky Child Clinical Hospital (City of Stavropol, Russia) and Child Regional Clinical Hospital of Krasnodar (Russia) within the period of 2010–2017. The patients of the main group, depending on the endocrinopathy compensation degree, were divided into two subgroups — Subgroup 1 included 46 children (52.9%) with compensated T1D, while Subgroup 2 included 43 children (47.1%) with decompensated T1D. According to the disease history of the children with T1D, 27 patients (30.3%) had had the disease for up to 1 year; 43 patients (48.3%) — 1 to 5 years, whereas in another 19 patients (21.4%) the disease duration exceeded 5 years.

In the category with the endocrinopathy duration up to one year, dominating were children with decompensated T1D (20 persons, 74.1%), whereas compensated T1D was observed in 7 children only (25.9%). The division of the T1D-diagnosed child population endocrinopathy based on the compensation degree followed the criteria of carbohydrate metabolism compensation (Dedov I. I., 2007). The glycemia level indicators were recorded subject to the child's clinical history.

The T1D diagnosis in the observed groups was made according to the laboratory test outcomes (general blood test; urine test; biochemical blood test with blood glucose level assessment), as well as following clinical examination data obtained from the Endocrinologist in a hospital.

The material used for the study of antioxidant defense indicators and lipid peroxidation was blood serum and hemolysate prepared from erythrocytes. Blood sampling from the ulnar vein was performed using a vacuum system (venipuncture), which was carried following the generally established algorithm for blood sampling from a vein, taken in the morning and on an empty stomach. The antioxidant protection status was evaluated through the following parameters:

— Total antioxidant activity (AOA). For this, a model system was used, which included a suspension of chicken egg yolk lipoproteins, that allowing studying the blood serum capacity to slow down the accumulation of active products by thiobarbituric acid (TBA) in the suspension (G.I. Klebanova, 1988).

— Superoxide dismutase activity (SOD). The SOD activity was evaluated on a spectrofluorophotometer ($\lambda = 320$ nm) using a curve that reflected the enzymatic inhibition of adrenaline auto-oxidation. The unit of enzymatic activity was taken as the amount of SOD required for a 50% inhibition of adrenaline

auto-oxidation into adrenochrome (H.P. Misra, I. Fridovich, 1972).

— Retinol and α -tocopherol were identified via the fluorometric method (R.Ch. Chernyauksene, 1984). All-trans-retinol (Sigma) and L,D, α -tocopherol (Serva) were used as the external standard.

— The content of reduced (GSH) and oxidized (GSSG) glutathione was identified through the fluorometric method under the same conditions for fluorescence recording (P.J. Hissin and R. Hilf (1976)). The measurements were taken on a spectrofluorophotometer at $\lambda = 350$ nm and $\lambda = 420$ nm, respectively.

Lipid peroxidation intensity was studied by the level of substrates with conjugated double bonds (DB). Diene conjugates (DC), ketodienes (KD) and conjugated trienes (CT) were identified using a spectrophotometric method based on measuring, in the optical region, the absorbance of electromagnetic radiation of conjugated lipid hydroperoxides' diene structures: DB ($\lambda = 220$ nm), DC ($\lambda = 232$ nm), KD and CT ($\lambda = 278$ nm) (J. Stocks method (1974), modification by I. Volchegorsky (1989, 2000)). The principle of the method for studying malondialdehyde (MDA), which is the end product of free-radical polyunsaturated higher fatty acids oxidation, is based on irreversible protein denaturation that occurs in case NH₂ protein groups interact with MDA aldehyde groups. The reaction of MDA with TBA produced a trimethyl complex (stained compound). The optical density of TBA-active lipoperoxidation products was assessed fluorimetrically ($\lambda = 532$ nm), and the MDA concentration was calculated based on the molar extinction coefficient of the trimethyl (stained) complex (V.B. Gavrilo, (1987)).

The total lipids level (TL) was studied with the spectrophotometric method using a semi-automatic biochemical analyzer BioChem SA (High Technology Inc., USA) using a reagent kit (Spinreact, Spain). Measurements were taken on an RF-5301PC spectrofluorophotometer (SHIMADZU, Japan) and a CM2203 spectrofluorometer (Solar, Belarus).

The oxidative stress coefficient (OSC) was calculated in order to reach an objective assessment of the antioxidant protection and lipid peroxidation. This coefficient is a ratio of the antioxidant protection and lipid peroxidation values in children with compensated T1D (Subgroup 1) and decompensated T1D (Subgroup 2) to the average values in healthy children (comparison group). When the OSC value exceeded 1, the oxidative stress was registered.

For a deeper in vivo study of the free-radical oxidation status in the studied groups, the functional activity of neutrophilic granulocytes was investigated employing the chemiluminescent (CL) method (De

Sole P, (1983)). The principle of the chemoluminescent analysis method is based on the registration of a quantum flux that emerges when a substance passes from an electronically excited state to the ground state. The assessment of luminol-dependent spontaneous chemiluminescence (LDCL) and zimosan-induced chemiluminescence (ZICL) was carried out for 90 minutes on a 36-channel analyzer CL3604 (Russia). The analyzer fluorescence intensity of 5.1×10^5 quanta per second was taken as 1 cu (Fig. 1).

The following indicators laid the basis for the

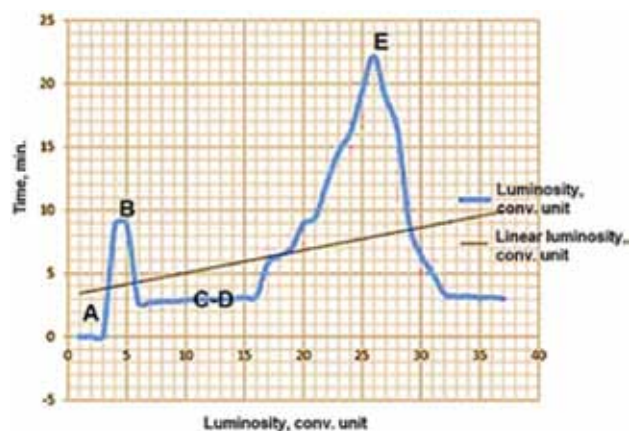


Fig. 1. Vein blood spontaneous LDCL curve: A — spontaneous fluorescence; B — fast flash; C, D — latent period; E — slow fluorescence phase

outcomes: T_{max} — time to reach the maximum; I_{max} — the maximum intensity level; S — the area under the CL curve; the activation index (AI) — the ratio of the ZICL area to the area of LDCL, which determines the CL enhancement induced by zymosan. The analyzer control along with the result record was performed through a PC. Statistical processing, including the data systematization as well as the graphic images and tables construction was carried out following variation statistics methods. The results can be seen as the arithmetic mean and its standard error. The differences significance between the groups (p) was assessed subject to Student's t -test. The differences in indicators were considered significant at $p < 0.05$. The calculations were performed employing the following software: STATISTICA 10.0, DBASE, STATGRAF, STAT4 (Stat Soft Inc., USA), as well as Med Calc (version 9.3.5.0), SPSS (version 7.5).

RESULTS AND DISCUSSION

The antioxidant defense system includes indirect and direct components. The indirect component im-

proves the basic metabolism, which does not involve the generation of excessive amounts of lipid peroxidation products and reactive oxygen species. Following this, an optimal way to regulate the oxygen-peroxide status and the dependent signaling pathways determining the course of all fundamental cellular processes is to change the mitochondrial base, which includes the activity, as well as quantitative and qualitative mitochondria components. The direct component of antioxidant defense includes a set of low- and macromolecular compounds of endogenous origin. A key role in the antioxidant defense system is played by antioxidant enzymes — the first defense line factors against free-radical oxidation and lipoperoxidation products, which include the enzymes complex of the glutathione system (GR, GPO, GST), peroxidase, catalase, myeloperoxidase, paraoxonase, aconitase, and superoxide dismutase.

Table 1 shows the indicators of antioxidant defense in the patients of the said groups.

Under physiological conditions, the human body reveals a balanced equilibrium between the level of oxidants (free radicals) and the antioxidant defense activity status. Oxidative stress provokes an increase in the number of free radicals that work a damaging effect on cellular structures. An increase (accumulation) of free radicals in body tissues disturbs the system balance. One of the significant parameters regulating the antioxidant defense system's buffer capacity is the total AOA, which includes a large number of non-enzymatic and enzymatic links. Of the basic enzymatic components, mention is to be made of fat-soluble vitamins (retinol, α -tocopherol) and superoxide dismutase. There is research-based evidence showing that α -tocopherol, which is an essential component of all plasma membranes, promotes the development of low-active radicals that are not capable of maintaining lipid peroxidation chain reactions. Besides, this fat-soluble vitamin makes membrane phospholipids less accessible for peroxidation by increasing their packing density. Children diagnosed with T1D, if compared with healthy ones, reveal activation of the antioxidant defense system (Table 2). In our opinion, this condition in the main group children, which demonstrated an increase in the total AOA (compensation stage — $11.7 \pm 0.7\%$; decompensation stage — $40.4 \pm 2.3\%$), a decrease in the retinol concentration ($5.6 \pm 0.3\%$ and $25.7 \pm 1.4\%$, respectively) and α -tocopherol ($6.1 \pm 0.2\%$ and $32.6 \pm 1.7\%$, respectively), is to be considered a protective mechanism in response to an increasing generation of reactive oxygen species (oxidative stress) aimed to reduce the severity of the endocrinopathology. Glutathione has been proven to perform its protective properties in its reduced (GSH) form only, while

Table 1. Indicators of antioxidant protection in patients of the studied groups, ($M \pm m$), ($p \leq 0,05$)

Indicators, units of measurements	Research groups		
	Comparison group	First group	The second group
Total antioxidant activity, c.u.	15,07 \pm 1,61	16,84 \pm 1,19	21,16 \pm 1,33
Retinol, mkmol / l	1,87 \pm 0,19	1,76 \pm 0,16	1,39 \pm 0,28
α -tocopherol, mkmol / l	6,69 \pm 0,58	6,28 \pm 0,43	4,51 \pm 0,67
Recycled glutathione, mkmol / l	2,72 \pm 0,13	2,66 \pm 0,11	2,57 \pm 0,16
Oxidized glutathione, mkmol / l	1,78 \pm 0,19	1,84 \pm 0,22	2,17 \pm 0,14
Superoxide dismutase, c.u.	1,52 \pm 0,08	1,46 \pm 0,06	1,27 \pm 0,11

Table 2. Indicators of lipoperoxidation in patients of the studied groups, ($M \pm m$), ($p \leq 0,05$)

Indicators, units of measurements	Research groups		
	Comparison group	First group	The second group
Conjugated double bond substrates, c.u.	1,41 \pm 0,14	1,53 \pm 0,11	1,92 \pm 0,19
Diene conjugates, mkmol / l	0,48 \pm 0,04	0,57 \pm 0,03	0,86 \pm 0,09
Ketodienes and conjugated trienes, c.u.	0,16 \pm 0,02	0,19 \pm 0,03	0,26 \pm 0,05
Malonic dialdehyde, mkmol / l	1,46 \pm 0,13	1,59 \pm 0,12	2,29 \pm 0,17
Total lipids, g / l	4,09 \pm 0,27	4,37 \pm 0,38	5,96 \pm 0,59

shifts in the glutathione status have a negative effect on complications development and the disease outcome. Enhanced glutathione development in its oxidized (GSSG) form ($3.4 \pm 0.2\%$ and $21.9 \pm 1.3\%$, respectively) against a decrease in the SOD activity ($3.9 \pm 0.4\%$ and $16.4 \pm 0.9\%$, respectively) and the glutamine content in the reduced (GSH) form ($2.2 \pm 0.2\%$ and $5.5 \pm 0.3\%$, respectively) in children with T1D, compared with healthy children's indicators, points not only at the activation of the antioxidant defense system and the stress in the the glutathione redox system, yet also is indicative of a slowing lipid chain oxidation, since the SOD action is aimed primarily at superoxide radicals removal. The study of the glutathione system in erythrocytes in children with T1D indicates a decrease in the activity of GSH — the main component of the antioxidant system, which, from our point of view, is a result of the damaging effect wrought by reactive oxygen species. Lower level of GSH increases the accessibility of membranes for the toxic action of lipid peroxidation products. A decrease in the cells antioxidant defense, which manifests itself in an increased GSSG concentration, accelerates the inactivation and oxidation of the thiol protein groups, thus aggravating the oxidative stress.

It has been scientifically proven that insulin deficiency (absolute, relative) in T1D contributes to an increase in the lipid peroxides concentration. The effect of the insulin hormone, which acts as a lipid peroxida-

tion inhibitor, is not only aimed at utilizing peroxide compounds and enhancing the membrane lipids mobility (lability), but also includes bidirectional changes in the non-enzymatic part (protein glycosylation). Along with an increase in the endocrinopathy severity, there is a progress in the lipid peroxidation activity, which is manifested through a cytotoxic effect. The development of this pathophysiological process that implies inactivation (inhibition) of membrane-bound enzymes (cytochrome oxidase activity), is seen as damage to erythrocyte membranes and lysosomes. Emerging morphological, structural and functional changes in endothelial cells and smooth muscle elements of the vascular wall, which often lead to rupture, facilitate vascular complications and diabetic angiopathies.

Table 2 shows the lipoperoxidation indicators in the patients of the involved groups.

Children with T1D, compared with healthy children, have all the respective indicators showing lipid peroxidation intensification: an increase in the substrates with conjugated double bonds (compensation stage, $8.5 \pm 0.5\%$; decompensation stage, $36.2 \pm 2.1\%$); DC accumulation (lipid peroxidation primary products) ($18.8 \pm 1.2\%$ and $79.2 \pm 3.7\%$, respectively); accumulation of KD and CT (the intermediate products of lipoperoxidation) ($18.7 \pm 1.4\%$ and $62.5 \pm 3.1\%$, respectively); an increase in the MDA level (the final product of lipid peroxidation) ($8.9 \pm 0.7\%$ and $56.8 \pm 2.7\%$, respectively); total lipids — $6.8 \pm 0.4\%$

and $45.7 \pm 2.3\%$, respectively. Note to be made that children with decompensated T1D have a significant accumulation of malonic dialdehyde, the most toxic product. From our point of view, in children with decompensated T1D, the most prominent increase in the lipid peroxidation initiation at the stage of primary, intermediate and final products — in comparison with the antioxidant defense system activation parameters — contribute to thickening of the blood vessel walls basement membrane, a higher blood viscosity, and a slower blood flow thus increasing the probability of intravascular coagulopathy (aggregation of blood cells) and disturbance through various hemostasis stages.

Table 3 shows the range of oxidative stress coefficient fluctuations in the studied groups.

Table 3. The range of fluctuation of the coefficient of oxidative stress in patients of the studied groups, (c.u.), ($M \pm m$), ($p \leq 0,05$)

Research groups		
Comparison group	First group	The second group
Less than 1	1,03 – 1,18	1,08 – 1,79

Antioxidant defense is a complex multilevel system that blocks the transition of lipid peroxidation processes from a physiological into a pathological status (oxidative stress). Oxidative stress of varying severity, developing due to disturbed antioxidant defense mechanisms, not only accompanies the course of classical stress, yet can also manifest itself as a key factor in the pathological condition. In children with long-term decompensated T1D, the probability of oxidative stress occurrence (OSC above 1) increases significantly due to disturbed components interaction (redox metabolism and vascular complications) in a single stress mechanism of all physiological systems.

An increase in the free-radical oxidation activity, regarded as a reliable indicator of the macroorganism status comes along with morphological and functional impairments in biological membranes. The set of these processes, which include a reduction in the membranes lipid layer stability, enhanced peroxidation of proteins, lipids, and ion permeability, serve the basis for the pathogenesis of various diseases at the molecular level. The use of CL analysis, which is highly informative, sensitive, and reliable, allows objective and reliable identification of potential morphological and metabolic disorders in the development and progress of the endocrine pathology at the molecular level (studying photochemical reactions, electronically excited molecule states, structure and properties of biological systems, and molecular transitions dynamics).

According to the available data obtained through investigating biological structures using CL analysis, there has been their connection identified with free-radical oxidation in a macroorganism, which is due to molecular oxygen reduction to active species (hydroxyl and superoxide anion radicals, singlet oxygen) has been established. The most important source of reactive oxygen species is lipid auto-oxidation, which occurs via release of free radicals. In case of peroxides recombination developing through interaction of free radicals with oxygen, there occurs emission of light quanta. The emission of photons is also observed upon excitation of ketones, oxygen dimer molecules, aldehydes, oxalates, cyclic hydroperoxides, aldehydes, biogenic amines, decomposition of intermediate products of reaction with molecular oxygen (peroxides). Inhibition of free-radical oxidation in the body goes on through natural antioxidants of hydrophilic (ascorbic acid, sulfhydryl compounds of the SH-group of proteins) and hydrophobic (flavins, tocopherols, steroids, carotenoids) phases.

Given this point of view, CL activity points at not excessive free-radical oxidation only, yet also reveals a low activity (lack) of antioxidants. Investigating the spontaneous emission intensity proportional to the free radicals recombination rate, does not offer a reliable picture of the reasons behind the change in the free-radical oxidation rate. In this connection, notable is the method of modifying free-radical reactions using luminol with a subsequent analysis of induced CL. In the presence of reactive oxygen species, luminol is oxidized to develop electron-excited carbonyl chromophores. The identified functional groups with a high quantum yield increase significantly the glow intensity due to the development of reactive oxygen species. This phenomenon is used successfully to study the functional level of phagocytic immunity. Insufficient generation of reactive oxygen species, aimed at antigens inactivation, means reduced activation rate of oxygen-dependent phagocytic metabolism, as well as incomplete phagocytosis.

There is scientifically proven data showing that the mechanisms of *non-specific immunity* are the initial stages where antigens (foreign agents) come into contact with the body. Neutrophil granulocytes that have a high reactivity, in response to numerous signals concerning disturbed internal environment can perform rapid functional restructuring, thus determining the nature of the inflammation course. The so-called *respiratory (oxygen) explosion*, which is caused by a sharp rise in the oxygen use through its conversion by phagocytes into active species, determines the neutrophils mobilization rate, potentiating the launch of the body's defense systems. The ability of neutrophilic

blood granulocytes to develop a sufficient number of reactive oxygen species is a prognostic sign of the nature (type) of inflammation, whereas the response to stimulation allows objective evaluation of the body defense activity. The model of neutrophilic granulocytes with high diagnostic significance used to study oxidative stress allows a significant expansion of the information pool to be obtained from the assessment of free-radical oxidation, which is viewed as a factor that indicates the health status through different phases of T1D in children.

Table 4 shows the indicators of luminol-dependent chemiluminescence of neutrophilic blood granulocytes in patients within the above-mentioned groups.

In case of an increasing severity of endocrinopathy in children with T1D, if compared with the main group (Subgroup1), there were also bidirectional changes registered in the spontaneous LDCL values (a 1.9 decrease in I_{max} , and a 1.7 times decrease in S ; T_{max} parameters growth — by 1.5 times) and zymosan-induced LDCL (I_{max} decrease — 1.5 times, S — 1.4 times; T_{max} parameters growth — 1.6 times). The reduction of nonspecific antimicrobial defense in children with decompensated T1D, occurring along with an increasing pancreas lesion area (destruction of insulin-producing β -cells of the Langerhans islets), is an effect of the following pathophysiological mechanisms:

Table 4. Indicators of luminol-dependent chemiluminescence of neutrophilic blood granulocytes in patients of the studied groups, ($M \pm m$)

Indicators	Research groups					
	Comparison group		First group		The second group	
	Value range	Average value	Value range	Average value	Value range	Average value
Spontaneous chemiluminescence						
T_{max}, s	573,4-1478,7	905,3 \pm 34,1	417,6-1084,9*	667,3 \pm 23,8*	614,6-1583,5*	968,9 \pm 31,7*
$I_{max}, o.e. \times 10^3$	3,03-12,96	9,93 \pm 0,67	28,87-80,33**	51,46 \pm 3,78**	16,23-43,91**	27,68 \pm 2,14**
$S, o.e. \times 10^5$	2,82-6,74	3,92 \pm 0,31	17,58-49,22**	31,64 \pm 2,06**	9,84-28,21**	18,37 \pm 1,95**
Zymosan-induced chemiluminescence						
T_{max}, s	772,8-1297,4	1035,1 \pm 38,6	593,9-1311,3*	717,2 \pm 26,3*	472,2-1559,2*	1087,0 \pm 43,1*
$I_{max}, o.e. \times 10^3$	9,72-29,06	19,34 \pm 1,26	36,63-135,16**	98,53 \pm 5,34**	34,18-99,57**	65,39 \pm 4,02**
$S, o.e. \times 10^6$	3,19-10,32	7,13 \pm 0,58	30,46-82,03**	51,57 \pm 3,29**	16,44-51,16**	34,72 \pm 2,19**
Activation index		1,82		1,63		1,89

Note: statistically significant differences with the children of the comparison group (* — $p < 0.05$; ** — $p < 0.01$).

The results of studying the luminol-dependent chemiluminescence parameters in neutrophilic blood granulocytes in the main group indicated that children with T1D in the compensation stage have bidirectional change dynamics in the spontaneous LDCL if compared with similar factors in healthy children (an increase of I_{max} — 5.2 times and S — 8.1 times; a decrease in T_{max} values 1.4 times). This type of change in the values indicates a proper generation of reactive oxygen species and blood cells oxygen-dependent metabolism processes in response to the early phases of selective organ-specific destruction of insulin-producing β -cells in the Langerhans pancreatic islets. A decrease in the maximum intensity growth rate value (I_{max}) during zymosan-induced LDCL in this subgroup, in comparison with the change dynamics of spontaneous LDCL, confirms that the development of the destruction initial stage in the islet cells correlates with a decrease in the reserve capacity of neutrophil granulocytes antimicrobial protection.

- reduced rate of metabolic processes, which is accompanied with a respiratory burst developing;
- reduced production of reactive oxygen species;
- depleted phagocytic activity of macrophages.

From our point of view, this condition points at a long chronic inflammatory process, which is combined with the depletion of defense & compensation mechanisms aimed at improving the body's vital processes under inflammation.

CONCLUSIONS

1. In children with T1D, through all the phases of the disease, the antioxidant defense system is activated against the negative effects of reactive oxygen species, including bidirectional changes in non-enzymatic mechanisms. The increase in the overall antioxidant activity (compensation stage, 11.7 \pm 0.7%; decompensation stage, 40.4 \pm 2.3%), a decrease in the retinol level (5.6 \pm 0.3% and 25.7 \pm 1.4%) and α -tocopherol (6.1 \pm 0.2% and

- 32.6±1.7%), compared with healthy children, is a protective response to the increasing generation of reactive oxygen species, the aim of that being reduction of the endocrinopathy severity course.
2. A significant increase in the content of oxidized glutathione (GSSG) (compensation stage, 3.4±0.2%; decompensation stage, 21.9±1.3%) in the venous blood of children with T1D, compared with healthy children, against a decrease in the superoxide dismutase activity (3.9±0.4% and 16.4±0.9%) and the level of reduced glutathione (GSH) (2.2±0.2% and 5.5±0.3%), is indicative of a stress in the glutathione redox system, as well as a slow chain oxidation of lipids. The redox system stress results in inhibited anti-peroxide enzymes and a decrease in the antioxidants level, which contribute to the stability of the antiperoxide and antiradical cell potential.
 3. Children with T1D, reveal intensified lipid peroxidation through all the stages of the pathology. Compared with healthy children, an increase is registered in the level of substrates with conjugated double bonds (compensation stage, 8.5±0.5%; decompensation stage, 36.2±2.1%), accumulation of diene conjugates (18.8±1.2% and 79.2±3.7%), accumulation of ketodienes and conjugate trienes (18.7±1.4% and 62.5±3.1%), as well as an increase in the malondialdehyde level (8.9±0.7% and 56.8±2.7%) and in total lipids, 6.8±0.4% and 45.7±2.3%, respectively.
 4. In children with decompensated T1D, prominent lipid metabolism disturbances combined with oxidative stress indicators, aggravate the course of the endocrine pathology, increasing significantly the likelihood of intravascular complications (coagulopathy).
 5. Highly reliable and diagnostically significant risk factors for early development of microvascular angiopathies should include the level of total antioxidant activity, as well as the content of diene conjugates and total lipids in the venous blood.
 6. The analysis of the outcomes obtained through the study of neutrophilic blood granulocytes functional activity in children with T1D, using luminol-dependent chemiluminescence indicates an increase in the intensity of reactive oxygen species development not only during a spontaneous chemiluminescent reaction, yet also zymosan-induced (stressed) chemiluminescence, if compared with healthy children.
 7. The method of spontaneous and induced luminol-dependent chemiluminescence employed to study oxidative stress using the model of neutrophilic granulocytes in children with T1D

is a reliable, cost-effective, highly sensitive express method for assessing the phagocytic immunity functional status, which, at the same time, allows registering the kinetic component of the phagocytosis process.

8. Children with decompensated T1D have changes in the Lipid peroxidation and antioxidant defense system, which is due to intensified lipid peroxidation against activated antioxidant defense mechanisms, and such changes correspond to the systemic inflammatory response syndrome that occurs with the maximum stress in the body's protective-compensatory mechanisms.

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THE SIGNIFICANCE OF DETERMINATION THE BODY'S ENERGY SUPPLY BEFORE AND AFTER COMPETITION AMONG YOUNG ATHLETES

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ABSTRACT — In 47 children 7–10 years old who are engaged in swimming there are studied the activity of myocardial and brain fractions of creatine phosphokinase, the level of troponin-T in blood serum and the main parameters of heart rate variability before and after the competition. The expenditure of usage this complex of energy supply of the myocardium and brain in young athletes has been established. The definitions of the studied laboratory and instrumental tests can be used in the diagnosis of the physiological, pathological *sports heart*.

KEYWORDS — children involved in sports, biochemical indicators of (MB-CFC, BB-CFC, troponin-T), spectral indicators of heart rate variability, physiological and pathological *sports heart*.

It is known that under physical and emotional stress, young athletes may experience energy problems with the body [1, 2]. Increased energy expenditure and energy (mitochondrial) deficiency lead to the formation of pathological *sports heart*, neurotic disorders and changes in other organs [2, 3].

To assess metabolic and energy changes in the myocardium, we use the determination of the activity of the MB-fraction of creatine phosphokinase (MB-CFC), troponin-T and the main spectral parameters of heart rate variability (HRV), reflecting the vegetative and energy supply of the organism. The activity of the BB-fraction of CFC characterizes the metabolic process of the brain and in combination with the change in the levels of the main parameters of HRV, may indicate the state of its energy supply [3, 4].

The particular interest is the study of energy supply of the heart and brain in young sportsmen before and after the competition.

Objective

To establish the significance of determination the body's energy supply before and after competition among young athletes.

The characteristics of children and research methods. 47 children aged 7–10 years (mean age 8.5 ± 1.5) involved in swimming were under observation. The clinical examination was held on the basis of the SBHI AR Regional Medical Exercise Center and sports club. Athletes with organic diseases of the cardiovascular and nervous systems and acute respiratory infections within 1 month were excluded.

The examination included the collection of anamnesis, examination of the organs and systems, with an accent for the cardiovascular and nervous systems. The levels of activity of MB-CFC, BB-CFC by ELISA, the content of troponin-T with the help of the enzyme-immune test-system Beringer Mannheim were studied in all the observed ones. From instrumental methods, standard electrocardiography (ECG), echocardiography (ECHO-CG) and electroencephalography were used according to indications, with the interpretation of the data obtained according to the standards. In addition, we studied the state of the main spectral parameters of HRV on the Polyspectr-12E apparatus of Neurosoft Company.

RESULTS AND DISCUSSION

Careful analysis of clinical, laboratory and instrumental data in 47 young athletes made it possible to form 2 groups of children. The first consisted of 22 (46.8%) athletes involved in 3–4 months. The second group consisted of 25 (53.2%) children, with experience in sport for 1.5–2 years.

In children of the first group, complaints of fatigue were noted after exercise in 7 (31.8%) cases, a decrease in heart tones was detected in 8 (36.3%), mild systolic murmur — in 5 (22.7%) cases.

Laboratory indicators of energy supply activity of MB-CFC, BB-CFC and the level of troponin-T did not significantly differ from the norm ($p_1 > 0.5$; $p_2 > 0.05$; $p_3 > 0.05$).

ECG detected: sinus bradyarrhythmia in 7 (31.8%) cases, T wave inversion in 2 or more leads in 2 (2.1%) athletes, segment ST depression in isolated cases. On the echocardiogram, left ventricular diastolic dysfunction in 3 (13.6%), an increase in its mass over 220 g/m^2 was detected in 4 (18.2%) children. The

spectral parameters of HRV were not significantly changed: TP>0,05; VLF>0,05; LF<0,05; HF>0,05 (Table 1).

All observed children were further examined after the competition in 1–2 days. Athletes of the first group had complaints of fatigue in 17 (77.3%) cases,

Table 1. The condition of laboratory and instrumental indicators before and after the competition

Data	MB-CFC (f/l)	BB-CFC (f/l)	Troponin-T (mg/l)	TP (mc2)	VLF (mc2)	LF (mc2)	HF (mc2)
Groups	Before competition						
First (n=25)	34,7±0,4	19,8±0,3	0,039±0,005	2740±616	1350±418	940±120	680±124
Second (n=22)	35,4±0,5**	28,1±0,3*	0,042±0,005**	2710±504*	1240±340*	1710±121**	970±120**
	After competition						
First (n=25)	29,5±0,3###	18,4±0,3##	0,042±0,005#	2450±512##	1280±41#	730±134##	810±130#
Second (n=22)	37,1±0,3###	32,5±0,4##	0,039±0,05#	2890±514##	904±141#	1600±450#	740±100##

Note: Reliability p^* — when comparing the indicators of the respective groups among themselves $p>0,05^*$, $p<0,05^{**}$, $p<0,01^{***}$
 $\#$ — when comparing the values of each group before and after the competition $p>0,05\#$, $p<0,05\##$, $p<0,01\###$

Thus, in children of this group, there were no marked disorders in the energy supply of the myocardium and the brain. This is confirmed by the values of the levels of activity of MB-, BB, CFC and troponin-T in combination with the stored relatively high levels of total spectrum capability (TP), low-frequency and high-frequency ranges. Identified deviations from the norm of clinical, laboratory and instrumental indices are due to not fitness or impaired adaptive abilities in athletes.

In the second group (25 observations), there were no complaints for long-term athletes, bradyarrhythmia was clinically observed — 11 (44.1%), loud heart sounds — 15 (60,0%).

Laboratory: indicators of energy supply of the organism, the activity of MB-CFC, BB-CFC was moderately increased ($p_1<0,05$; $p_2>0,05$), with unchanged levels of troponin-T ($p_3>0,05$).

ECG detected: sinus bradyarrhythmia in 11 (44.0%) cases, deviation of the electrical axis of the heart to the left — 10 (40.0%), moderate left ventricular hypertrophy 7 (28.0%). The echocardiography revealed an increase in the mass of the myocardium of the left ventricle in 9 (36.0%) children and diastolic dysfunction in 2 (8.0%).

When analyzing the spectral parameters of HRV, changes in the low-frequency (LF) and high-frequency (HF) ranges were found in 8 (32.0%) cases at normal values of the total power of the spectrum (Table 1). The changes correlated with the increase in the activity of MB-CFC and BB-CFC ($k^1=0,9$; $k^2=0,7$).

Consequently, the young athletes of the second group determined a sufficiently high energy supply of the body. The revealed changes in clinical and instrumental indices are probably due to the development of the *sports heart*.

half of the heart sounds were muffled in half, mild systolic murmur in 5 (22.1%) and bradyarrhythmia with the same frequency.

Laboratory parameters were characterized by an increase in the levels of MB-CFC ($p_1<0,01$) BB-CFC ($p_2<0,05$) with moderately reduced troponin-T ($p_3>0,05$) compared with those before the competition (Table 1).

On the electrocardiogram, the changes detected before the competition were maintained after. The frequency of distolic dysfunction on echocardiography increased in 15 (68.2%) with a preserved level of intex myocardial mass in 9 (40.9%). The overall power of the spectrum was reduced ($p<0,05$) at a low level of the low frequency range LF ($p<0,05$). It indicates the lack of energy in the organism.

When comparing clinical, laboratory, and instrumental data before and after the competition, a decrease in the energy of the myocardium and brain associated with the lack of fitness of young athletes was established. This clearly reflects changes in the levels of myocardial and brain fraction of CFC ($p_1<0,05$; $p_2<0,05$) in combination with reduced overall power of the HRV spectrum ($p_3<0,05$; Table 1).

Further observation after 1 month among these young athletes, we managed to single out a subgroup (9 people) with significantly changed clinical, laboratory and instrumental indices. Clinically, they had muffled heart sounds, half had mild systolic murmur, sinus bradyarrhythmia-7 (77.8%), tachyarrhythmia-2 (25.8%). Levels of MB-CFC, BB-CFC were below normal ($p_1<0,05$; $p_2<0,05$). On ECG, sinus arrhythmia was detected in all children, signs of impaired repolarization in 7 (77.8%). On echocardiography, diastolic dysfunction was detected in 7 (77.8%).

These young athletes were at risk of developing the pathological *sports heart*. In the future, after 2–3 months, their examinations confirm this condition.

In the observables of the second group, 1–3 days after the competition, the frequency of occurrence of bradyarrhythmia and changes in heart tones remained the same as before the competition. They showed ECG sinus bradyarrhythmia-15 (60,0%) with signs of left ventricular hypertrophy-8 (32,0%) and diastolic dysfunction on echocardiography-7 (28,0%). These disorders can be interpreted as a physiological *sports heart*. When comparing the results of HRV before and after the competition, an increase in the levels of indicators MB-CFC, BB-CFC and the spectrum of TP ($p_1 < 0,01$; $p_2 < 0,05$; $p_3 < 0,05$; Table 1). Consequently, the body's energy supply after the competition was quite high, or probably due to the formation of *sports heart*.

Thus, the determination of the levels of activity of MB-CFC, BB-CFC, the content of troponin-T in serum, variations in HRV ranges before and after the competition may allow to do the objective assessment of the body's energy supply. The use of this laboratory and instrumental complex makes it possible indirectly to characterize the combined energy changes in the myocardium and brain. The disorders occurring in these organs in young athletes are probably related to

cerebrocardiac syndrome of physical and emotional stress. Investigation of the activity of MB-CFC, BB-CFC and the condition of the main indicators of HRV (TP, HF, LF) can be assumed to diagnose the pathological *sports heart*, and the degree of fitness of young athletes.

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MECHANISMS OF METABOLIC ADAPTATION AND OXIDATIVE STRESS IN HERPESVIRUS INFECTIONS

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The pathogenesis of a chronic course and the complications of herpesvirus infections remains poorly understood nowadays despite the extreme relevance, associated with the pandemic of these infections and the severe complications in the activation of its latent forms.

Recent research has found that redox processes and, primarily, processes of free radical oxidation mainly determine the stability of the homeostasis of a living organism. As a result of the disturbance of the activity of this system, toxic products accumulate, which is one of the reasons for the imbalance in the regulation of homeostasis, leading to serious metabolic disorders, changes in the immune status, hormonal disorders, deep disturbances in the detoxification system, etc. [1].

The activation of free radical oxidative reactions is the main pathogenetic factor of many diseases and pathological processes, including herpesvirus infections, accompanied by lesion of the biological barriers of cell membranes [2].

The features of herpesvirus infections allow us to consider them as diseases of the immune system, with the development of variety of immunopathological reactions, which create the conditions for genesis of prolonged endotoxemia, aggression of proinflammatory cytokines and free radicals causing various complications.

In this connection, in evaluation of the severity of endotoxemia, the relevance of the study of its immunobiochemical component is widely recognized, because the development of endogenous intoxication is accompanied by metabolic disorders of varying severity. At the same time, in non-physiological concentrations, fluids and tissues accumulate intermediate and final products of normal and impaired metabolism.

Malonic dialdehyde is considered to be a universal marker, which represents the level of pathological metabolism, correlating with the main clinical laboratory prognostic criteria of metabolic disorders.

Malonic dialdehyde is a secondary product of free radical oxidation of lipids and proteins, interacts with the N-terminal residues of amino acids, proteins and amino groups of phospholipids with the formation of

conjugated fluorescent Schiff-type compounds [4]. The increase in malondialdehyde indicates excessive activation of free radical oxidation, the decrease indicates inhibition of lipid metabolism. Malonic dialdehyde is very toxic and chemically active, has a damaging effect associated with the lesion of the structural and functional state of biomembranes. Their utilization in the body occurs at a very low rate, and as a result they accumulate, being a ballast that disrupts the functional state of cell biomembranes.

The rate of free radical oxidation and the concentration of free radicals in humans are normally maintained at a defined level by an antioxidant system that counteracts the processes of starting and developing free radical reactions. The action of pathogenic factors and the activation of endogenous mechanisms of free radical oxidation lead to a strain of the antioxidant defense mechanisms. In this regard, we were additionally presented the study of the level of catalase, which represents the first line of defense against free radicals.

Catalase is an enzyme of the class of oxidoreductases found in the cells of practically all aerobic organisms. Along with the degradation of hydrogen peroxide and thus the protection of the cell from its toxic effects, the enzyme catalyzes a number of metabolically significant protective reactions. Catalase activity in the blood is one of the prognostic tests of endotoxemia severity in the human body [3].

It is known that the protein of the acute phase ferritin has antioxidant activity, it is a protein of the acute phase of inflammation, the main feature of which is a rapid and significant change in concentration as a result of disturbed homeostasis independent of the reason and location of the calling stimulus [3, 4].

Detection of pathogenetically significant metabolic disorders is not only theoretical, but also practical value, as it determines the direction of the search for effective means of correction of these disorders to optimize the treatment of infection caused by the stirpes of herpes.

The aim of research

Is to study the role of lipid peroxidation and antioxidant system in the pathogenesis of herpesvirus infection.

Materials and methods

We studied the data of 80 patients with herpesvirus infection who received treatment in A.M. Nichoga Regional infectious clinical hospital in the city of Astrakhan. Molecular diagnostic methods (PCR) and detection of specific antibodies to herpes viruses (HSV-1, 2) in the diagnostic titer by three-phase enzyme immunoassay (EIA) were used to verify the diagnosis. The tested group consisted of 46 (57.5%) boys and 34 (42.5%) girls. The mean age of patients was 3.4 ± 0.5 years. The control group consisted of 30 healthy individuals. The research took into account all legislative and ethical requirements.

The object of the laboratory analysis were blood samples of patients with active form of herpesvirus infection. Blood for the preparation of serum was obtained by puncture of the cubital vein. The serum was separated from the blood cells by centrifugation at 3000 rpm for 10 minutes in the first 2 hours after blood taking. The status of lipid peroxidation was determined by the level of malondialdehyde in the blood serum by the method of Jagi K. (1968) in modification of Kuzmenko D. I. and Laptev B. I. (1999) by reaction with thiobarbituric acid. For evaluation the antioxidant system, the serum ferritin level was determined by enzyme-linked immunosorbent assay using a set of reagents "Ferritin-ELISA-BEST" (Novosibirsk, Russia). Catalase activity was determined using the method of Korolyuk M. A. (1988).

Statistical data processing was carried out by standard methods of variation statistics using statistical indicators: Student's criterion and correlation coefficient. Mathematical data processing was carried out using Excel and for Windows.

RESULTS AND DISCUSSION

During the dynamic analysis, a significant increase in level of malondialdehyde in blood serum was found during the period of infection activity ($p < 0.001$), which indicated the activation of the body's prooxidant system. During the period of clinical remission, in parallel with the positive dynamics of the disease, there is a significant decrease in malonic dialdehyde in blood serum ($p < 0.001$) (Table 1).

Analysis of the level of ferritin — a high-molecular iron-containing antioxidant protein involved in the metabolism and reallocation of iron in the body, revealed its significant increase in patients with herpesvirus infection by 71.3% in the main (271.1 ± 7.5) ng/ml relative to the control group (77.8 ± 3.9) ng/ml ($p < 0.01$). After the therapy in patients with herpesvirus infection, a decrease in the index relative to the baseline by 56.1% to (118.9 ± 7.6) ng/ml was revealed, which corresponded to the normal value interval (Table 1).

Table 1. Indicators of free radical oxidation in patients with herpesvirus infection

The indicator	Group of surveyed	Research stage	$\bar{X} \pm m$	p
Malonic dialdehyde, mkmol/l	healthy		0.73 ± 0.072	$p < 0.001$
	sick	before treatment after treatment	12.39 ± 0.73 $0.77 \pm 0.29^*$	
Catalase, mkat/l	healthy		0.95 ± 0.084	$p < 0.001$
	sick	before treatment after treatment	0.023 ± 0.008 $1.05 \pm 0.013^*$	
Ferritin, ng/ml	healthy		77.8 ± 3.9	$p < 0.001$
	sick	before treatment after treatment	$271.1 \pm 7.5^*$ $118.9 \pm 7.6^*$	

In the study of the activity of intracellular antioxidant catalase in patients with herpesvirus infection, there was a significant decrease before treatment ($p < 0.001$). After treatment patients with herpesvirus infection registered a significant increase in the level of catalase to normal values (1.05 ± 0.013) mkat/l ($p < 0.001$) (Table 1).

Thus, in the dynamics of the disease in patients with herpesvirus infection there are nonspecific metabolic disorders in the form of activation of the processes of lipoperoxidation, increased acute-phase blood protein-ferritin and decreased activity of catalase.

The first time we found changes in metabolism allow us to deepen the understanding of the pathogenesis of herpesvirus infection, which contributes to solve clinical problems of medical science, especially the improvement of diagnosis and treatment.

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DYNAMICS OF PERIODONTAL FIXING CAPACITY THROUGH ORTHODONTIC TREATMENT EMPLOYING EDGEWISE TECHNIQUE

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Out of the major periodontal functions orthodontists take great interest in its fixing capacity [1]. This term means the counterwork of the dentofacial segments (teeth with surrounding tissues) to chewing loads under physiological conditions, and to the forces developed by orthodontic appliances of various action, and by prosthetic structures replacing defects of the dental arches [2, 3, 4]. The fixing capacity of periodont, as experts claim, is determined by the dentofacial arches type as well as by their shape and size, even in case of physiological occlusion [5, 6, 7]. Given the high prevalence of dental caries and its complications, which are the etiological factors behind dentition defects and, accordingly, maxillofacial anomalies and deformities, the periodontal fixing capacity needs investigation for further selection of prosthetic structures and orthodontic appliances [8, 9, 10]. The effectiveness of dental prosthetics, taking into account the periodontal tissues status, has been described in clinical observations [11, 12]. Nevertheless, of particular importance is knowledge of the periodontal fixing capacity when choosing the optimal loads and their dosing in orthodontic treatment dynamics, in particular when using arch equipment (edgewise technique).

Aim of study

To identify the dynamics in the periodontal fixing capacity in order to regulate the optimal load through orthodontic treatment employing the edgewise technique.

MATERIALS AND METHODS

27 patients underwent treatment for dental arches shape anomalies. The treatment was carried out using non-removable arc equipment (edgewise technique) following the protocol for the occlusion issues treatment. The first stage of leveling dental arches implied using nickel-titanium alloy arcs of circular cross section. When measuring the periodont fixing capacity, the load was dosed taking into account the tooth deviation distance. The tooth was moved only halfway through its moving range. Tooth mobility was measured using the L.P. Ivanov tool, while Stens impression compound was used to fix it on the teeth in the central occlusion position. The device included a circular eccentricity scale with a probe coming to it, which allowed evaluating tooth mobility with an accuracy of 0.01 mm. The probe was installed from the lingual surface of the upper incisors, after which the scale was set to the zero position. The pressure was generated with a dynamometer, whose probe was applied to the incisors vestibular surface and the device pressure force was measured in grams. The upper incisors mobility measurements were taken before treatment, and then one day, one week, two weeks, and three weeks into the active phase of the treatment. The tooth shift was done at 0.07 mm, 0.1 mm, 0.2 mm, 0.25 mm, and 0.3 mm.

RESULTS AND DISCUSSION

The study showed that prior to treatment, moving a tooth by 0.07 mm required a force of 58.91 ± 6.90 grams. An increase in the power up to 99.21 ± 16.94 grams, would result in the medial incisors shifted by 0.1 mm. Moving a tooth by 0.2 mm would require a force of 149.38 ± 5.83 grams. Any further power increase would not lead to the tooth shift. Therefore, prior to treatment, the maxillary medial incisors would not move more than 0.2 mm, which allowed selecting the optimal load for treatment, not exceeding 100 grams. However, a day later already, after applying the device, the periodontal fixing capacity decreased and it took an effort of 50.60 ± 9.88 grams to move the teeth by 0.07 mm. As the power was taken up to 70.87 ± 12.58 grams, the medial incisors

shifted by 0.1 mm. To move a tooth by 0.2 mm, an effort of 115.00 ± 15.75 grams was required, which was significantly lower than prior to the treatment, and indicated a decrease in the periodontal fixing capacity. The tooth mobility increased to 0.25 mm when subjected to a force of 135.17 ± 9.67 grams. Further power increase did not lead to any tooth shift. A week later, after the device was applied, the periodontal fixing capacity decreased and an effort of 32.17 ± 8.09 grams was enough for a 0.07 mm tooth shift. With an increase in power load up to 38.11 ± 10.13 grams, the medial incisors shifted by 0.1 mm. Shifting the tooth by 0.2 mm would take an effort of 62.61 ± 13.39 grams, which was significantly lower than before the treatment and revealed a decrease in the periodontal fixing capacity. Shifting a tooth by 0.25 mm would take an effort of 83.51 ± 11.10 grams. The mobility of the tooth increased to 0.4 mm when subjected to an effort of 144.41 ± 7.84 grams. Any further increase in the power did not lead to the tooth shift. Two weeks later, after applying the device, the periodontal fixing capacity remained almost unchanged and was close to the values obtained a week into active treatment. Shifting the teeth by 0.07 mm would take a force of 28.91 ± 5.83 grams. As the power load increased up to 31.92 ± 7.81 grams, the medial incisors showed a 0.1 mm shift. Ensuring a 0.2 mm shift would take an effort of 60.87 ± 14.82 grams was required, whereas a force of 82.61 ± 8.81 grams was required for a shift of 0.25 mm. When the tooth was shifted by 0.4 mm, a force of 143.68 ± 6.24 grams was required. A further increase in the effort applied did not lead to a shift. After three weeks, the values remained virtually unchanged.

CONCLUSION

The periodontal fixing capacity decreased through the dynamics of orthodontic treatment, while a lower force was required for the teeth shift.

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MANUFACTURING METHODS FOR INDIVIDUAL ALIGNERS AND TRAINERS FROM THERMOPLASTS AND CLINICAL INDICATIONS FOR THEIR APPLICATION

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Standard preorthodontic trainers are now widely used in the clinical orthodontics to treat patients with dentofacial anomalies and deformities [1, 2]. However, their use is limited due to the mismatch between the size of the trainers and the dental arches. The nowadays available literature offers data on the dental arches linear dimensions that are recommended to be used for identifying the orthodontic treatment tactics [3, 4]. Modern methods of studying dental arches have been shown in view of the face and head measurements [5, 6]. The need for forecasting the dental arch shape, taking into account the individual parameters of teeth, has been explained [7, 8]. Dental arch anomalies reveal a variety of etiopathogenetic features [9, 10]. There have been advanced methods proposed for orthopedic and orthodontic treatment of children and adults, using advanced prosthetic structures and taking into account the increased aesthetic requirements [11, 12]. However, it has been shown that many designs of prostheses and devices made from acrylic plastics have a negative effect on the oral mucosa and affect the oral cavity microbiota. Given that, there is specific interest to be taken in the use of orthodontic and orthopedic structures made from thermoplastic materials, which served the basis for this study.

Aim of study

To identify indications for the methods of manufacturing aligners and trainers from thermoplastics of various rigidity.

MATERIAL AND METHODS

26 children were examined and treated in the period of mixed and permanent occlusion (11–16 years old) with various types of occlusion anomalies caused by disturbed shape and size of the jaws or their abnormal position. While studying the jaws cast models, modern methods of diagnostics were used, also taking into account the classification of the dental arches shape and size. To simulate the shape of the forecasted dental arch, a method of mathematical and graphic reproduction was applied, taking into account the recommended torque and angulation of permanent teeth. Constructive occlusion was identified taking into account the X-ray analysis of the temporomandibular joint elements. The recommendation was to use aligners for 8–10 hours a day while treating patients with impaired shape and size of the dental arches, and to use aligners at night for children with occlusion that is abnormal due to improper jaw location.

Results and discussion. We produced 28 aligners and trainers for treating patients with abnormal dental arches shape and size, and 31 trainers to treat occlusion disturbances caused by the mandible posterior position. While making the aligners, the stamping method (using a Ministar machine, Germany, Scheu-Dent) was employed. The patients had their respective pick-up impressions taken and then cast on two pairs of die stone, one of which was diagnostic, the other being working. The working model was cut into fragments depending on the occlusion anomaly, and preformed in view of the forecasted dental arch shape, which was built through mathematical and graphical modeling. Photocomposite materials were used to eliminate undercuts and close the seams connecting the model fragments on the preformed model. The stamping was performed in the Ministar machine following the manufacturer's recommendations for working with Bioplast materials of various thickness and rigidity. The aligners were made for one or both jaws, depending on the type of occlusal relationships pathology. To treat occlusion anomalies in the sagittal direction, in particular, in case of distal occlusion issues, both aligners were interconnected in a constructive bite.

Different thickness and rigidity of the aligner ensured due adjustment through treating patients with various types of disclusion. In case of teeth crowding, the aligners proved to be better made of soft and thin material. At the final stage of distal occlusion treatment, after improving the dental arches shape, trainers from hard materials were used. The study outcomes showed that subjective adjustment to the aligners took place in the first week of using the aligner or trainer. The dental arch shape improved during the first year of treatment. Improving the jaws position and the achieving stable occlusive relationship took at least 16 months, which is consistent with the data reported by other experts.

CONCLUSION

To improve the shape and size of the dental arches, we recommend using tailor-made aligners made of soft and thin thermoplastic material. At the final stage of treating distal occlusion, once the dental arches shape becomes normal, using trainers made from rigid thermoplastic materials can be recommended.

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COMPARATIVE EVALUATION OF THE MAJOR GROUPS OF MANUAL TOOTHBRUSHES EFFICIENCY AND THEIR EFFECT ON THE ORAL CAVITY HYGIENIC STATUS

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ABSTRACT — There is a lot of importance attached currently to individual selection of hygiene products depending on the person's dental and hygienic status. This present study focused on the effectiveness of various toothbrushes, and involved 76 patients aged 18–35 years old with a *good* (OHI-S = 0–0.6) and a *satisfactory* (OHI-S = 0.7–1.6) levels of oral hygiene. The teeth periodont was assessed as healthy, *healthy* also implying mild gingivitis. All the brushes were divided into the following categories: depending on the bristles shape — cylindrical, needle-shaped, rubberized, textured; depending on the material — nylon, polyester; depending on the hardness — medium, soft. The hygiene level was evaluated with OHI-S (Green, Vermillion, 1964) before, 1, 2 and 3 months after the tested toothbrushes were taken for use. A visual inspection and microscopy were carried out using a Levenhuk light microscope (4× magnification). The bristles quality was considered satisfactory if their tips had no sharp and uneven edges, and the surface was smooth. Based on the data obtained, the wear of the bristles is linked directly to the oral hygiene quality as the brush field shape changes significantly through the operation period. Using of a manual toothbrushes made of the Tynex brand nylon and the Curen brand polyester significantly improves the individual hygiene quality and allows recommending it use to patients seeking to increase cleaning efficiency and lengthen their durability.

KEYWORDS — manual toothbrush, oral hygiene, hygienic status, dental plaque.

INTRODUCTION

There is research data available suggesting that dental plaque is one of the most significant etiological and pathogenetic factors for the development of caries and inflammatory periodontal diseases, while effective oral hygiene is the main way to remove it [1–7]. At the same time, incorrect methods of teeth cleaning and improper selection of toothpastes have an adverse effect on the hard tooth tissues thus contributing to a decrease in the hygiene quality, rapid development and complication of decay, as well as the development of non-cariou lesions (wedge-shaped defects) [8–13].

The need for dental preventive measures in various parts of the Russian Federation is known to be up to 96.8%. This situation is aggravated by a low dental health culture and poor patient compliance [14–16].

There are a large number of electric toothbrushes featuring different performance principles available now on the market; however, mostly due to economic reasons, manual toothbrushes in Russia still remain very popular [17–19].

Nowadays, toothbrushes include natural bristles or synthetic fibers (nylon, setron, perlon, dederlon, polyurethane). However, compared with synthetic fiber, natural bristles reveal a number of issues — a median canal filled with microorganisms, trouble keeping the brush clean, the bristles impossible to be made perfectly smooth while processing the tips, and trouble making it stiff as much as needed [20]. Besides, the surface and the tips of such bristles cannot be polished or rounded, which makes them potentially traumatic (Fig. 1).

Different manufacturers use synthetic bristles of different thickness and configuration. Advanced technologies allow now producing bristles with twisted hairs (the twister type) and the so-called micro-texture bristle, which is made through applying microvilli-shaped polymer coating on each bristle. Structured bristles clean the teeth not with the tips only, yet also with their side surfaces, which increases the toothbrush efficiency. Based on the degree of the bristles hardness (increasing order), manual toothbrushes can be ranged as follows: very soft (marked as *ultrasoft*, *extrasoft* or *sensitive*); soft (*soft*); medium hardness (*medium*); hard (*hard*); very hard (*extra hard*). Young children (up to 3) should use toothbrushes with very



Fig.1. Microphotograph of pork bristle. Magnification $\times 4$

soft bristles, while for the preschoolers and primary schoolers soft toothbrushes are recommended. The best type of brushes for teens and adults are medium. However, in case of periodontal tissues inflammation, oral mucosa diseases and non-caries lesions of hard dental tissues, soft toothbrushes are recommended. Brushes with hard bristles can only be used for a short course in case of a tendency to an increased development of plaque. Medium and soft brushes are most effective, their bristles being more flexible and penetrating better into the interdental spaces, tooth fissures and subgingival areas. In many cases nowadays, manufacturers combine bristles of different hardness — the harder ones (they are often made shorter) central bristles are to clean effectively the chewing surface of the teeth, whereas the softer (and often longer) peripheral bristles clean the teeth perigingival areas [21].

The degree of brush hardness is largely due to the thickness of the bristles. Nylon bristles of medium hardness, for instance, have a diameter of about 0.20 mm, soft ones — 0.15–0.18 mm. When combining bristles of different hardness in one brush, they sometimes may be marked with different colors. However, manufacturers often use bristles with different fiber diameters yet indicate one degree of hardness. By the type of the tips processing, bristles can be rifled, polished, rounded, ground, combined. The rounded tips of the bristles will not only increase the cleaning capacity of the toothbrush, but also will prevent damage to the tooth enamel, periodontal tissues and oral mucosa. Synthetic bristles made from materials available nowadays can be processed very well, due to which bristles with cone-shaped rounding and ultrathin tips can be obtained, which in turn offers better penetration into natural deepening in the tooth enamel.

Most studies focus on comparison of the features specific of manual and electric toothbrushes, their effectiveness and safety, as well as the capacity to eliminate issues pertaining to gingivitis, never taking into account the material and shape of the bristles [22]. The authors here believe that effective removal of plaque

and maintaining oral hygiene at a proper level will be achieved not only through the development of correct manual skills, yet also by due selection of personal products used to maintain oral cavity hygiene [23]. The wide range of such hygiene products offered by national and foreign manufacturers stirs among many authors a lot of interest in identifying the optimal material and shape of toothbrush bristles, as well as identifying their best acceptable service life.

Aim of study

To improve the efficiency of oral hygiene by selecting the optimal material and shape of toothbrush bristles and identifying their acceptable service life.

MATERIALS AND METHODS

The study involved 76 patients aged 18–35 years old with a *good* (OHI-S = 0–0.6) and a *satisfactory* (OHI-S = 0.7–1.6) levels of oral hygiene. The teeth periodont was assessed as healthy, while *healthy* also implied mild gingivitis. The study also included 10 popular manual toothbrushes of different size, shape, as well as the bristle hardness and material. To ensure more correct comparison in the future, depending on the bristles shape all the toothbrushes were conventionally divided into the following groups: cylindrical, needle-shaped and rubberized bristles (Table 1).

The total number of the toothbrushes included was 200, 20 brushes per group. The study was conducted subject to the GOST R52379-2005 requirements (Good clinical practice), with a written consent obtained from each of the participants. Each patient underwent the standard training method to develop due teeth-cleaning skills (method by N.G. Pakhomov, 1982). Prior to the study, all the patients were trained to brush their teeth properly with the *ROCS PRO* toothpaste up until their level of oral hygiene could be regarded as *excellent* or *good* (0–0.6 points by OHI-S index). To study the changes in the bristle structure when cleaning was performed improperly, an additional group was established, which included 20 different toothbrushes

Table 1. Study groups and their characteristics

Nº	Toothbrush name	Bristle shape	Bristle material	Bristle stiffness	Bristle length	Bristle thickness
1	"Aquafresh family"	Cylindrical	nylon "Tynex"	medium	0,95/1,1	0,23
2	"Colgate 360° Comprehensive Cleaning"	Cylindrical	nylon "Tynex"	medium	0,8/1,2	0,22
3	"Colgate 360° Charcoal"	Acicular	nylon "Tynex"	soft	1,1	0,23/0,15/0,01
4	"Colgate Premier Whitening"	Cylindrical	nylon 612	medium	1,0	0,21
5	"CURAPROX 5460 Ultrasoft"	Cylindrical	polyester	soft	0,9	0,1
6	"LACALUT aktiv"	Acicular	nylon "Tynex"	soft	1,0/1,3	0,2/0,11/ 0,01
7	"ORAL-B PRO-EXPERT"	Cylindrical	nylon "Tynex"	medium	1,0/1,1/1,2	0,18/0,2
8	"R.O.C.S. Black Edition"	Textured	nylon "Tynex"	medium	0,8/1,3	0,18/0,2
9	"SPLATCOMPLETE"	Acicular	nylon "Tynex"	medium	1,1	0,22/0,17/0,01
10	"SPLATWHITENING"	Rubberized	nylon "Tynex"	medium	1,1	0,22

(2 brushes from each group). Throughout the study (3 months), these brushes were used by patients cleaning their teeth mostly with horizontal movements and exerting excessive pressure on the brush.

Prior to use, the bristles on all the toothbrushes were subjected to microscopic inspection to assess the initial quality of the bristles. To do this, 50 bristles were cut from each brush (10 out of 5 different areas of the brush spot) (Fig. 2).



Fig. 2. Five areas of the brush spot where bristles were cut for the study

Visual inspection and photographing was carried out using a Levenhuk light microscope (magnification — 4×). The quality of the bristles was considered satisfactory if their tip had no sharp and uneven edges, while the surface was smooth. Similarly, 1, 2 and 3 months into using the brushes, a comparative assessment of the bristles wear in each of the groups was carried out. To understand the link between the bristle wear and the oral hygiene quality, the patients of all groups were assigned a simplified index of oral hygiene (OHI-S; Green, Vermillion, 1964) before, 1, 2 and 3 months into using the toothbrushes. The data statistical analysis was carried performed following the variation statistics method with the identification of

the mean value (M), standard deviation (σ). For statistical data processing, the statistical packages Microsoft Excel 2007 and Stat Soft Statistica v6.0 were used.

The critical significance level when testing statistical hypotheses in this study was taken as 0.05.

RESULTS AND DISCUSSION

The evaluation of the initial quality of the bristles in new toothbrushes revealed that the share of well-treated bristles in the study groups varied from 77.2% to 94.4%. At the same time, the group with the Colgate Premier Whitening toothbrush (belongs to the economy-class) showed the worst results. The best quality of bristles was observed on the CURAPROX, R.O.C.S., and ORAL-B brushes (Table 2).

Cylindrical bristles in Colgate Premier Whitening brushes (Nylon 612) proved prone to deformation through use. By the end of Month 3 into use, the bristles revealed moderate longitudinal stratification. At the same time, the tips erasability in this group was the highest, and could be observed during the first month already. By the end of Month 3, many bristles (76%) had had their tips significantly deformed ($p < 0.001$) (Fig. 3, 4).

The cylindrical bristles made of the Tynex nylon proved to be more wear-resistant compared to Nylon 612 (number of unsatisfactory bristles by the end of Month 3 went up by 21.3%).

Despite the thickness, polyester bristles showed good resistance to deformation, abrasion and stratification (increase in the number of unsatisfactory bristles by 20.4% by the end of Month 3) ($p < 0.001$) (Fig. 5, 6).

Needle-shaped bristles were most susceptible to deformations and stratification due to their minimal thickness. Through Month 1 already they showed the fiber dissociation reaching its significant degree by Month 3. Over a period of 3 months, the number of

Table 2. Initial quality of bristles and their wear through use, ($M \pm m$), ($p \leq 0,05$)

№	Toothbrush name	Percentage (%) of bristles with satisfactory quality			
		Before use	After 1 month of use	After 2 months of use	After 3 months of use
1	"Aquafresh family"	84,73 \pm 2,41	75,63 \pm 1,67	63,69 \pm 1,58	57,27 \pm 1,01
2	"Colgate 360° Comprehensive Cleaning"	82,49 \pm 1,94	75,24 \pm 1,52	63,25 \pm 1,74	54,18 \pm 1,32
3	"Colgate 360° Charcoal"	85,26 \pm 1,83	54,37 \pm 1,46	37,26 \pm 1,29	15,62 \pm 0,87
4	"Colgate Premier Whitening"	77,23 \pm 1,79	54,18 \pm 1,21	36,68 \pm 1,14	24,39 \pm 1,06
5	"CURAPROX 5460 Ultrasoft"	94,41 \pm 0,89	84,83 \pm 1,19	81,27 \pm 1,74	74,88 \pm 2,13
6	"LACALUT aktiv"	77,65 \pm 1,46	46,87 \pm 1,35	19,61 \pm 0,66	8,43 \pm 0,41
7	"ORAL-B PRO-EXPERT"	92,48 \pm 2,59	86,84 \pm 1,72	84,49 \pm 1,26	80,07 \pm 1,61
8	"R.O.C.S. Black Edition"	92,84 \pm 2,31	87,61 \pm 2,08	82,34 \pm 1,44	75,12 \pm 1,59
9	"SPLATCOMPLETE"	86,78 \pm 1,48	53,12 \pm 1,14	31,26 \pm 0,91	14,36 \pm 1,02
10	"SPLATWHITENING"	85,29 \pm 1,64	84,04 \pm 2,07	80,47 \pm 2,23	77,44 \pm 1,69

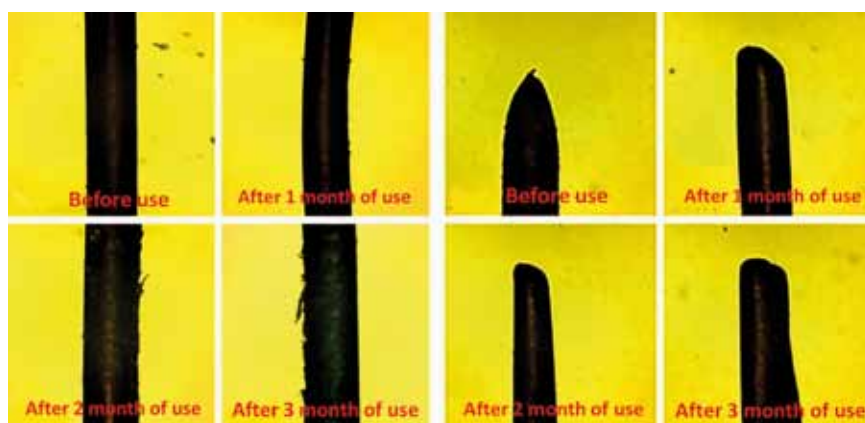
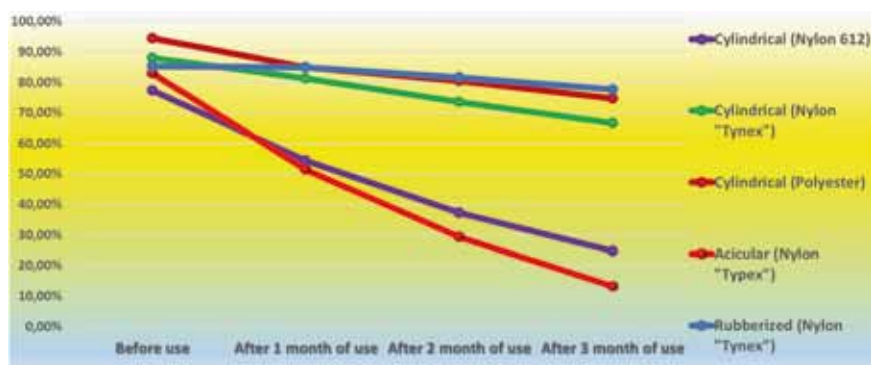
Fig. 3. External change in cylindrical bristles made of Nylon 612 at various stages of use (Colgate Premier Whitening). Magnification $\times 4$ 

Fig. 4. Bristles wear-resistance depending on the material and shape within 3 months

bristles with a quality level to be considered as unsatisfactory increased by 69.73% ($p < 0.001$) (Fig. 4, 6).

Prior to use, rubberized bristles have a raised surface. There was no bristle stratification, abrasion, or deformations detected reliably through their use (an increase in the number of unsatisfactory quality bristles by 7.6% after 3 months) ($p > 0.05$) (Fig. 4). However, note to be made that this texture of the

bristle surface is not as beneficial from the point of cleaning the bristles. Fig. 6 (2-B) shows toothpaste crystals accumulated in the bristles relief.

The results of dynamic changes in the oral cavity hygiene (based on OHI-S index) revealed a significant deterioration of oral hygiene in patients using brushes with needle-shaped bristles as early as by the end of Month 1. In most cases, the level of hygiene was

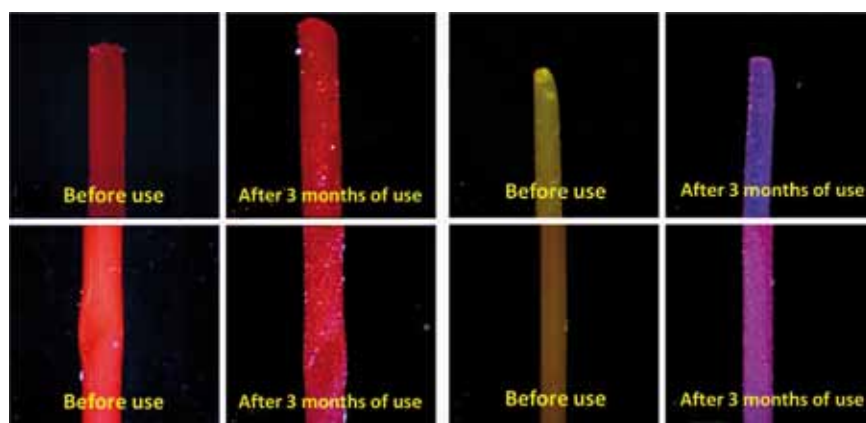


Fig. 5. External change in textured Tynex nylon bristles, R.O.C.S. Black Edition (1) and polyester bristles CURAPROX 5460 Ultrasoft (2) through various stages of their use. Magnification $\times 4$.

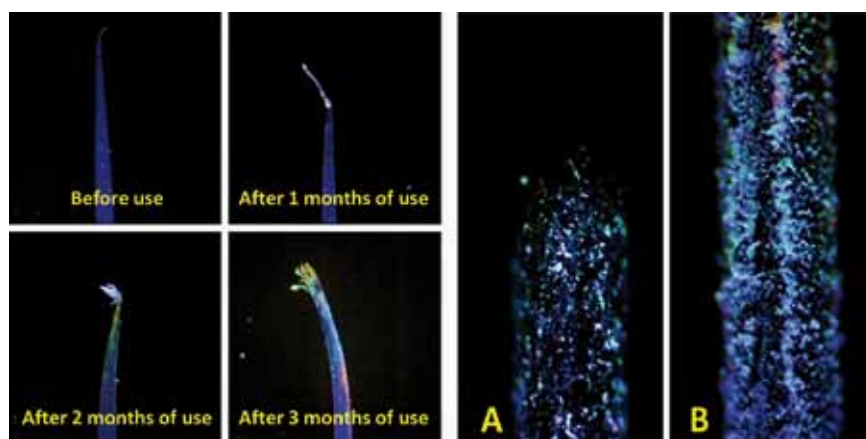


Fig. 6. External change in needle-shaped bristles, LACALUTaktiv and SPLATCOMPLETE (1), and rubberized bristles, SPLATWHITENING (2) through various stages of their use. A — before use; B — after 3 months. Magnification $\times 4$

rated as *unsatisfactory* (up to 2.5 points). By the end of Month 3, these values exceeded 2.6 points ($p < 0.001$). A similar dynamics was observed in the group using cylindrical bristles made of Nylon 612 (Table 3).

The patients using toothbrushes with cylindrical and rubberized bristles made of Tynex nylon featured no significant change in the hygiene level ($p > 0.05$). The group of patients using improper brushing techniques showed that in addition to the visible deformation of the bristles, their significant dissociation was also present. These changes were to be seen already through Month 1, and were significantly aggravated by Months 2 and 3. At the same time, the bristles had their edges getting sharp (Fig. 8).

CONCLUSIONS

1. The quality of bristles depends on the manufacturing material. The best processing quality was observed in bristles made from the Tynex nylon and polyester by Curen.
2. The wear-resistance of bristles directly depends on the thickness, shape and material. Nylon 612 showed a poorer resistance to abrasion than other

materials. The most resistant to stratification were cylindrical bristles, made of the Tynex nylon.

3. Needle-shaped bristles are prone to deformation and stratification by as soon as 1 month into use. This feature will not allow enjoying the advantage offered by the bristles shape, which provides free penetration into harder-to-clean areas.
4. Polyester bristles are most prone to stratification in case of improper brushing techniques are employed. However, they featured good abrasion-resistance despite their small thickness.
5. Bristles with rubber coating have good wear-resistance, yet have a rough surface, which may make their cleaning complicated.
6. The wear of bristles directly affects the quality of oral hygiene, as the use of toothbrushes changes significantly the shape of the brushing field, which is due to the pressure exercised by the bristles on the teeth surface, so in old brushes the bristles contact spot around the precervical part of the tooth will be incomplete thus making cleaning improper.
7. Using a manual toothbrush made from the Tynex brand nylon and the Curen brand polyester will

Table 3. Dynamic change in the oral hygiene, ($M \pm m$), ($p \leq 0,05$)

№	Toothbrush name	Indicators hygienic index OHI-S			
		Before use	After 1 month of use	After 2 months of use	After 3 months of use
1	"Aquafresh family"	0,48±0,04	0,58±0,03	1,48±0,08	2,36±0,11
2	"Colgate 360° Comprehensive Cleaning"	0,46±0,05	0,52±0,04	1,46±0,09	2,35±0,08
3	"Colgate 360° Charcoal"	0,32±0,03	1,56±0,07	1,98±0,11	2,36±0,12
4	"Colgate Premier Whitening"	0,28±0,04	1,52±0,08	2,02±0,06	2,56±0,09
5	"CURAPROX 5460 Ultrasoft"	0,44±0,06	0,76±0,07	1,24±0,09	1,48±0,05
6	"LACALUT aktiv"	0,37±0,03	1,88±0,09	2,36±0,14	2,72±0,13
7	"ORAL-B PRO-EXPERT"	0,52±0,05	0,56±0,04	1,42±0,07	1,56±0,09
8	"R.O.C.S. Black Edition"	0,54±0,02	0,77±0,06	1,29±0,08	1,58±0,07
9	"SPLATCOMPLETE"	0,43±0,03	1,86±0,08	2,27±0,12	2,67±0,09
10	"SPLATWHITENING"	0,39±0,02	0,83±0,03	1,18±0,06	1,43±0,08

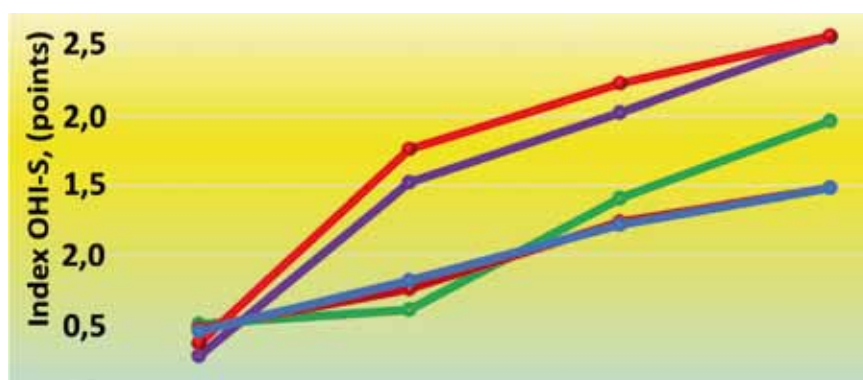
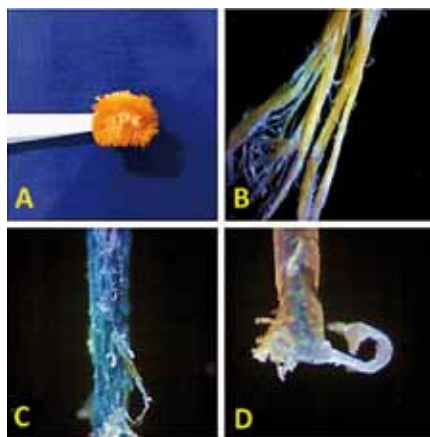


Fig. 7. Change in the oral hygiene level depending on the bristles shape and material through various stages of use

Fig. 8. Bristles after 3 months of improper tooth brushing. A — general view; B, C, D — bristles stratification. Magnification $\times 4$

improve significantly the quality of individual hygiene, which allows recommending it to patients as a way to improve the cleaning effect as well as to extend the toothbrush service life.

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MORPHOLOGICAL FEATURES OF DENTOFACIAL AREA IN PEOPLE WITH DENTAL ARCH ISSUES COMBINED WITH OCCLUSION ANOMALIES

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The level of development of each era determines the specifics of recognizing diseases and teaching about them. Nowadays, there is an increased interest taken by patients in their own appearance as well as in the structural features of the facial part of their heads [1, 2]. Another issue currently faced by the dentistry is the growing prevalence of dentofacial anomalies and deformities among various population groups [3, 4]. The etiological factors behind anomalies and deformities include dental system congenital and acquired pathologies, and especially dental arch defects [5, 6, 7]. The effect of the dental arches pathology on the craniofacial status has been proven in numerous works written by clinical experts [8, 9]. It has been noted that the timely treatment and preventive measures offered to patients with dental arches defects through different age periods, has a beneficial effect on the growth, development and condition not only of the masticatory system, yet also on the adjacent organs and body systems [10, 11, 12]. Given the above, studying maxillofacial morphology in people with dental arch defects will remain an urgent issue for dentistry.

Aim of study

To identify anatomical and physiological dentofacial features in people with dental arch defects combined with occlusion anomalies.

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MATERIAL AND METHODS

The maxillofacial area status was assessed in 312 people in their first mature period (21–35 years of age). Out of the total number of patients, a representative sampling was done involving 127 patients who needed pre-prosthetic orthodontic treatment. Subjective and objective research methods were employed following the protocol for the managing patients with partial absence of teeth.

RESULTS AND DISCUSSION

127 people out of 312 patients had a combined pathology, which accounted for $40.7 \pm 0.16\%$. Out of the patients with dental arches defects in combination with occlusion pathology, 50 patients were found to have individual teeth position anomalies, which was $39.4 \pm 0.38\%$ of the number of patients with combined pathology. Dental arches anomalies and deformities were observed in 35 people ($27.56 \pm 0.35\%$), while another 42 patients had pathological occlusion, which in relative terms was $33.1 \pm 0.37\%$ of the number of patients with the dental system combined pathology. Anatomical and physiological maxillofacial features, as a rule, had a pathology localization in the dental arch. Anomalies and deformities of the dental arches anterior part entailed aesthetic and functional impairments. There were frequent speech disorders and disturbed food bite. An incorrect position of the front teeth was the etiological factor behind periodontal disease accompanied by impaired blood circulation, while it contributed to the development of traumatic occlusion. There was pathological teeth mobility observed as well as disturbed teeth position in different directions. Patients with anomalies and deformities in the chewing segment, experienced discomfort in the mouth while chewing food. There was frequent overload of antimers, which suffered from additional stress in case of unilateral defects. In case of bilateral defects of the dental arches, patients often complained of the functional status of the temporomandibular joints. Patients with abnormal eruption terms, abnormalities in the number of teeth (hypodontia), and abnormal position of the teeth,

were found to have varying degrees of teeth deviation from their normal position.

CONCLUSION

The results of the study indicate a high level of occlusion anomalies prevalence in people with dentofacial arches defects. Anatomical and physiological dentofacial features were typically attributed to the dental arch pathology localization.

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INFLUENCE OF ANATOMICAL FACTORS ON MAXILLARY SINUS MEMBRANE PERFORATION DURING SINUS FLOOR AUGMENTATION SURGERY

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ABSTRACT — The Schneiderian membrane perforation is the most common intraoperative complication during the sinus floor elevation. The aim of the study was to evaluate different anatomical factors that can lead to the development of perforations and to identify significance of each of them. Those factors were: the membrane thickness, the presence of septa and the angle made by the medial and the lateral walls of the sinus. Preoperatively was analyzed CBCT data of 24 patients (32 sinuses) and compared them with the intraoperative data (the perforation rate within the whole groups was 34%). The results showed that the most significant factor in the present investigation was the angle between the medial and the lateral walls (the perforation rate varies from 0% to 63%).

KEYWORDS — maxillary sinus, the Schneiderian membrane, perforation, sinus-lift surgery, cone-beam computer tomography.

INTRODUCTION

The Schneiderian membrane perforation — is the most common complication of sinus lift surgery. The frequency of its occurrence varies from 11 to 56% according to literary dat [1]. The presence of perforation increases the risk of inflammatory complications by 5–10% and reduces the survival rate of implants by up to 15% [2, 3, 4]. Also, damage to the Schneiderian membrane often leads to cicatricial changes and disruption of normal mucociliary clearance [5]. The use of Pieszosurgery allows to reduce the frequency of development of this complication due to minimal traumatization of soft tissues during the formation of a bone window with lateral access and separation of

the Schneiderian membrane [6, 7]. It is fundamental to assume that the anatomical features of the structure of the maxillary sinus may play a role in the development of this complication [8, 9, 10].

Aim

The aim of the study was to identify the anatomical risk factors for the development of perforation of the mucous membrane of the maxillary sinus during sinus lift surgery. The following tasks were set:

1. at the preoperative stage to study the thickness of the mucous membrane, the features of the relief of the bottom of the sinuses (septa) and the angle between the anterior-lateral and medial walls of the sinus;
2. estimate the number of perforations arising intraoperatively;
3. determine the relationship between the above factors and the number of perforations.

MATERIAL AND METHODS

For the study, 24 patients were selected from whom the data of a cone-beam computed tomography and protocol data for 32 sinus-lifting operations in these patients were studied.

The criteria for inclusion of patients in the study were:

1. the absence of teeth in the distal upper jaw;
2. the need for a sinus lift operation using the lateral window method;
3. performance of all operations by one surgeon.

Criteria for non-inclusion:

1. the presence of violations of the structure of the osteomeatal complex;
2. the presence of pathological changes in the mucous membrane of the maxillary sinus.

RESULTS

Based on the preoperative analysis of CBCT data, the expected risk factors for perforation were:

1. thickness of the sinus mucosa, less than 1.5 mm in 17 cases and more than 1.5 mm in 15 cases (Fig. 1);

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- the angle between the anterior-lateral and medial walls of the sinus in the area where the operation was necessary. According to this criterion, all the sinuses were divided into 3 groups: group A — with an angle of up to 30° (N = 8); Group B — with an angle value from 30 to 60° (N = 15); Group C — with an angle of more than 60° (N = 9) (Fig. 2);

Moreover, if the angle exceeds 60°, then even if there are other anatomical risk factors (thickness of the mucosa less than 1.5 mm, the presence of septa), the likelihood of this complication is significantly reduced (Fig. 5).

CONCLUSION

When analyzing the data obtained, it was found that the angle between the anterior-lateral and medial

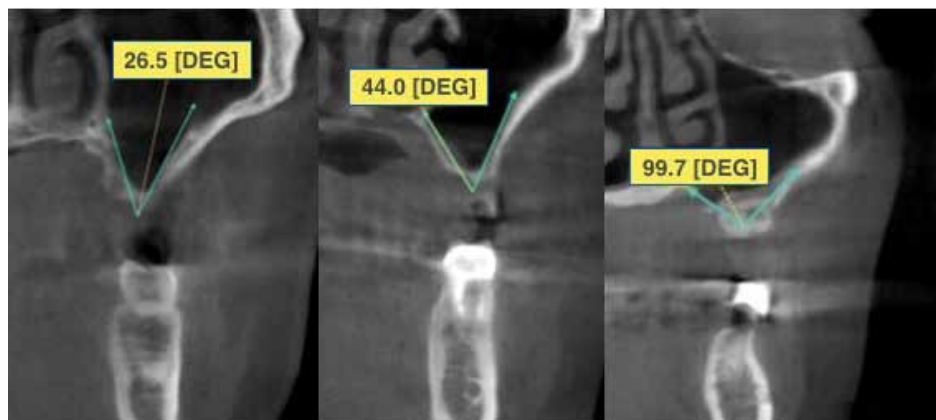


Fig. 1. Khorguani Thick sinus membrane

Fig. 2. Khorguani Angle degree between medial and lateral walls

- the presence of septa in the region of the bottom of the maxillary sinus (in the course of the work, the septa was found in only one case, therefore this criterion was excluded from further research) (Fig. 3).

Analysis of the protocols of the performed operations showed that in 32 operated sinuses, perforation occurred in 11 cases (34%) (Fig. 4).

Comparison of intraoperative data with CBCT data allowed to determine that:

- at a mucosal thickness of up to 1.5 mm, perforation appeared in 7 cases out of 17 (41%); with a thickness of 1.5 mm or more — in 4 out of 15 (27%);
- with the angle between the anterior-lateral and medial wall up to 30° (group A), the perforation of the Schneiderian membrane occurred in 5 cases out of 8 (63%); when the value is from 30 to 60° (group B) — in 4 out of 15 (27%); at a value of 60° and more (group C) — in no case did the perforation occur (0%).

DISCUSSION

The results of the study showed that most often perforation occurs at small values of the angle between the anterior-lateral and medial walls of the sinus.

walls of the maxillary sinus can be a leading risk factor for the occurrence of mucosal perforation. CBCT allows to measure the angle and predict the development of perforation of the Schneiderian membrane. It is recommended to start exfoliation of the mucous membrane from the distal parts of the maxillary sinus, where the angle is at its maximum, which will reduce the tension of the membrane, and reduce the frequency of occurrence of this complication.

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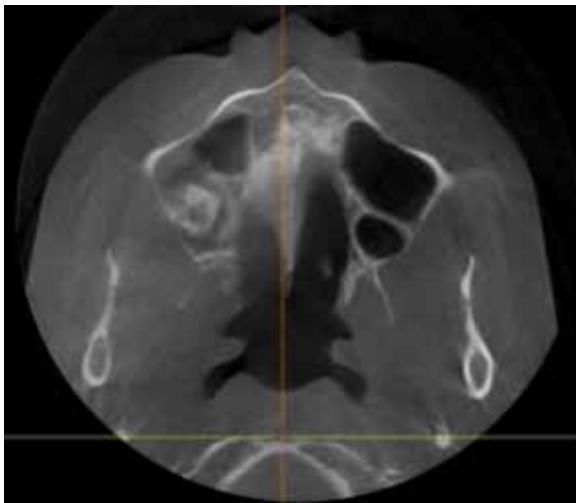


Fig.3. Khorguani Maxillary sinus septa



Fig.4. Khorguani Perforation of sinus membrane



Fig.5. Khorguani Maxillary sinus septa intraoperatively

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EVALUATION OF BIOLOGICAL INDIFFERENCE OF NEWER DENTAL LIGHT-CURED MATERIALS BASED ON OUTCOMES OF CLINICAL AND MORPHOLOGICAL STUDIES IN EXPERIMENT

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INTRODUCTION

Of numerous reasons that affect the reliability and durability of restoration, the oral hygiene level is among the top ones [1,2]. Poor oral care is known to be a factor facilitating cariogenicity [3,4,5,6,7,8]. At the same time, improper oral hygiene can also cause complications occurring after restoration (hyperesthesia, edge permeability and edge adaptation, secondary caries) [9]. The patient's hygiene status is of special importance when there are light-cured composite materials involved.

Currently, there is a large selection of chemical and light-cured composites. Different materials have certain advantages and disadvantages. All filling materials have their own features that determine the restoration reliability and aesthetics [10,11]. The major properties for composite materials include strength, polymerization,

ABSTRACT — THE AIM OF INVESTIGATION was to study the histological and immunohistochemical picture of periodontal tissues in experimental animals when exposed to the light-cured nanohybrid dental restorative material *Restaurin* with and without *Easy Glaze* coating. **MATERIALS AND METHODS.** A cariogenic model in the experiment on animals (50 rats), an artificial defect of hard tissues (Black class V) was created with further filling with the nanohybrid material *Restaurin* + sealant *Easy Glaze* (1st main group — P-1), *Restaurin* (2nd main group — P-2) and microhybrid composite *Filtek Z-250* (control group). **RESULTS.** In the study of periodontal segments in the comparison group and the group P-1, morphological differences were not determined. In the study of biopsy specimens taken from animals of the control group and group P-2, a number of dystrophic and inflammatory changes were detected. An immunohistochemical study of biopsy specimens in the comparison group and the P-1 group did not establish differences in the qualitative signs of immunocytes from their number and localization. In the study of biopsy specimens taken from animals of the control group and group P-2 there was a significant increase in the number of HLA-DR⁺ and CD3⁺ cells in the mucosal lamina propria; a slight increase in CD8⁺ cells in the mucosa itself. In the epithelium of animals in the control group and the group P-2, a decrease in CD4⁺ cells was recorded compared with the group of intact animals and the group P-1. In a number of drugs in animals of the control group and group P-2 there was a significant infiltration of CD16⁺ NK cells, CD20⁺ B cells of the papillary layer of the mucous membrane itself, CD23⁺ cells were observed, however, there was no pronounced infiltration of CD16⁺, CD20⁺ tissues and cells. **CONCLUSION.** Established in the course of the experiment on animals, the facts of the expression of molecules on gingival cells, antigen-presenting dendritic cells at different stages of maturation, B-lymphocytes carrying a low affinity receptor for immunoglobulin E, in our opinion, can be associated with a violation of periodontal contact during filling of artificially created solid defects tissues, as well as the penetration of aggressive microflora into the deeper layers of the mucous membrane and periodontal due to the low level of hygiene and lack of solid food in the diet of the animals. In addition, the lack of infiltration of the studied tooth-gingival segments of rats by CD23⁺ cells may indirectly indicate the hypoallergenicity of the restoring material *Restaurin*.

KEYWORDS — dental filling material *Restaurin*, sealant *Easy Glaze*, microhybrid composite *Filtek Z-250*, hypoallergenic.

elasticity modulus, wear resistance, thermal expansion, and hardness [12, 13].

The constantly developing market of dental materials offers new filling materials and even new groups of materials [14, 15, 16]. One of such materials is the light-cured nanohybrid dental filling material *Restaurin* manufactured in Russia (*Technodent*).

The issue of filling material functional properties, aesthetics and durability under poor hygiene conditions, as well as its impact on the oral cavity tissues, appears to be of considerable interest [17, 18].

Aim of study:

To investigate the histological and immune-histochemical profile of periodontal tissues in experimental animals when exposed to the light-cured nanohybrid dental restorative material *Restaurin* used with and without the *Easy Glaze* sealant.

MATERIALS AND METHODS

The experiment implied modeling a cariogenic situation in the oral cavity involving white rats (the experiment was conducted on the premises of the Research & Development Department of the Kuban State Medical University, Ministry of Health, Russia. The animals were selected based on the same type of housing conditions (limited cell area), yet with different diets and types of food, which served basis for the caries development. A total of 50 animals (six months old) were used through the experiment (Table 1).

After the cariogenic situation modeling was completed under general anesthesia (viz. intraperitoneal thiopental anesthesia, 0.1 ml of 5% sodium thiopental per 100 grams of animal weight) a spherical bur was used to go 2–3 mm under the gum thus making an artificial defect of hard tissues in the cervical area of mandibular incisors from the vestibular and lingual sides. Subject to the research plan, the created hard tissues teeth defects were filled with the nanohybrid material *Restaurin* + the *Easy Glaze* sealant (1st main group, R-1, n = 15), *Restaurin* (2nd main group, R-2, n = 15) and the microhybrid composite *Filtek Z-250* (3M ESPE) (control group, n = 10). Besides, immunohistochemical studies were carried out in the comparison group (intact animals, n = 10). 30 days later, with anesthesia, the animals had their dentoalveolar segments cut to be further fixed in a buffered formalin 10% solution, and decalcified in a nitric acid 20% solution. After processing through ascending alcohols the samples were embedded in paraffin. The histological sections were stained with hematoxylin-eosin, by Mallory and Masson. The morphometric examinations were performed using the Video-Test-Morphology 5.1 for Windows software. The identification of the subpopulation markers for immunocytes of the dentoalveolar segments tissues was performed through indirect biotin-extravidine-peroxidase method. For the study control, reaction was performed with normal mouse serum, which has no staining, rather than with primary antibodies.

Table 1. Comparative features of the animal groups involved in the study, ($M \pm m$)

Animal groups	Number of animals	Distribution by gender	Age of introduction to the experiment	The average body weight at the beginning of the experiment	The duration of the experiment
Comparison group	10	5 males, 5 females	6 months \pm 3 days	230,5 \pm 20,5gm	60 days
First group	15	7 males, 8 females	6 months \pm 3 days	230,5 \pm 20,5gm	60 days
Second main	15	8 males, 7 females	6 months \pm 3 days	225,5 \pm 22,5gm	60 days
Control group	10	5 males, 5 females	6 months \pm 3 days	225,5 \pm 24,5gm	60 days

The animals were assigned to groups in view of having an equal representation of male and female animals in each group as well as based on the limited average mass deviations (no more than 10%).

The caries model was developed within 1 month by keeping the animals of the main groups on the cariogenic Stephan diet. To boost the simulation, the rats' diet mentioned above was enriched with sunflower oil (2 ml per animal). The animals of the control group and of the comparison groups were kept on the standard balanced diet including solid food (cereals) and water with no limit.

The experiments were carried out following the International Principles of the European Convention for the Protection of Vertebrate Animals Used for Experiments and Other Scientific Purposes (Strasbourg, 1986), Common Ethical Principles of Animal Experiments (Russia, 2011), subject to the principles of good laboratory practice (The national standard Principles of Good Laboratory Practice GOST R 53434-2009) and the positive conclusion from the Ethics Committee of the Kuban State Medical University, Ministry of Health of Russia. Statistical data processing was

performed using Statistica 6.0. Data treatment was carried out through attribute control charts and non-parametric criteria testing.

RESULTS AND DISCUSSION

As the experimental study showed, in the comparison group (intact animals, $n = 10$), the basal layer of the buccal epithelium included cells of mainly prismatic shape with basophilic cytoplasm and nuclei located in 1–3 rows. The granular layer itself consisted of several rows of flattened cells with elongated hyperchromic nuclei, while the epithelium mucous membrane appeared as papillae penetrating deep into the buccal epithelium. Cells near the basement membrane had shortened processes and resembled HLA-DR⁺ cells located in the spinous and granular layers, which also had a process-like structure. The obtained data on the autokinesis of antigen-presenting dendritic cells from capillaries straight through the basement membrane into the entire epithelium thickness, and then back through the lymphatic bed to the secondary lymphoid organs, is within the norm. The results in the comparison group revealed that CD3-positive cells were found in small quantities in the spinous layer, could be occasionally detected in the papillary layer of the proper mucous plate (lamina propria), and sometimes — in the reticular layer. The tissue distribution of the detected CD3⁺ cells, which were represented by the CD4⁺ and CD8⁺ subpopulations (where CD4⁺ were, actually, the helpers/inductors, and the CD8⁺ — the cells), in general, corresponded to the distribution specific of CD3⁺ cells. CD4⁺ cells, in turn, were localized in a small amount in the spinous or basal epithelium layers, while CD8⁺ cells — only in the basal layer and, significantly less often, in the adjacent rows of the spinous layer. A number of preparations revealed the presence of CD8⁺ cells on the tops of the interdental papillae, while CD4⁺ cells were identified between the papillae of the proper mucous plate, in an amount of 3–5 per microscope field.

CD20⁺ cells were observed in 2 preparations only, while the majority of immunocytes were represented by antigen-presenting HLA-DR⁺ cells and a subpopulation of T cells (Fig. 1).

Consequently, in the comparison group, CD23⁺ cells (B-lymphocytes mediating the low-affinity receptor for immunoglobulin E) basically were not to be observed. The papillary layer contained HLA-DR⁺ cells, from 6 to 9 per one field, which lined up along the basal membrane. An immune-histochemical examination of biopsy specimens obtained in group R-1 (*Restavrin* + *Easy Glaze* sealant) revealed the impaired keratinisation of the keratinocytes, which manifested itself as isolated parakeratosis. Vacuolar cell degeneration was mainly observed in the epithelium spinous layer;

moderate round cell infiltration was mainly recorded in the lamina propria papillary layer. Collagen fiber thickening was observed in the reticular layer only. In the spinous epithelium, HLA-DR⁺ cells were detected near the basal membrane, as well as in the papillary and reticular layers in an amount of 5 to 7 per one field (Fig. 2).

The number of CD3⁺ cells in the preparations of this group increased if compared with the norm, while 3 to 5 cells per 1 field were localized in the spinous layer, near the basal membrane, and from 2 to 3 — in the mucosa papillary layer. CD4⁺ cells, in turn, in an amount of 3 to 6 per one field were located in the main, spinous and basal epithelium layers as well as along the basal membrane of the proper mucous plate. Special mention is to be made that the number of cells decreased significantly compared to the intact animals group, whereas specific CD8⁺ cells (4 to 6 per one field) were located both in the basal and in the adjacent spinous layer. The epithelial layer of the mucous membrane revealed no changes in the number of CD16⁺ cells, and the number of CD20⁺ cells which mediate the B-cell population was also not significantly different from the similar index in the comparison group (intact animals) where CD23⁺ cells were detected (Fig. 3).

The biopsy specimens of the R-1 group neither morphologically nor immune-histochemically confirmed the signs of chronic nonspecific inflammation involving cellular and humoral immunity. As the results of the study in the R-2 group showed, immuno-histological preparations featured moderate transformations in the morphological structure of the periodontal disease manifested as mild keratinisation disturbance. Actually, the parakeratosis manifestations were significantly less prominent than in the biopsy specimens of the R-1 group. Edema and round-cell infiltration of the proper mucous plate were detected in a small part of the biopsy specimens. Collagen fibers were visualized in the reticular layer, they had a predominant view of slightly thickened and compacted plates, while no round-cell infiltration was detected. In the R-2 group, CD3⁺ cells were detected near the basal membrane; their number in the mucosal epithelium did not change compared with this index in the comparison group and the R-1 group; however, a significant number of CD4⁺ cells were identified (3 to 9 per one field). The total number of CD4⁺ cells located directly near the basal membrane and in the papillary mucosal layer, if compared with the R-1 group, did not change and ranged from 4 to 6 per one microscope field (Fig. 4).

CD8⁺ cells were located in the depth of the spinous layer and near the basal membrane (Fig. 5).

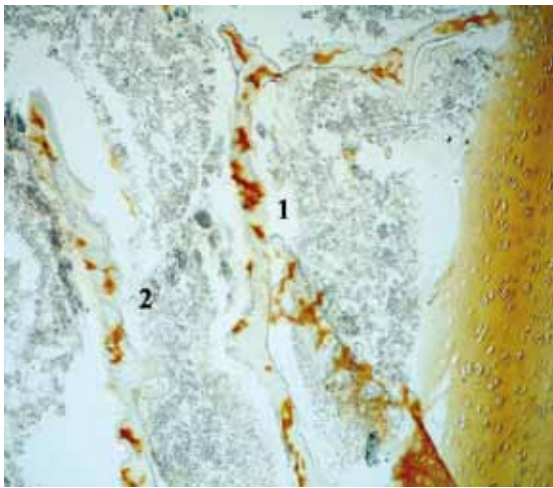


Fig. 1. Micro-photograph of the intact papilla fragment of an animal from the comparison group, $n = 10$. Cryostat section; mcAT1-anti-HLA-DR; AES development; contrasting — Mayer's Hemalum; Oc. 15, Obj. 60. Numerical designation: 1. HLA-DR+ cells in the basal membrane thickness; 2. HLA-DR+ papillary mucosal cells.

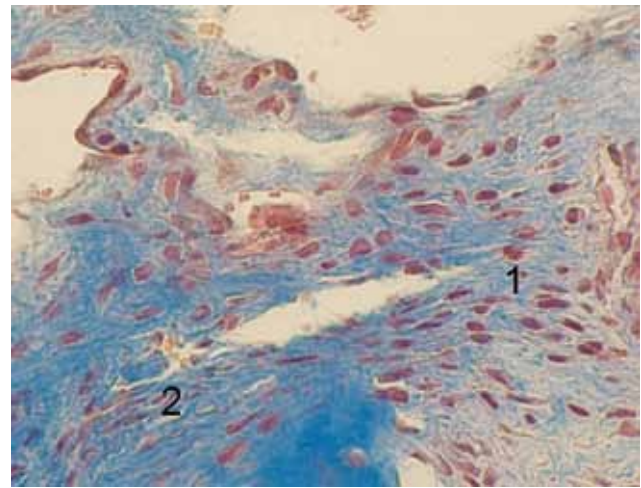


Fig. 2. Micro-photograph of the papilla fragment of an animal from group R-1, $n = 15$. Cryostat section; mcAT1-anti-HLA-DR; AES development; Contrast — methylene blue; Oc. 15, Obj. 60. Digital expression: 1. HLA-DR+ cells of the epithelium spinous layer; 2. HLA-DR+ cells of the mucosa

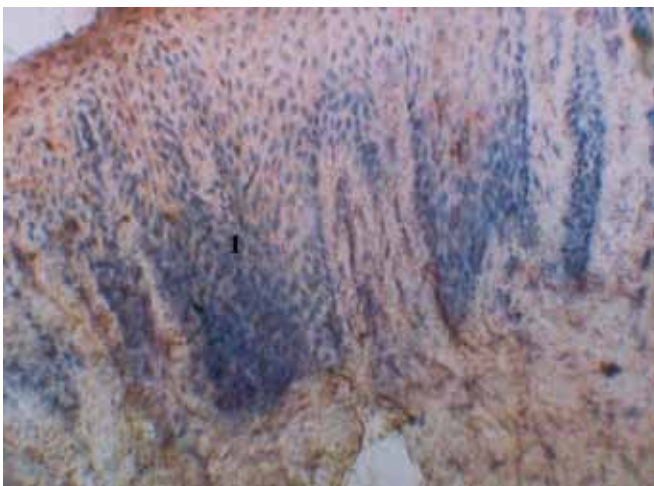


Fig. 3. Micro-photograph of a gingival papilla fragment in group R-1, $n = 15$. Cryostat section; mcAT1-anti-CD20; AES development; Contrast — methylene blue; Oc. 15, Obj. 60. Numerical designation: 1. CD20+ cells

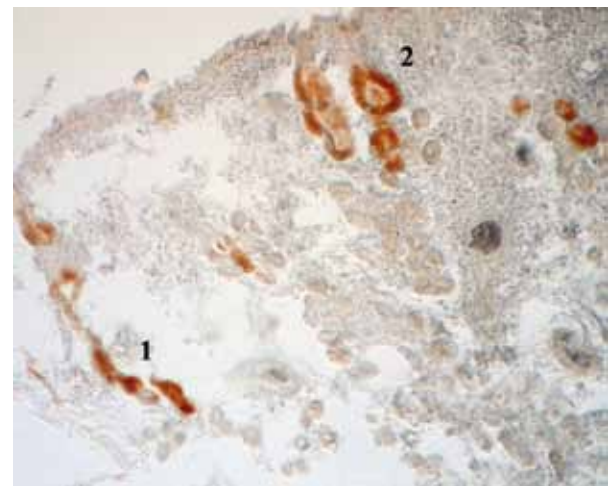


Fig. 4. Micro-photograph of a gingival papilla fragment in group R-2, $n = 15$. Cryostat section; mcAT1-anti-CD4; AES development; contrasting — Mayer's Hemalum; Oc. 15, Obj. 60. Numerical designation: 1. CD4+ cells of the epithelium spinous layer; 2. CD4+ cells of the mucosal papillary layer

It should be noted that there were basically no CD23⁺ and CD16⁺ NK cells, while the number of CD20⁺ cells was insignificant (1 to 3 per a field), which helps describe the morphological compartment of the isolated tissues as specific. The expression of HLA-DR molecules, which was particularly evident in the mucous membrane, was also observed in cells located in the spinous layer above the interdental papillae tops, near the cells of the basal layer, in an amount of 8 to 15 per microscope field (Fig. 6).

Besides, infiltration of the papillary layer of proper mucous plate the CD3⁺ cells in an amount of 5 to 10 per microscope field was registered. The number of CD3 positive cells was reduced in the epithelium of the proper mucous plate (2 to 4 per one field). When studying the biopsy specimens of the control group (*Filtek Z-250*), parakeratosis were observed in up to 2/3 of the studied preparations (increased keratinocyte keratinization) and mild vacuolar dystrophy. Spongiosis was observed in 1/3 of the preparations. The

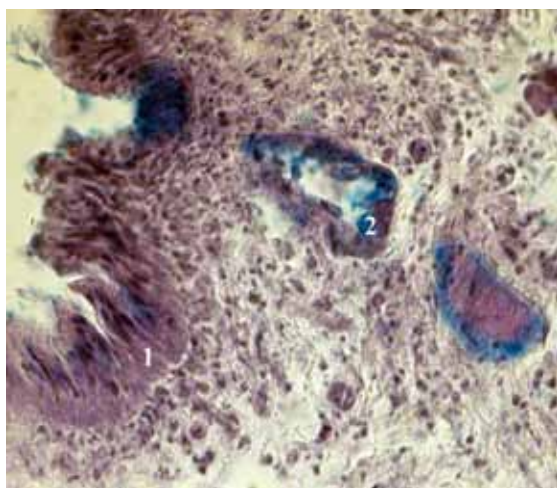


Fig. 5. Micro-photograph of a gingival papilla fragment in group R-2, $n = 15$. Cryostat section; mcAT1-anti-CD8; AES development; contrasting — Mayer's Hemalum; Oc. 15, Obj. 60. Numerical designation: 1. CD8⁺ spinous layer cells; 2. CD8⁺ basal layer cells

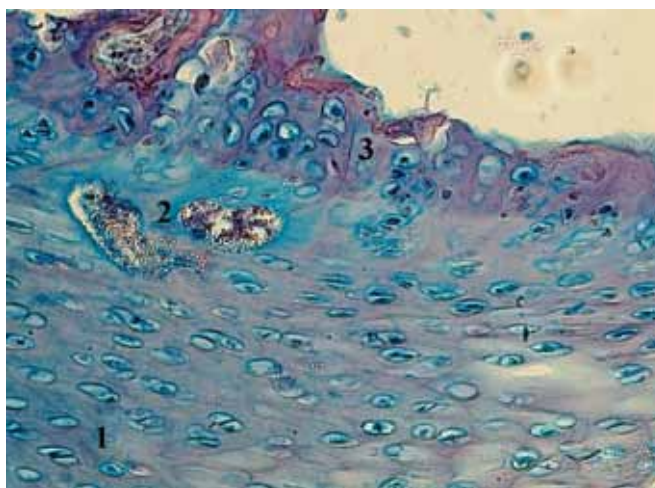


Fig. 6. Micro-photograph of a papilla fragment in group R-2, $n = 15$. Cryostat section; mcAT1-HLA-DR; AES development; contrasting — Mayer's Hemalum; Oc. 15, Obj. 60. Numerical designation: 1. HLA-DR⁺ spinous layer cell; 2. HLA-DR⁺ cells near the basal membrane; 3. HLA-DR⁺ cells of the mucous membrane

papillary layer at the peripheral vessels mainly localized HLA-DR⁺ cells (5 to 12 per one field). Moderate CD3⁺ cells infiltration of the epithelial layer was also observed (2 to 5 per one field) and partly of the mucous papillary layer (5 to 9 per 1 field) (Fig. 7).

CD4⁺ cells located in the spinous layer, and less (1 to 3 per one field) in the epithelium basal layer; their number basically revealed no change compared to the intact periodont in the reticular and papillary layers of the lamina propria. CD8⁺ cells were also observed in the papillary and reticular layers of the proper mucous plate (4 to 9 per one field).

CONCLUSIONS

1. The immune-histochemical study revealed no qualitative difference between the number of immune cells in the biopsy specimens of the gingival papillae in intact animals and animals of the R-1 group (*Restavrin* + *Easy Glaze* sealant). A morphological study of gingival papilla biopsy specimens in the control group (*Filtek Z-250*) and the R-2 group (*Restavrin*) revealed signs of an inflammatory process characterized by an increase in the number of HLA-DR⁺, CD3⁺, CD8⁺ cells in the epithelium along with a reduced number of HLA-DR⁺, CD4⁺ cells and an unchanged number of CD3⁺, CD16⁺, CD20⁺, CD23⁺ cells in the lamina propria among the dentoalveolar segments.

2. Objective facts of molecules expression on the studied cells, as well as the revealed cytological signs manifested as antigen-presenting dendritic cells at different maturation stages, the presence of B-lymphocytes carrying a low affinity receptor for

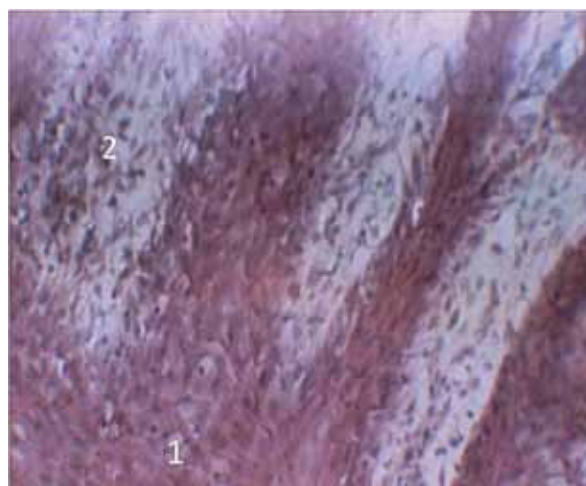


Fig. 7. Micro-photograph a gingival papilla fragment in the control group, $n = 10$. Cryostat section; hematoxylin and eosin staining; Oc. 15, Obj. 60. Numerical designation: 1. vacuolar dystrophy; 2. papillary layer lymphoid infiltration

immunoglobulin E – indicate disturbed intercellular cooperation and penetration of pathogenic microflora into the deeper layers of mucous membrane and periodont due to poor hygiene and lack of solid food in the experimental animals' diet. The absence of intercellular CD23⁺ infiltration in the studied biopsy specimens is an indirect indication of hypoallergenic properties of the *Restavrin* and *Restavrin* + *Easy Glaze* sealant used in the experiment.

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DEPENDENCE OF STRESS STRAIN OF DENTAL HARD TISSUES AND PERIODONT ON HORIZONTAL DEFORMATION DEGREE

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The cause-and-effect connection for dental arches deformations is high prevalence of hard dental tissues pathology and associated anomalies of occlusal relations [1,2,3]. Besides, the morphological features of the dentofacial segments, dental arches and the dentofacial area have a significant impact on pathology development [4,5,6]. Clinical dentistry attaches particular importance to dental arches deformation in the horizontal direction. Totally opposite treatments have been proposed: in some cases, the orthodontic treatment is recommended prior to prosthetics, while in others the treatment policy implies odontopreparation of the proximal surfaces of the teeth, which limit the defect, before creating parallel walls [7,8,9]. Teeth and morphological structures of the dentofacial area get stress-strained under various effects, both physiological and pathological [10,11,12]. However, issues related to selecting the optimal location for the teeth roots when performing dental arch defect prosthetic treatment, still remain relevant. The points that cause issues include questions regarding stress-strain status of abutment teeth located at a certain angle towards each other, which stands behind the aim of the present study.

Aim of study

To identify the dependence of the stress-strain status of dental hard tissues and periodont on the horizontal deformation.

MATERIAL AND METHODS

To conduct this study, a mathematical model was developed, which allowed assessing the stress-strain status occurring in the dental hard tissues and in the periodont against the chewing load. The stress status was measured in megapascals (MPa). At the same time, the elastic properties of model materials (Young's modulus, Poisson's ratio) for dentin tissue were 1,560 MPa, $\nu = 0.32$; for periodontal tissues they were significantly less ($E = 15$ MPa, $\nu = 0.45$), whereas for the bone tissue they reached the maximum values of 20,000 MPa ($\nu = 0.3$). The models were distributed into 4 groups. Group 1 included the deformation simulation of 10° to 15°. Group 2 consisted of models where the medial inclination of the first mandibular molar varied from 16° to 25°. In the third group, the horizontal deformation was 26–35°. The fourth group had a teeth inclination varying from 36° to 50°. When estimating the deformation status, displacement scales (mm) and von Mises equivalent stress patterns (SEQV) were used.

RESULTS AND DISCUSSION

In case of a mesial inclination of the mandibular molar towards the defect, the observed models of the dentofacial segments featured redistribution of the loads, the dependence of which was determined by the respective tooth inclination. Where the inclination was 10–15° at the mesial occlusal surface of the crown near the first order central groove, the stress status was 5.0 ± 0.13 MPa. With an increase in the tooth inclination from 16° to 25°, the value increased up to 7.0 ± 0.13 MPa. As for Groups 3 and 4 models, the indicators were 9.5 ± 0.11 MPa and 14.5 ± 0.11 MPa, respectively. At the mesial root, in its cervical third, the stress status was 1.28 ± 0.46 MPa. In Groups 2, 3 and 4, the parameter in question was 1.88 ± 0.22 MPa, 2.7 ± 0.21 MPa and $2.87, 8 \pm 0.18$ MPa. The stress status at the septum interradiculare in Group 1 was an average of 0.98 ± 0.26 MPa, and slightly decreased beyond the tops of the teeth roots going down to 0.64 ± 0.12 MPa. In Group 2, the stress status at the area of the septum interradiculare, was 1.12 ± 0.22 MPa; in Group 3, the

indicators increased up to 1.5 MPa, while in case of the tooth inclination of 36° to 50°, the parameter was 1.82 ± 0.16 MPa. The deformed status value also varied in view of the tooth inclination. In the model plane image of the total displacements, the deformed status value at the central fissure (with the tooth inclination of 10° to 15°) was 0.045 ± 0.004 mm. In the bone tissue, deformation was observed at the tooth neck and the cervical third of the root, while the deformation status value, based on vectors, was 0.033 ± 0.002 mm. An inclination increase up to 16–25° resulted in bringing the studied parameters at the tooth crown to 0.06 ± 0.005 mm, which exceeded significantly similar values for deformation of up to 15°. From the distal molar neck surface to the cervical third of the root, the deformed status value was 0.045 ± 0.003 mm. In Group 3, the deformed status indicators at the tooth crown were 0.065 ± 0.004 mm, and in the bone tissue — 0.047 ± 0.003 mm. In Group 4, the indicators were 0.10 ± 0.005 mm and 0.088 ± 0.003 mm, respectively.

CONCLUSION

Horizontal deformation of the dental arches, accompanied with a distal tooth mesial inclination, comes along with changes in the stress-strain status in the teeth hard tissues as well as in the periodontal complex tissues, whose severity is determined by the inclination degree and the type of deformation. The data obtained can be used in clinical practice of orthopedic dentistry for diagnostic purposes and to select methods for preprosthetic orthodontic treatment.

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CLINICAL MANIFESTATIONS OF TEMPOROMANDIBULAR JOINT DYSFUNCTION IN PATIENTS WITH FREE-END EDENTULOUS SPACE

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INTRODUCTION

The most common pathology in clinical orthopedics that affects adult population is dentition issues localized in various parts of the dentition [1–6]. The worst thing here — from the topography view — is free-end edentulous space, which, in case of lacking timely treatment will develop into masticatory muscle and temporomandibular joint (TMJ) pathology [7–12].

Aim of study

To identify the major clinical symptoms of masticatory muscle and TMJ pathologies, and to determine their prevalence in patients with free-end edentulous space.

MATERIALS AND METHODS

The study involved 280 patients with free-end edentulous space, of them 160 (57.1%) being females, with another 120 (42.9%) males aged 24–65. Through diagnosing the TMJ dysfunction we identified the maximum value of the mouth opening at vertical, lateral, and frontal mandibular movement; the type and the steadiness of the mandibular movement; pain symptoms in the TMJ and in the masticatory muscles at palpation and at various movements; the presence and the degree of articular noise.

RESULTS OF STUDY

Studying mandibular movements allowed identifying their limit at maximum mouth opening in 42.9%

of the patients, while in 28.6% of them the maximum opening was reduced to 25–37 mm, and in another 14.3% of the patients that value was below 25 mm. 57.1% of the patients had mandibular vertical movements within the normal values (38–56 mm).

Restricted lateral mandibular movement was registered in 42.9% of the patients, whereas 32.2% of them had lateral movements values now exceeding 5–9 mm, and in another 10.7% — less than 5 mm. In 57.1% of the patients, lateral movements were within the normal range (10–11 mm).

The frontal (protrusional) movement of the mandible was restricted in 14.3% of the patients, including 10.7% of the patients who had the respective value in between 3–5 mm, while 3.6% of the patients had it below 3 mm. In 85.7% of the patients the mandibular movement forward was within the full range (5–7 mm).

The asymmetric nature of the mandible movements relative to the midline at the mouth opening was observed in 21.4% of the patients. At the same time, 17.8% of the patients had the mandible shifting to the right or left in the initial phase of the mouth opening, and then returning to the midline. In 3.6%, the mandible shifted to the side without returning to the midline, and in the final phase of the mouth opening, it featured a shift to the side by more than 2 mm. In 78.6% of the patients, no mandible movements asymmetry was identified, while the mandible lateral shift did not exceed 2 mm.

A pain response from the TMJ during mandibular articulation was to be observed in 17.9% of patients, while in 10.7% of the patients it was observed with one mandibular movement, and in 7.2% of the patients — with two or more movements. 81.1% of the patients manifested no pain symptoms.

Pain symptoms through mandible articulation which localized in the masticatory muscles were observed in 17.9% of the patients. In 82.1% of the patients, no signs of pain were registered when the masticatory muscles were not moving.

The lateral and distal palpation of the TMJ produced pain symptoms in 17.9% of the patients. At the

same time, 10.7% of the patients had mild pain symptoms, while in another 7.2% of the cases pronounced soreness in the TMJ was registered. 81.1% of the patients reported no pain or discomfort at palpation.

The masticatory muscles palpation was painful in 17.9% of the patients. At the same time, as a rule, painful palpation of one to three masticatory muscles was determined. Painful response was more often observed at palpation of the external pterygoid and masticatory muscles. Less frequently, pain was reported in case of temporal muscles palpation. Painless palpation of the muscles under examination was observed in 82.1% of the patients.

Articular noise in the TMJ was registered in 35.7% of the patients. At auscultation, articular noise revealed crunch, friction, and clicking sounds. In 64.3% of the patients, auscultation showed uniform and soft sounds, with no signs of pathological articular noise.

CONCLUSIONS

The above shows that in patients with free-end edentulous space, the leading clinical symptoms of the TMJ and masticatory muscles pathology include restricted maximum mouth opening at vertical, lateral and anterior movements of the mandible; asymmetry of mandibular movements at mouth opening; pain symptoms in the TMJ and masticatory muscles through palpation and various mandibular movements; articular noise.

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SCANNING ELECTRON MICROSCOPY AND X-RAY SPECTRAL MICROANALYSIS IN STUDYING DENTAL TISSUE RESISTANCE

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INTRODUCTION

The results of the multinational pilot research project *European Oral Health Indicators* (EGO-HID-2005 system) for 2013–2018 revealed that the lowest level of hard tissues mineralization in permanent teeth was observed in the first years after their eruption. Thus, in the key age categories for 12-year-old children, the prevalence of caries was 81.1–100% with an intensity of 3.51–5.03, while for the 15-year-olds the numbers amounted to 84.3–100% and 4.17–6.27, respectively [1–7].

Experts studying caries believe that the pattern of increase in the prevalence and intensity of carious lesions in permanent teeth in children through 6 to 15 years of age is due to the following factors: diet imbalance; physiological hypomineralization of the teeth hard tissues due to incomplete enamel maturation; increased pathology in pregnant women; chronic maternal diseases leading to fetal hypoxia; use of medication; genetic susceptibility to caries; environmental issues; reduced overall resistance in children [8–14]. One of the negative factors is premature transfer to formula feeding, which entails overstrain in adjustment mechanisms and immunity. Failure of the physiological systems in case of changed type of feeding leads to a rapid increase in weight & height parameters with the redistribution of calcium-phosphorus ratio, which is not in favor of hard tooth tissues. An important role also belongs to physical development acceleration, which leads to earlier eruption of not milk teeth only, yet also of permanent teeth [15–21].

ABSTRACT — AIM. Potential use of scanning electron microscopy with X-ray spectral microanalysis to determine the structural, functional and acid resistance of tooth enamel through mineralization stages.

MATERIALS AND METHODS. A VEGA II LMU high-resolution scanning electron microscope with an INCA Energy 350XT X-ray microanalyzer, were used to identify the degree of packing, size, and shape of enamel prisms and interprismatic intervals, as well as the content of chemical elements in the upper layer of permanent teeth enamel. Structural, functional and acid resistance of enamel was studied using the enamel resistance test (V.R. Okushko, 1984). The material used included 47 premolars (removed for orthodontic reasons) with no sign of carious lesions in children belonging to the age group of 11–16 with a mineralization period of 6–60 months from the time of eruption.

RESULTS. The results of X-ray spectral microanalysis regarding the chemical elements content in weight percent, revealed that through the maturation (mineralization) stages, the surface enamel layer featured a significant trend towards increasing the Ca, P, and F concentration, as well as Ca/P ratio, along with a decrease in the level of C, Na, O. An investigation into children undergoing the early stages of physiological maturation revealed that tooth enamel had a hypomineralized structure of the hydroxyapatites crystalline grid with disturbed spatial orientation and boundaries accuracy, changed organic matrix depth, increased shell size and polymorphisms in the enamel prisms structure along with a reduced density of their packing. The combination of these signs is indicative of incomplete development of prismatic enamel structures with an unbalanced ratio of the mineral component and the organic matrix.

CONCLUSION. The obtained results demonstrate potential use of high-resolution electron microscopy with X-ray spectral microanalysis to study dental hard tissues. Development and introduction of personalized approaches to caries prevention based on selective usage of remineralizing drugs and vitamin-mineral complexes, would improve resistance to caries through all stages of physiological maturation.

KEYWORDS — scanning electron microscopy, X-ray spectral microanalysis, caries resistance, enamel mineralization, enamel chemical composition.

Most specialists claim that the central role in caries development belongs to the local situation in the oral cavity. Lack of proper hygienic care, for instance, as well as increased microbial contamination, excessive

development of dental plaque deposits, hypo-salivation, periodontal inflammatory issues, and the development of multiple retention spots act as conditions facilitating rapid caries progress [22–26].

Some researchers, however, question the key role of the previously identified factors, because in people featuring high resistance to caries, these issues do not lead to carious lesion. In their opinion, caries resistance is due to morphological features of the enamel structure, the structure specifics, the teeth shape and microrelief, and the presence and size of the gaps between the teeth [27–34].

In children, during eruption or soon after it is complete, poorly mineralized hard tooth tissues have no time to be saturated with micro- and macroelements, and are in the phase of structural and functional immaturity being most susceptible to intensive saturation with mineral components. The enamel of immature teeth reveals high variability of morphological structures. This morphology features immature enamel microroughness, where depressions, niches, micropores, and areas of minor packing density of crystalline structures are combined with wide interprismatic intervals and unclear boundaries of enamel prisms. An erupted tooth enamel has a volume of micropores reaching 6%, while in mature enamel this index will not exceed 0.2%. In immature enamel, apatites are mainly represented by the hydroxyapatites that are least resistant to dental plaque acids [35–41].

Experts state that the chemical composition specifics, incomplete mineralization and the specific morphology combined with the microroughness of immature enamel in the children lay the ground for a cariogenic situation entailing high risk of carious lesions due to significant enamel solubility, low acid resistance, a tendency towards focal demineralization, and poor resistance to the aggressive action of cariogenic factors [42–47]. Despite the significant amount of published studies focusing on the permanent teeth enamel caries-resistance at the maturation stages, given the modern clinical and diagnostic approaches, the available data on the chemical composition and microstructure of the surface during intensive tertiary mineralization is scarce and isolated, which determined the purpose of this study.

Aim of study

To investigate potential use of scanning electron microscopy and X-ray spectral microanalysis in identifying the structural & functional, as well as acid resistance of tooth enamel through the mineralization stages.

MATERIALS AND METHODS

On the premises of Department of Pediatric Dentistry, Orthodontics and Oral and Maxillofacial Surgery (Kuban State Medical University) we carried out an evaluation of the dental status in 38 children aged 11–16 undergoing orthodontic treatment and diagnosed with Class (K07) “Oral and maxillofacial anomalies [including bite anomalies]”, subclass (K07.3) “Anomalies of the teeth: crowded teeth” (ICD-10).

The criteria for the inclusion in the study were: I–II health groups (by Yu.E. Veltischev, 1994); a good level of dental health: DMF index below 2.6; oral hygiene index (OHI) (Yu.A. Fedorov, V.V. Volodkina, 1970) below 2.0; OHI-S (Green, Vermillion, 1964) below 1.6; Type I–II microcrystallization of oral fluid; teeth (premolars) recommended to be removed for orthodontic reasons with no signs of carious lesions.

At the first stage of the work, the assessment of the structural & functional and acid resistance of the enamel on the premolars to be removed for orthodontic reasons, was performed using the enamel resistance test (ERT-test, V.R. Okushko, L.I. Kosareva, 1984). The diagnostics of enamel focal demineralization in the teeth to be removed for orthodontic reasons was performed through the method of vital staining (Axamit L.A., 1978) and Caries Indicator (Omega Dent, Russia). The enamel staining intensity was evaluated with a colorimetric scale featuring shades of blue from slightly bluish to dark blue.

At the second stage, atraumatic removal of teeth that erupted simultaneously was performed in order to save the surface layer of enamel in the maximum possible way. The teeth (47 premolars of children aged 11–16, yet no later than six months after the eruption) with no carious signs were removed for orthodontic reasons. All the extracted teeth were divided into three groups. Group 1 included 13 teeth extracted from children aged 11–12 (hard tissues mineralization term 6–12 months from eruption). Group 2 included 19 teeth removed from children aged 13–14 (hard tissues mineralization term 13–36 months from eruption). Group 3 included 15 teeth that were removed from adolescents, 15–16 years old (hard tissues mineralization term 37–60 months from eruption). Immediately after extraction, the teeth were immersed in a 2% Monochloramine B aqueous solution for 30 minutes with further careful ultrasound treatment to remove the remaining periodontal ligaments, soft tissues, and dental plaque. Then the teeth roots were separated at the level of the enamel-cement joint point, while the coronary segments were further polished with brushes and the Cleanic® (Kerr) universal polishing paste. To prevent artifacts typical of chemical fixation of sam-

ples, as well as to inhibit biochemical reactions in the enamel samples, they were stored in a solution of artificial saliva (T. Fusayama, 1975) in a glass container with a ground-in lid placed in a thermostat ($\text{pH} = 7.0 \pm 0.2$; $t = 10.0^\circ \text{C}$).

The third stage, including the study of the chemical composition and microstructure of the enamel samples surface, was carried out at the Department of Nanomaterial Technology, Engineering Institute, North-Caucasus Federal University. While preparing the teeth for the study, the conventional method was employed: with water cooling and a 0.2 mm diamond disc, enamel was cut at the equator area from the oral and vestibular surfaces of the crowns, to be further treated with ultrasound, degreased, and subjected to vacuum. The chemical composition and microstructure of the enamel surface layer samples was studied in a VEGA II LMU scanning electron microscope («Tescan») with the INCA Energy 350XT X-ray microanalysis system (Oxford Instruments Analytical, England). The samples surfaces were fixed on a glass slide and then sprayed with carbon ($h = 12\text{--}15 \text{ nm}$) in a VUP-5 vacuum unit for electrical conductivity thus ensuring optimal conditions for microscopy (Fig. 1).

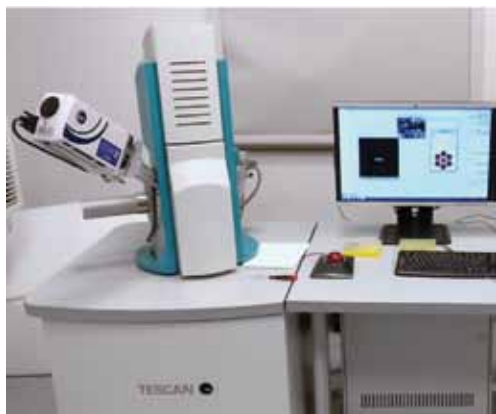


Fig. 1. Scanning electron microscope VEGA II LMU ("Tescan") with an Oxford Instruments INCA Energy 350XT X-ray energy dispersive microanalysis system

The statistical processing was performed using the statistical software packages Excel and Statistica 10.0. To assess the differences in categorical variables in the groups, the exact Fisher's or χ^2 method was used. When describing quantitative indicators, the mean value (M) and standard deviation (m) were used. To analyze the significance of the differences among the compared groups, the Kruskal–Wallis criterion was used. The critical level of significance when testing the statistical hypotheses was taken as 0.05.

RESULTS AND DISCUSSION

Table 1 shows the status of structural & functional, and acid resistance of tooth enamel at the equator area through various mineralization stages.

Analysis of the clinical and diagnostic data in groups involved in the study shows that an increase in the time of hard tooth tissues mineralization came along with an increase in the structural and functional, as well as acid resistance of the tooth enamel, which is also accompanied with a decrease in the enamel staining intensity. We suppose that statistically significant dynamics of improvement in structural, functional and acid resistance (reduced enamel permeability), as well as prolonged enamel maturation period are due to an increased activity in the fluoroapatite development mechanisms, obvious prevalence of morphological completeness (structural maturity), and consistent salivary homeostasis along with proper self-regulation of calcium-phosphorus metabolism in the oral cavity. Table 2 shows the change dynamics in the content of chemical elements in the surface layer of permanent teeth enamel through mineralization.

The study of the chemical composition of the permanent teeth enamel surface through various mineralization stages reveals that the most common elements in the enamel are oxygen (O), calcium (Ca), phosphorus (P), and carbon (C). The remaining elements, whose mass content exceeds 0.01% are nitrogen (N), sodium (Na), chlorine (Cl), magnesium (Mg), fluorine (F), and silicon (Si). Evaluation of the chemical composition of the permanent tooth surface enamel suggests that the maturation stages (mineralization) show a prominent tendency towards an increase in the concentration of Ca, P, F, Ca/P ratio along with reducing levels of C, Na, and O. In Group 2, the increase in the chemical elements content in the enamel surface layer was: Ca — $7.97 \pm 0.46\%$, P — $2.17 \pm 0.21\%$, F — $33.33 \pm 2.18\%$; in Group 3: Ca — $14.04 \pm 0.93\%$, P — $4.75 \pm 0.34\%$, F — $55.56 \pm 4.08\%$.

In our opinion, higher resistance and mineralization through an increase in the macro- and microelements that are part of fluorapatite $[\text{Ca}_{10}(\text{PO}_4)_6\text{F}_2]$, hydroxyapatite $[\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2]$, chlorapatite $[\text{Ca}_{10}(\text{PO}_4)_6\text{Cl}_2]$, carbonapatite $[\text{Ca}_{10}(\text{PO}_4)_5\text{CO}_3(\text{OH})_2]$ during enamel maturation is due to the following factors:

1. Intracrystalline ion exchange reaction in the hydroxyapatite grid with the introduction of ions (Ca^{2+} , PO_4^{3-} , CO_3^{2-} , F^{2-}) from the crystals surface deep into the ion grid.
2. Possible displacing of isomorphous ions (Ca^{2+} antagonists) in the crystalline grid of hydroxyapatite by Ca^{2+} or replacing vacant sites with calcium due to an increase in the Ca^{2+} concentration in the oral fluid.

Table 1. Structural & functional resistance and acid resistance of tooth enamel in the equatorial region at various stages of mineralization, ($M \pm m$)

Parameters	Terms of mineralization of hard tissues of teeth from the moment of eruption		
	6–12 months	13–36 months	37–60 months
ERT-test, %	27,19±1,04	24,72±1,38*	18,63±0,96*
Enamel staining intensity, points	2,58±0,16	2,31±0,19*	1,67±0,12*

Note: * — statistically significant in relation to the indicators of the first group, ($p \leq 0.05$).

Table 2. The concentration of chemical elements in the surface layer of enamel permanent teeth during the stages of tertiary mineralization, (in mass %), ($M \pm m$)

Chemical element	Terms of mineralization of hard tissues of teeth from the moment of eruption		
	6–12 months	13–36 months	37–60 months
Ca	21,08 ± 0,93	22,76 ± 1,12*	24,04 ± 0,85*
P	14,74 ± 0,39	15,06 ± 0,63*	15,44 ± 0,49*
Ca/P	1,43 ± 0,07	1,51 ± 0,05*	1,56 ± 0,08*
C	8,03 ± 0,56	7,68 ± 0,39 *	7,04 ± 0,41*
O	53,66 ± 5,17	51,96 ± 4,77*	51,07 ± 4,93*
F	0,09 ± 0,02	0,12 ± 0,03*	0,14 ± 0,01*
Mg	0,24 ± 0,03	0,21 ± 0,05*	0,23 ± 0,04*
Na	0,59 ± 0,09	0,57 ± 0,04*	0,51 ± 0,03*
Cl	0,43 ± 0,06	0,47 ± 0,03*	0,42 ± 0,05*
Si	0,03 ± 0,006	0,03 ± 0,008*	0,04 ± 0,009 *
N	1,11 ± 0,17	1,14 ± 0,11*	1,07 ± 0,16 *

Note: * — statistically significant in relation to the indicators of the first group, ($p \leq 0.05$).

3. Reaction of isomorphic substitution of HO^- groups for F^- in the hydroxyapatite ionic grid, with the development of hydroxyfluoroapatites or fluorapatites (fluoridation), which has a protective effect. This helps increase the hydroxyapatite crystals size due to increased precipitation from the oral fluid, as well as increases the enamel acid resistance.
4. Considerable total surface of the apatites in mineralized tissues allows them to absorb not charged particles alone, yet also electrically neutral molecules.
5. The enamel surface layer, as a hyper-mineralized area, features a maximum concentration level of nearly all mineral elements, especially *calcium*, *phosphorus*, *fluorine* with a gradual decrease in the content following the direction from the surface to the enamel-dentin boundary.
6. Fluoride maximum concentration in the enamel surface layer is considered a key caries-resistant factor, as well as an inhibitor of pathogenic (opportunistic) oral cavity microflora. The fluorine content in the deeper enamel layers

decreases, yet the Ca/P ratio increases since at the approach to the dentin-enamel border, the number of carbonate-apatites increases. Rise in the molar Ca/P ratio in the enamel surface layer (patients of Group 2 — $5.59 \pm 0.37\%$, patients of Group 3 — $9.09 \pm 0.62\%$) with an increase in the enamel maturation (calcification) term up to the maximum level (2.0) in adolescents aged 15–16, indicates almost complete mineralization, low intensity of demineralizing processes, and absence of prominent ionic substitutions for mineral components.

An increase in the hard tooth tissues maturation (mineralization) time has been observed to come along with a decrease in the levels of oxygen, carbon and other light elements shaping the organic basis of enamel, as well as chlorine and sodium. The decrease in the chemical elements concentration in the enamel surface layer in Group 2 was: O — $3.17 \pm 0.19\%$, C — $4.36 \pm 0.27\%$, Na — $3.39 \pm 0.24\%$; in Group 3: O — $4.83 \pm 0.22\%$, C — $12.33 \pm 0.74\%$, Na — $13.56 \pm 0.86\%$. The variability of other chemical elements by mass

ratio (magnesium, chlorine, silicon, nitrogen) had no statistically significant differences.

The connection between morphological features and chemical composition of the permanent teeth enamel surface layer through various mineralization stages has been confirmed with the data from scanning electron microscopy. The enamel surface in teeth with a mineralization period of 6–12 months reveals clearly visible perikymata (Retzius striae). Perikymata are areas of extremely low mineralization that are transverse to enamel prisms and have a thickness of 200–400 nm. Perikymata border shows enamel prisms outing, while the enamel surface itself is unclear (dim) and not smooth featuring a high degree of roughness. Microscopic examination of the dental enamel in children through early maturation revealed the following morphological features — hypomineralized structure of hydroxyapatites crystalline grid with a disturbed spatial orientation (chaotic arrangement) and clear boundaries; changing depth of the organic matrix; increased shell size and polymorphisms in the enamel prisms structure (pentagon and hexagon); reduced size of enamel prisms in vertical and horizontal planes; a decrease in the enamel prisms packing density per volume unit (increased interprismatic distance and the height of the interprismatic intervals). The total of these morphological features indicates an incomplete prismatic enamel structure due to disturbed relations between the mineral component and the organic matrix, a low level of maturation (mineralization) of its surface, deficient protective layer on the surface, significant permeability degree of immature enamel, as well as the presence of extra retention spots for microflora. Systematizing the obtained data regarding the surface morphology, we can speak of low caries resistance and acid resistance of immature enamel with a high risk of susceptibility to caries in children aged 11–12 (Fig. 2).

In Group 2 (mineralization term of 13–36 months) perikymata on the tooth enamel surface were less prominent, while there was a tendency to their smoothing, whereas the perikymata surface itself was smooth and homogeneous. Compared to patients in Group 1, the number of enamel prism outings (open, closed cup-shaped depressions — craters) not only within the perikymata, yet also at their borders, was significantly reduced, while the craters on the enamel surface were obviously deeper and much smaller in the area. The enamel surface featured some shine, also becoming smoother and more uniform. The appearance of scratches, grooves and microcracks, which surround enamel prism groups, while creating a honeycomb-shaped structure, indicates an insufficient degree of mineralization. Electron microscopy of tooth enamel

allows identifying the following morphological features: relative orderliness of the hydroxyapatite crystals spatial orientation; prevalence of the enamel prisms close to the normal (standard) size in the vertical and horizontal planes, with an arcuate shape and clear boundaries; the averaged amount of enamel prisms per volume unit (packing density); a slight increase in the height of interprismatic intervals and distances. In our opinion, the mineral layer deposited on the enamel surface inhibits full performance of the protective function due to insufficient calcification (mineralization). Visualization of the available morphological data shows that children aged 13–14, if compared with children aged 11–12, feature better caries and acid resistance of enamel along with reduced enamel caries susceptibility (Fig. 3).

Patients of Group 3 (mineralization term of 37–60 months) featured enamel surface with a significantly lower number and area of the open cup-shaped depressions (craters), if compared with similar indicators in Groups 2 and 3. The outer surface of the enamel, as a dense, amorphous, transparent structure, features the highest homogeneity and specific shine. Electron microscopy of child tooth enamel at the final stages of its maturation revealed the following qualitative morphological features: a stable, spatially oriented microstructure represented with ordered hexa- and heptagonal arcuate types of enamel prisms that have clearly cut boundaries; proper location of the organic matrix in depth; enamel prism size corresponding to the normal (standard) ones in vertical and horizontal planes; high packing density of enamel prisms per volume unit (minimal interprismatic distance and height of interprismatic intervals). The high-endurance surface layer separates the end surfaces of enamel prisms thus ensuring isolation of their contact surfaces from the aggressive effect of oral fluid, and preventing antagonists from abrading hard tissues. From our point of view, adolescents aged 15–16, if compared to younger children, due to the conditions facilitating high-grade mineralization, have a significantly lower total component (share) of organic matter, while enamel maturation (calcification) is almost complete. The combination of visual morphological signs pointing at a significant increase in the enamel surface mineralization in Group 3 (compared with patients in Groups 1 and 2) indicates a sufficient level of caries and acid resistance with minimal caries susceptibility of the enamel (Fig. 4).

Analysis of the obtained results demonstrates the feasibility of employing the scanning electron microscopy method with X-ray spectral microanalysis to identify the hypomineralization of tooth enamel as a condition promoting caries.

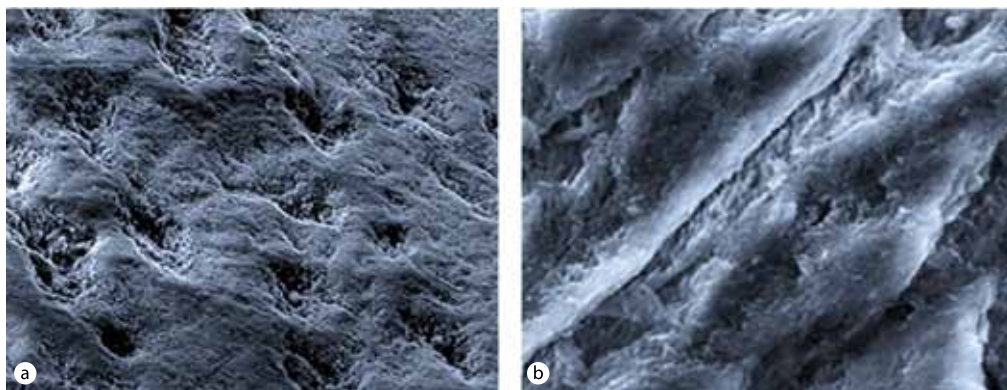


Fig. 2. Scanning electron microscopy of the enamel surface of a permanent tooth with a mineralization period of 6–12 months. The magnification $\times 10\,000$ (a), $\times 30\,000$ (b)

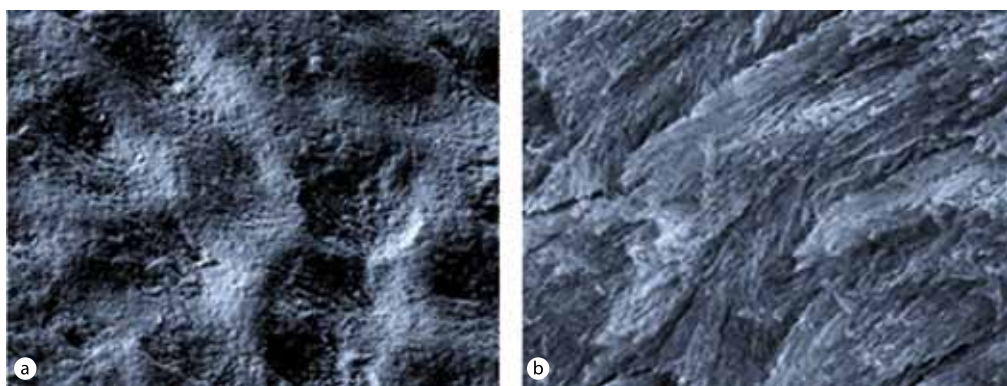


Fig. 3. Scanning electron microscopy of the enamel surface of a permanent tooth with a mineralization period 13–36 months. The magnification $\times 10\,000$ (a), $\times 30\,000$ (b)

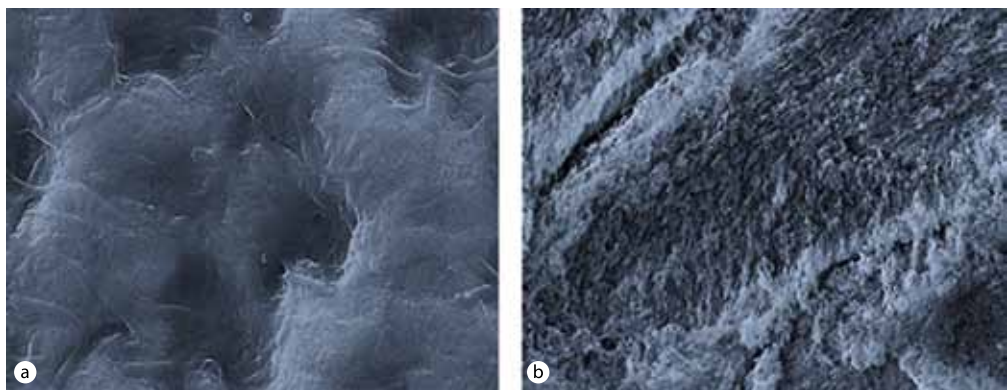


Fig. 4. Scanning electron microscopy of the enamel surface of a permanent tooth with a mineralization period 37–60 months. The magnification $\times 10\,000$ (a), $\times 30\,000$ (b)

CONCLUSIONS

1. Studying the morphology and chemical composition of the tooth enamel surface layer employing scanning electron microscopy with an energy dispersive microanalysis system allows obtaining a proper image of the changes typical of various enamel maturation stages. High resolution with possible ratio identification for organic and inorganic components of enamel, allows spotting foci of insufficient tertiary mineralization, which
2. cannot be diagnosed with the available clinical methods (ERT-test, vital staining method).
3. The results of electron probe X-ray spectral microanalysis for the concentration of elements in the mass share indicate that the stages of enamel surface layer maturation reveal a steady trend towards an increase in the content of Ca, P, F, as well as Ca/P ratio, with a decrease in C, Na, and O.
4. Tooth enamel in children through the early stages of physiological maturation reveal the following

morphological features: hypomineralized structure of hydroxyapatites crystalline grid with a disturbed spatial orientation and clear boundaries; changing depth of the organic matrix; increased shell size and polymorphisms in the enamel prisms structure; reduced size of enamel prisms in vertical and horizontal planes; a decrease in the enamel prisms packing density. The combination of morphological features in children belonging to the age group of 11–12 year-olds indicates low caries and acid resistance with high caries susceptibility in immature enamel, which lays the ground for cariogenic situations.

4. The specifics of the macro- and microelement composition, which determines the nature of pathological changes in the hypomineralization center, can be well used for the development and implementation of caries preventive (individual, professional) programs for children. Reasonable introduction of remineralizing and fluorine-containing drugs as well as vitamin-mineral combinations will help stabilize demineralization, establish conditions for saturation of the oral fluid with macro- and microelements, increase caries and acid resistance at the molecular, tissue, organ and system levels, and will also help improve the enamel permeability.

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ORAL CAVITY AND PERIODONT MICROBIOME STATUS THROUGH EMOTIONAL STRESS

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ABSTRACT — AIM. To study the effect of emotional stress on the microbial status of the gingival sulcus, going through eubiosis and dysbiosis, observed in law enforcement officers. **MATERIALS AND METHODS.** The study involved 67 law enforcement officers aged 30–49. The microbiological study focused on the gingival sulcus total microbial contamination and its colonization with certain types of microbes, employing aerobic and anaerobic cultivation methods. **RESULTS.** When in a state of relative rest, 100% of the persons with no gum issues were observed to have the eubiotic state of the gingival sulcus microbial status, while in 100% of persons with mild periodontitis the microbial status of the gingival sulcus was found to be in a state of dysbiosis. **CONCLUSION.** The stressor effect along with a microbial homeostasis imbalance in the dentogingival gap causes an increase in the microbial associations imbalance, which manifests itself as a decrease in the commensal microflora and an increase in the potentially pathogenic (opportunistic) one.

KEYWORDS — microbial status, gingival sulcus, emotional stress, dysbiosis, eubiosis, aerobes, anaerobes.

INTRODUCTION

Oral cavity and periodontal microbiome is one of the most investigated microbial communities. This is due to its complex composition and its abundant interaction with the human body. The oral cavity is one of the most densely populated human ecosystems, which contains over 1,000 different types of eubacteria, archaea, fungi, protozoa and viruses. The oral microbiota status is directly related to a wide range of health issues, such as oral cavity diseases (caries, periodontal diseases), diabetes, cardiovascular diseases, cancer etc. Oral microbiome has been shown to have

a comprehensive effect on the development of diseases — the decisive role belongs not to a particular micro-organism, yet a combination of these [1–7].

In the oral cavity, typically several standard types of biological material are studied, which reflect a particular microbial community status — saliva, soft plaque, subgingival and supragingival dental calculus, as well as the contents of the gingival sulcus and of the periodontal pocket. All these biotopes, except the gingival sulcus and periodontal pocket biocenosis, are extremely unstable and depend significantly on the oral hygiene type and intensity. The unique feature of the gingival sulcus biotope is that quantitative and qualitative changes in these microecological system's microbial communities can lead to major dental issues — gingivitis, periodontitis, and caries. Structural and functional disorders of the gingival sulcus biofilm result in pathological changes that are not only of local, yet also of systemic importance [8–12].

Modern life environment is full of stress inducing factors, which make the body respond with a set of psychological, physiological and biochemical reactions that are indicative of psychological and emotional stress. In particular, a high level of emotional effects can be seen in law enforcement officers who are exposed to excessive loads under various social conditions. In case of emergencies, the emotional pressure experienced by a law enforcement officer goes up many times reaching the top peak of psycho-emotional stress [13, 14].

Most researchers studied the effect of emotional stress on the body's microbiome relying on the intestinal microbiota example. Stress factors have been proven to promote the intestinal microbiota imbalance and the growth of pathogenic microflora [15, 16]. A limited number of works highlight the effect of emotional stress on the oral cavity microbial status. It is important to study the level of the effect that emotional factors have on the oral cavity areas that are responsible for the development of the most common dental diseases, such as periodontal tissues inflamma-

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tory diseases [17, 18]. Studying changes in the gingival sulcus microbial status under various microecological situations in the oral cavity would allow a deeper analysis into the interaction between bacteria and the immune response under stress-response of the body [19].

Aim of study

To elucidate the effect of law enforcement officers' emotional stress on the microbial status of the gingival sulcus, which is under eubiosis and dysbiosis.

MATERIALS AND METHODS

The study involved 67 law enforcement officers aged 30–49 years with no somatic diseases. Group 1 included 22 persons (11 males, 11 females) who had no clinical manifestation of periodontal or dental lesions. Group 2 included 45 persons (29 males, 16 females) diagnosed with chronic moderate periodontitis.

Law enforcement officer implies emotional stress — interaction with criminals, strict deadline for important tasks, night shifts. We used the C.D. Spielberger scale (adjusted by Yu.L. Khanin) to determine the level of personal and reactive anxiety. An indicator below 30 revealed low anxiety; 30–45 points — moderate anxiety, while exceeding 45 points — showed high anxiety [20].

A microbiological study was carried for the total microbial contamination of the gingival sulcus and its colonization with certain microbial species; the methods used were those involving aerobic and anaerobic cultivation [21]. Samples of the gingival sulcus were taken in the morning on an empty stomach, with a sterile standard-size paper endodontic pin (#30), 1 cm long, which, after soaking, was put in a sterile saline solution and washed thoroughly. Standard dilutions were plated on special, selective and differential diagnostic media — blood agar, yolk-salt agar, Sabuoraud's medium, Endo medium, sugar agar, followed with cultivation under aerobic and anaerobic conditions. For the inoculations obtained under aerobic cultivation conditions, the gingival fluid microbial content with aerobic and facultatively aerobic bacteria (further called aerobes) was identified. On the inoculations obtained under anaerobic cultivation conditions, microbial colonization of facultative and obligate anaerobes was determined (hereinafter referred to as anaerobes). Identification of the isolated pure cultures was carried out following morphological, tinctorial, cultural, and biochemical features. The results of the quantitative study were expressed in a decimal logarithm of colony-forming units per 1 ml — lg CFU/ml. The frequency of identifying certain species of colonizing microflora was identified, too. The statistical analysis of results

was performed using SPSS 17.0 and Microsoft Excel 2007 software. The total sample was analyzed with parametric methods after a preliminary check for the normal distribution with the Kolmogorov-Smirnov test. The differences between the studied parameters were evaluated with Student's t-test. The detection rates for individual microorganisms were compared with the ϕ Fisher criterion [22].

RESULTS AND DISCUSSION

The first stage of the study involved identifying the gingival sulcus microbial condition (eubiosis or dysbiosis) in individuals with different dental status in a state of relative rest.

The microbial homeostasis of the gingival sulcus biofilm in individuals with periodontitis was different from that in persons with intact gums (Table 1). In the state of relative rest, the microbial load on the gingival sulcus biofilm in Group 2 exceeded the same index in Group 1. Our studies revealed that gingival sulcus colonization with aerobic and anaerobic microflora in people with periodontitis exceeded the same indicators in people with intact gums, 3.4 times ($p < 0.05$) and 8.3 times ($p < 0.05$), respectively.

The qualitative composition of the gingival sulcus microbial status in relative rest depended on the dental status, too. The frequency of the gingival sulcus colonization with *S.viridans* spp. in persons with periodontitis was 63.9% lower ($p < 0.05$) than in those without gums issues (Tables 2 and 3). Also, the development of dental diseases came along with a 3.0 times decrease ($p < 0.05$) in the density of colonization of the gingival sulcus with *S.viridans* spp. (Table 2).

The gingival sulcus colonization with γ -hemolytic streptococci, which include *S.mutans*, in patients with periodontitis is 3.5 times ($p < 0.05$) above that of persons without the pathology.

Neisseria spp. were 37.3% ($p < 0.05$) more often detected in people with periodontitis, while the colonization density with *Neiserias* was also higher (28.2 times ($p < 0.05$)) in that group, compared with those with no gums issues.

The density of epidermal staphylococcus colonization in patients with periodontitis was 3.2 times ($p < 0.05$) above that in healthy individuals. In Group 2, potentially pathogenic (opportunistic) microorganisms were more common (the percentage of increase is bracketed): *Bacillus* spp. (20.4% ($p < 0.05$)), *S.aureus* (21.1% ($p < 0.05$)), *S. β -haemolyticus* spp. (19.0% ($p < 0.05$)), *Actinomyces* spp. (8.8% ($p < 0.05$)), *Enterobacteriaceae* (26.3% ($p < 0.05$)), *Candida* spp. (26.3% ($p < 0.05$)). We observed a decrease in the *Lactobacillus* spp. colonization frequency in patients with periodontitis (by 18.6% ($p < 0.05$)).

Table 1. Effect of emotional stress on gingival sulcus general colonization, lg CFU/ml ($M \pm m$)

Indicators	Groups	Intact gums		Periodontitis	
		Relative rest state	Voltage condition	Relative rest state	Voltage condition
Aerobe colonization		7,26 \pm 0,04	7,40 \pm 0,03 [^]	7,79 \pm 0,03*	7,85 \pm 0,03*
Anaerobic colonization		6,81 \pm 0,04	7,07 \pm 0,08 [^]	7,73 \pm 0,03*	7,76 \pm 0,03*

Notes: * — the reliability of indices differences in persons with periodontitis compared with a group of persons with intact gums, Student's t-test, $p < 0.05$;

[^] — the reliability of indices differences in persons under emotional stress compared with those in the state of relative rest, Student's t-test, $p < 0.05$.

Table 2. Effect of emotional stress on gingival sulcus microbiota in people with no periodontal issues, % of persons / lg CFU/ml ($M \pm m$)

Microorganisms	Relative rest state	Emotional stress
<i>S. viridans</i> spp.	95,5 / 6,91 \pm 0,09	81,8 / 6,79 \pm 0,05
<i>S. y-haemolyticus</i> spp.	81,8 / 6,81 \pm 0,10	95,5 / 7,08 \pm 0,06
<i>S. β-haemolyticus</i> spp.	9,1 / 5,80 \pm 0,30	9,1 / 6,51 \pm 0,39
<i>Neisseria</i> spp.	36,4 / 5,88 \pm 0,26	36,4 / 7,07 \pm 0,10 [^]
<i>Corynebacterium</i> spp.	31,8 / 5,84 \pm 0,25	4,5 [^] / 5,30
<i>Lactobacillus</i> spp.	27,3 / 5,30 \pm 0,10	9,1 [^] / 5,25 \pm 0,25
<i>S. epidermidis</i>	31,8 / 4,99 \pm 0,13	31,8 / 5,65 \pm 0,23 [^]
<i>Bacillus</i> spp.	18,2 / 5,28 \pm 0,19	9,1 / 5,50 \pm 0,20
<i>Actinomyces</i> spp.	0/0	0/0
<i>S. aureus</i>	0/0	0/0
<i>Enterobacteriaceae</i>	0/0	0/0
<i>Candida</i> spp.	0/0	0/0

Note: [^] — probability of frequency difference by the ϕ Fisher criterion and lg CFU/ml, Student's t-test, under emotional stress compared with those in the state of relative rest, $p < 0.05$.

Here below we will look at how the gingival sulcus microbial status changed in eubiosis and dysbiosis in those exposed to emotional stress. In Group 1 (relative rest, the eubiotic state of the microbiota was identified) *Lactobacillus* spp. were detected 18.2% less often ($p < 0.05$), *Corynebacterium* spp. – 27.3% less often ($p < 0.05$). At the same time, an increase in the microbial count of *S. epidermidis* (4.6 times ($p < 0.05$)) and *Neisseria* spp. (15.4 times ($p < 0.05$)) was detected.

In Group 2 we identified dysbiotic microbial status, where *S. viridans* spp. were detected 19.3% ($p < 0.05$) less often, *Corynebacterium* spp. – 17.5% ($p < 0.05$) less often, *S. epidermidis* (19.3% ($p < 0.05$)) less often; on the other hand, *Neisseria* spp. and *Enterobacteriaceae* were found more often (15.8% ($p < 0.05$) and 15.8% ($p < 0.05$), respectively), whereas the *Neisseria* spp. and *Bacillus* spp. colonization density was higher (1.9 times ($p < 0.05$) and 6.6 times ($p < 0.05$), respectively).

Describing the changes in the dentogingival gap microbiocenosis in case of emotional stress, note is to be made that 2 out of 22 persons in Group 1 (9.1%) were found to have microbial populations imbalance, which could be described as a dysbiotic shift. All persons in Group 2 exposed to stress factors against the al-

ready existing microbial dysbiotic changes, showed an increase in the microbial associations' imbalance. Out of the 45 persons examined, a dysbiotic shift was found in 18 people (31.6%), another 27 showing Degree 1–2 dysbiosis (68.4%).

Under emotional stress in individuals with eubiosis, the total gingival sulcus microbial colonization by aerobic and anaerobic microorganisms went up, with *Lactobacillus* spp. and *Corynebacterium* spp. found less often, while a higher microbial count was observed for *S. epidermidis* and *Neisseria* spp.

Individuals with dysbiosis showed no significant change in the total microbial load of the gingival sulcus, which remained at a high level; the *Neisseria* spp. and *Bacillus* spp. colonization density increased, while a decrease was observed in the detection rate for *S. viridans* spp. and *Corynebacterium* spp.; the *Bacillus* spp. and *Enterobacteriaceae* colonization frequency increased as well.

Under emotional stress, 9.1% of persons with eubiosis revealed a dysbiotic shift in microbial populations. Those who already had microbial dysbiosis, demonstrated an increase in the microbial associations imbalance. Stress-induced alterations in the microbial status may be of different nature depending on the ini-

tial state of the bacterial populations ratio in the biofilm. The eubiotic type of the microbial populations interaction is a stabilizing factor and offers adaptive maintenance of the biofilm homeostasis. The stressor effect along with an imbalance of the dentogingival gap microbial homeostasis leads to the aggravated imbalance in the microbial associations, which reveals itself as a decrease in the commensal microflora and an increase in the potentially pathogenic one.

The above shows that emotional stress had an impact on the quantitative and qualitative features of the gingival sulcus biofilm in both groups; this effect, however, was more significant in Group 2. The biofilm, which already manifested a microbial populations imbalance, responded to the stress factor with a more intense disturbance in the relationships between the symbiotic and potentially pathogenic microflora. The frequency of symbiotic *S. viridans* spp. colonization in individuals with the gingival sulcus biofilm dysbiosis was 69.5% lower ($p < 0.05$) compared with persons with eubiosis. In Group 2 opportunistic microorganisms (*Bacillus* spp., *Actinomyces* spp., *S. aureus*, *Enterobacteriaceae*, *Candida* spp.) were detected in the gingival biofilm significantly more often. The highest detection rate in Group 2 was observed for *Bacillus* spp. (47.0% ($p < 0.05$) more often than in Group 1), *S. aureus* (in 26.3% of cases ($p < 0.05$)), *Actinomyces* spp. (8.8% of cases ($p < 0.05$)), *Enterobacteriaceae* (42.1% of cases ($p < 0.05$)), *Candida* spp. (28.1% of cases ($p < 0.05$)).

CONCLUSIONS

1. The resident microflora of each biotope performs numerous functions related not only to maintaining its functioning, yet also to the homeostasis as a whole. We have shown that the microbial status is a highly sensitive indicator system, which responds with quantitative and qualitative changes when subjected to external and internal factors. While law enforcement officers perform their public duties, they undergo an emotional load that is many times above normal, often reaching the level of emotional stress. Subjective view on the significance of a specific task can turn it into a strong emotional stressor [21, 22].
2. The study has revealed that psycho-emotional stress affects the gingival sulcus microbial status, although the level of this effect depends on the initial microbial associations balance. In case of eubiosis, the gingival biofilm is an important component of the natural anti-infectious protection system for periodontal tissues, ensuring the stability in the microecological homeostasis and the colonization resistance of this biological niche. Under dysbiosis, the initial microbial

populations imbalance increases the susceptibility to pathogenic invasion [23–26].

3. Emotional stress affecting law enforcement officers, as our data shows, leads to a lower level and frequency of the gingival biofilm colonization with a stabilizing microflora. A decrease in the antagonistic action of these bacteria contributes to the gingival sulcus colonization with opportunistic microorganisms, and increased manifestations of dysbiosis, which is most intense in persons with a microbial populations initial imbalance. An imbalance in the resident microflora with a shift towards opportunistic microflora sets ground for the development of infectious diseases in the oral cavity.

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CAUSES BEHIND DISTAL OCCLUSION

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INTRODUCTION

The etiology and pathogenesis of distal occlusion have been the focus of a large number of works [1,2,3,4]. Most authors claim that the causes behind this pathology are very diverse [5,6,7,8]. It is also known that, various etiological factors lead to morphological and functional issues in the dentofacial system, including issues affecting the temporomandibular joint and masticatory muscles [9,10,11,12].

Aim of study

To identify the most significant factors contributing to and predisposing for distal occlusion. The object of this study included 156 patients with distal occlusion.

MATERIALS AND METHODS

Depending on the upper front teeth position, all the patients were divided into two groups. The first group included 82 patients with the upper front teeth protrusion, while the other group included 74 patients with the upper front teeth retrusion. The clinical histories and examination outcomes of all the patients allowed identifying factors contributing to the development of the said pathology.

RESULTS OF STUDY

In case of distal occlusion of the first clinical type, the most frequent causes included disturbed nasal breathing due to various pathological changes in the nasopharyngeal area — 73%. Such pathological processes imply narrowed airways, displaced or thickened nasal septum, tonsils hypertrophy, partial or complete

nose obstruction due to hypertrophic catarrh, polyps, adenoids. All of these lead to impeded nasal breathing, while the role nasal breathing issues play in the development of distal occlusion has been confirmed by many authors. Our research shows that distal factors contributing to the mandible displacement could be bad habits such as sucking thumb, lower lip, dummies etc. (63%). Besides, the occurrence of first clinical type distal occlusion has been linked to artificial feeding — 20%, childhood rickets — 20%, genetic predisposition — 16%, and premature removal of milk teeth — 14%.

The second clinical type of distal occlusion is due to a similar issue in the family — 63%; however, during that it is important to take into account the general body status as well as the effect of the environment. For instance, we identified chronic and acute maternal diseases during fetal development, gestoses, abnormal fetal position, higher pressure of the amniotic fluid during polyhydramnion, mismatch between the volume of the amnion and the fetus, amniotic cords, which lead to distal occlusion. The factors observed in case of the second clinical type included: poor habits — 40%, artificial feeding — 34%, premature removal of milk molars — 28%, disturbed nasal breathing and rickets — 23% each, respectively.

CONCLUSION

Distal occlusion typically develops as a result of a set of etiopathogenetic factors. For instance, when calculating the average number of factors contributing to the development of first clinical type of distal occlusion, there is an average of three factors as per each patient, and two — for one patient with the second clinical type of distal occlusion. The data from our study allows us to design a more detailed picture of the leading role that certain etiopathogenetic factors have in the development of distal occlusion, which enables us to opt for the most reasonable treatment method that should be comprehensive and take into account the diversity of etiological factors.

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ASSESSMENT OF THE REPRODUCTIVE POTENTIAL OF WOMEN WITH HY-POTALAMIC SYNDROME

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ABSTRACT — The reproductive potential was evaluated in 87 women aged 19 to 32 years with hypothalamic syndrome in the Astrakhan region. Analysis of the survey results showed that 72,4% of the patients had menstrual and reproductive disorders. In the structure of menstrual dysfunction, hypomenstrual and hypermenstrual syndromes predominate, while among reproductive ones — primary infertility and miscarriage.

KEYWORDS — hypothalamic syndrome, menstrual function, reproductive function, infertility, miscarriage, women.

INTRODUCTION

Protection of reproductive health is a state priority. Recently, there has been a steady increase in neuroendocrine pathology. According to various authors, hypothalamic syndrome (HS) occurs in 18-25% of women of reproductive age. Hypothalamic syndrome (HS) is a pathological symptom complex based on the primary lesion of the hypothalamus and associated central nervous system structures [1, 2, 3]. Various adverse factors during pregnancy can affect the structure of the hypothalamus and the formation of its connections. In most cases, HS without treatment transforms into neuro-endocrine syndrome, in which chronic anovulation causes infertility in 25–72% of women [5]. Chronic anovulation on the background of overweight and metabolic disorders can contribute to the development of hyperplastic processes and endometrial cancer [4, 6].

MATERIALS AND METHODS OF THE RESEARCH

The reproductive function was assessed in 87 women with hypothalamic syndrome aged 21 to 32 years (main group). The women of the main group were divided into 2 subgroups depending on body mass index (BMI). Subgroup 1 included patients with $BMI \geq 30$ — 45 people, subgroup 2 ($BMI \leq 30$) — 43 patients. The control group consisted of 52 women without hypothalamic syndrome during the examination. The average age in the main group was 31.6 ± 0.5 years, in the control one — 30.9 ± 1.2 years. All subjects

were comparable in history. All women were assessed by the levels of follicle-stimulating (FSH) and luteinizing hormone (LH), prolactin (Prl), cortisol (K), testosterone (T), estradiol (E2) on the 5th day of the menstrual cycle and progesterone (P) in serum on the 212th day of the menstrual cycle. Hormonal studies were carried out using the enzyme-linked immunosorbent assay (ELISA) with “Hema-Medika” LLC (Russia) and “Diagnostic” (USA) kits in accordance with the attached instructions. The medical history was collected in 2 ways: 1 — questionnaire, 2 — information from medical records.

Statistical data processing was carried out using the software package “Statistica-6”. The hypothesis on the equality of general means in the 2 compared groups was tested using the non-parametric Mann-Whitney U-test for independent samples. The difference between the general fractions (frequencies) was estimated using the Student t-test. The study of the relationship between quantitative traits was carried out using correlation analysis by the Pearson method.

RESEARCH RESULTS

Pronounced neuroendocrine disorders were revealed in mothers of the surveyed girls with puberty HS. Among them, obese women predominated — 45 (52,1%) ($p < 0,05$), with vegetative disorders — 33 (37,9%) ($p < 0,05$), with hyperplastic processes and hormone-dependent tumors of the reproductive system — 20 (22,9%) ($p < 0,05$). A high percentage of other gynecological diseases was revealed — 24 (27,5%) ($p < 0,05$). In addition, 39 (44,8%) mothers had a history of infertility, 18 (20,8%) — miscarriage. Analysis of the course of pregnancy and childbirth revealed complications in 76 (87,5%) mothers of the subjects in the main group and 15 (28,8%) — in the control one ($p < 0,001$). 83,3% of women in the main group had the perinatal history aggravated by the formation of cerebral disorders ($p < 0,001$).

The study of the nature of the menstrual function showed that 75 (86,4%) women of the main group had anovulatory menstrual cycles in adolescence ($p < 0,05$). 37,9% had dysmenorrhea ($p < 0,05$) and 25 (29,1%) — premenstrual tension syndrome ($p < 0,05$). Further analysis of menstrual function showed a difference in the age of onset of menstruation ($p < 0,001$) (table 1).

In 22 (34%) recorded cases menstruation was not steady yet in the reproductive age ($p < 0,001$).

Table 1. The nature of menstrual function in the studied groups

Types of menarche disorders	Main group n=87 M±m	Control n=52 M±m	p
Menarche age, years	12,1±0,8	13,7±0,7	<0,001
Cycle establishment time, years	2,8±1,6	1,5±1,1	<0,05
Duration of menstruation, days	6,2±1,8	4,3±1,7	<0,05
Duration of cycle, days	38,9±2,5	28,4±2,2	<0,001
Cycle disorders, abs (%)	76(87,3%)	13(24,8%)	<0,001

Note: p — significance of differences in relation to the control group

Oligomenorrhea occurred in 58 (67%) patients of the main group, and polymenorrhea — in 20 (23%) ($p = 0,05$, $p = 0,03$). The most common in the main group was a rhythm disorder — in 77,1% and 67,8% of women, respectively to subgroups ($p < 0,001$). In addition, in the main group, with a BMI of < 30 women with hyperpolymenorrhea prevailed significantly at 73,6% ($p < 0,001$), with a BMI ≥ 30 — 33,3% ($p < 0,001$). Acyclic uterine bleeding occurred in 27,5%, and 36,7% in both subgroups with HS ($p < 0,001$), and algomenorrhea in 37,9% ($p < 0,001$). In subgroup 1 of patients with HS ($p < 0,05$) primary amenorrhea was more common. Secondary amenorrhea was registered in both groups almost equally ($p > 0,05$).

A retrospective analysis of reproductive function revealed that 55 women (63,2%) of the main group had spontaneous miscarriages, and in the control group this indicator was 9 patients (17,3%) ($p < 0,001$). In addition, 29 (33,3%) patients in the main group suffered from habitual miscarriage, and a significantly larger percentage of 19 (21,8%) were women in subgroup 2 with a BMI < 30 ($p < 0,05$). A significant number of patients in the main group with a BMI ≤ 30 suffered from primary infertility ($p < 0,001$). Cases of secondary infertility were less common (8 (9,1%) in the main group and 1 (1,9%) in the control one, $p < 0,05$).

Table 2. Indicators of the hormonal status of the surveyed women

Indicators M±m	BMI ≥ 30 subgroup 1, n=45	BMI ≤ 30 , Subgroup 2, n=43	Control, n=52	P ₁ (1-Control)	P ₃ (2-Control)
FSH, mme / l	4,2±1,7*	8,3±1,8	6,6±1,7	$p < 0,01$	$p < 0,05$
LH, mme / l	14,3±2,4*	7,7±2,6	6,4±2,2	$p < 0,002$	$p < 0,05$
Prl, mme / l	558,2±29,2*	358,2±28,7	197,1±25,1	$p < 0,05$	$p < 0,001$
E2, pg / ml	67,7±19,4*	54,8±23,8	48,5±22,3	$p < 0,05$	$p < 0,05$
P, nmol / l	13,6±3,4**	29,2±23,8	57,8±4,4	$p < 0,001$	$p < 0,05$
K, nmol / l	224,2±21,8**	427,4±26,6	127,3±25,4	$p < 0,05$	$p < 0,001$
T, nmol / l	1,3±0,6*	1,9±0,9	0,8±0,7	$p < 0,05$	$p < 0,05$

The significance of differences * $p_1 < 0,05$, ** $p_1 < 0,001$ — relative to subgroup 2. p_2 , p_3 — relative to the control group

Against the background of the pathological activation of the hypothalamic-pituitary-ovarian system in subgroup 1 of the main group, increased secretion of LH ($p < 0,001$), prolactin ($p < 0,05$), cortisol ($p < 0,001$) and testosterone ($p < 0,05$) was detected, as well as a decrease in FSH ($p < 0,05$), E2 and progesterone ($p < 0,05$) (table 2).

CONCLUSION

Research results indicate a decrease in reproductive capacity in 72,4% of women in the Astrakhan region with the hypothalamic syndrome. Amenorrhea, hyperpolymenorrhea, acyclic uterine bleeding prevailed among the disorders of menstrual function. The structure of reproductive disorders was remarkable for primary infertility and miscarriage with a high frequency.

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