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EDITORIAL



Dear colleagues,

All of us this year found ourselves in a completely new reality. We have to cope with the outbreak of COVID-19. Health care systems in many countries proved to be not ready for a pandemic. This costed patients and doctors their lives.

Let me thank, on behalf of the Editorial Board, all doctors that have risked their lives and have rescued and are going on to rescue lives of their patients.

Today, in many countries, despite surge in coronavirus cases, the restrictions are eased and life is returning to normal. However, we understand that the world has changed and we still have to live with restrictions. In particular, we have to limit physical contact and communication, whereas the educational process has been transferred online by using video, smartphones and social networks.

This occurs not only as a result of the pandemic but it reflects the spirit of the time: life and business are becoming more digital. Medicine is one of the fields, where the potential of digitalization has already been used widely. For instance, Digital Supply Act adopted in Germany on Dec. 19, 2019 enables to render a series of measures such as health apps, digital medical reports and online consultations.

Many patients have already started to use health apps, for instance, for timely intake of medications or monitoring blood sugar levels. Doctors are allowed to prescribe medications using smartphone applications.

The Act foresees many other new applications for doctors and patients. Doctors will get initial funding for conducting video consultations with patients. It should promote a further extension of the online services. The services of distant consulting are provided for home care patients and are paid from non-budget sources. To implement this, doctors can place corresponding offers on their websites.

Of course, such form of medical services cannot fully substitute physical connection between doctor and patient but may significantly improve the consultant-patient relationship. Besides, deeper knowledge of different formats and online methods is therefore required.

We should evaluate the experience we are living through today as a lesson that is not only going to transform our future. It is a lesson that accelerates digital transformation in medicine and dramatically changes the forms of rendering medical services in future.

Yours,

Editor-in-Chief
Dr. Georg Tyminski

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Dear clinicians, research fellows, colleagues and friends!

Multitude of nosological forms, their individuality and variability among different patients — all this make the process of diagnosis fairly complicated. Moreover, the outcome of a treatment depends on knowledge and skills of a doctor, which may often be insufficient.

Therefore, a special attention in clinical medicine is paid to the latest achievements in biology, physics, chemistry, as well as in engineering and electronics. Thus, objective testing methods, which are incorporated in clinical practice, extend the volume and enhance the informativeness of acquired data.

The feasibility for development of clinical laboratory diagnosis or laboratory medicine is determined by emerging technologies for in vitro testing of human biomaterials using hematologic, general clinical, parasitic, biochemical, immunological, serological and many other methods of laboratory examinations.

In modern health care system, 70% of medical decisions, practically in all clinical disciplines, are based on laboratory results. Laboratory tests are responsible for not less than 93% of objective diagnostic examinations; they are included into the programs of obligatory checkups as well as in standards of medical treatments for most somatic symptoms.

The results of laboratory tests have a special priority for early and accurate detection of the signs of pathological conditions. They establish an evidence-based approach to solution of social and legal issues. The contribution of laboratory tests to the development of evidence medicine is indisputable.

Among most important components of laboratory medicine, a special place belongs to the pathobiological section, which is based on fundamental theoretical knowledge and advancements, a section of laboratory (clinical) analytics dealing with systemization of the means and methods for conducting the tests. It also contains a section of clinical-laboratory diagnosis, which gives evidence on the informativeness of laboratory data and solutions for concrete medical problems.

Interdisciplinary interaction between laboratory clinical diagnosis and general therapy, gastroenterology, pulmonology, endocrinology, pediatrics, cardiology, neurology, nephrology, dentistry takes place as a rapidly growing cooperation, promoting incorporation of innovative technologies, extension of medical knowledge and update of methods of early diagnosis.

Today, laboratory diagnostics demands even more differentiation of the object and methods of diagnostics. Therefore, it is so important to join the efforts of laboratory doctors and clinicians brought together by an interdisciplinary approach.

Adding the section *Clinical Laboratory Diagnostics* to the journal *Archiv Euromedica* will highlight new publications on such subjects as preclinical verification of pathology, differential diagnosis of clinical manifestations, assessing the efficiency of preventive and therapeutic measures.

Executive Editor

Prof. Dmitry Domenyuk

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THE USE OF PRINCIPAL COMPONENT ANALYSIS FOR EVALUATION OF MORPHOFUNCTIONAL CHANGES IN RED BLOOD CELLS UNDER THE INFLUENCE OF DIFFERENT GLUCOSE CONCENTRATIONS

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ABSTRACT — The article presents findings of the research investigating the effect of various glucose concentrations on the morphometric parameters of red blood cells. The principal component method was employed in order to determine the most significant indicators in the experiment. The experiment was aimed to investigate the effect of hyperglycemia on the shape, size and functional parameters of erythrocytes depending on the glucose concentration and exposure time. It was established that characteristic changes in the shape and size of erythrocytes induced by hyperglycemia are correlative with concentration of glucose and exposure time.

KEYWORDS — glucose concentration, red blood cells, morphometric parameters, principal component analysis.

INTRODUCTION

Glucose is an osmotic and chemically active substance and a long-term increase in its concentration is undesirable either in the interstitial medium or in the cell. Hyperglycemia disrupts the osmolarity of the interstitial medium and the high reactivity of glucose changes the chemical composition of structural proteins and the activity of enzymes [1].

Many authors have identified various disorders of the erythrocyte membrane resulting from the toxic effect of glucose [2]. As a result of these disorders the surface architectonics of red blood cells changes and abnormal forms of red blood cells appear [3].

The purpose of this work was to identify the possibility of using the principal component method in the assessment of morphofunctional parameters of red blood cells that were displayed under the influence

of different glucose concentrations. The state of red blood cells was assessed in accordance with biophysical properties, morphofunctional parameters, indicators of poikilocytosis, anisocytosis and ovalocytosis.

Aim of study

To identify the dependence between the content of matrix metalloproteinases, their tissue inhibitors and the periodontological status in children with Type 1 DM through different endocrinopathy stages.

MATERIALS AND METHODS

During the experiment 11 control blood samples were examined, the reference values (number of er (RBC-erythrocytes or in abbreviated form — er), concentration of HB, Ht and glucose concentration) of which were determined within the normal range [4]. Blood in the amount of 4 ml was taken under standardized conditions, centrifuged at 1000 rpm, the supernatant was separated, then the er was washed in an isotonic NaCl solution three times. During the study, a series of diluted glucose solutions were prepared on buffered isotonic NaCl solution (pH 7.4) and deionized water: 1) isotonic NaCl solution — glucose concentration 0 mmol/l; 2) glucose-containing isotonic NaCl solutions — 6.5; 7.5; 10.0 and 15.0 mmol/l. Glucose concentrations corresponded to the degree of compensation of glycemia in diabetes mellitus, so the concentration of glucose in the blood up to 6.5 mmol/l corresponds to compensation, 7.5-sub-compensation and higher-decompensation [5]. Each of the 5 test tubes was filled with 0.3 ml of the corresponding glucose solution on an isotonic solution with an er mass of 0.2 ml until HT — 40% was obtained. For the reliability of the results the concentration of glucose in the prepared solutions was determined using a semi-automatic stat Fax 1904 biochemical analyzer. After that, blood preparations were prepared: from the first test tube — before incubation (control) and then from all five test tubes — 10, 30, 60 and 120 minutes after incubation in a thermostat at 37° C. A total of 21 smears were obtained from a single blood sample. At each stage of incubation the preparations were previewed under a microscope at low magnification

without immersion. Preparations with all glucose concentrations incubated for 120 min were poorly visualized and were not subject to further cytomorphometric analysis. Under microscopy in these smears, normal discocytes were globulated, glued together and located in the fields of vision as aggregates and coin columns and were prone to hemolysis. Thus, in our study we worked with the morphofunctional properties of er under the influence of different glucose concentrations for 10, 30 and 60 minutes. The study of the obtained smears was carried out on the computer hardware and software complex *mekos-C-3*, the program — *Erythrocytometry*. It is known that the morphology of shaped blood elements has long been recognized as an important clinical indicator. Among the numerous hematological indicators, er morphometry is successfully used for the diagnosis of a number of different pathologies, as well as for General health assessment. The modern Arsenal of morphometric methods for analyzing peripheral blood cells is quite extensive [6]. In the study of er analysis the following characteristics were used: average diameter, area, polarization, shape factor, red blood cell formula (distribution into the main morphological types), as well as the coefficients of ovalocytosis, poikilocytosis, anisocytosis and anisochromia. The study of the nanostructure of peripheral blood erythrocytes of wounds was carried out using a scanning probe microscope NTegraPrima (NT-MDT, Russia). In the study, specially prepared microprobes were used in semi-contact mode with the use of *misalignment errors*. A preliminary selection of the area was made in an optical microscope at a magnification of 40×0.65 , a glass cutter was used, the marked area was selected, and the sample was placed on the object table of a scanning probe microscope. The mode was used using the NT-MDT NSC 10 cantelever [7]. Two-dimensional and three-dimensional images were obtained using atomic force microscopy in 3D mode (Fig. 4).

RESULTS AND DISCUSSION

We used the principal component method to determine a small number of linear combinations of initial morphometric features of er in relation to glucose concentration which explains most of the variability of the data as a whole. Statistical data processing was performed using nonparametric analysis methods (the principal component method) and using Microsoft Office software Microsoft Exel, STATISTICA Edition and STATGRAPHICS Plus. All stages of the experiment were performed at the Department of Biomedicine and physiology of the North Caucasus Federal University. The use of the above-mentioned morphometric and statistical methods allowed us to evaluate the properties of er as an indicator of adaptation and adaptability of the body to changed conditions of the internal environment (high concentrations of glucose).

As a result of the analysis, 3 main components were identified in the control blood sample, describing 100% dispersion of morphofunctional features of er. It turned out that in the first main component, which describes 68.5% of the variance of the analyzed er features, the greatest weight among the features was

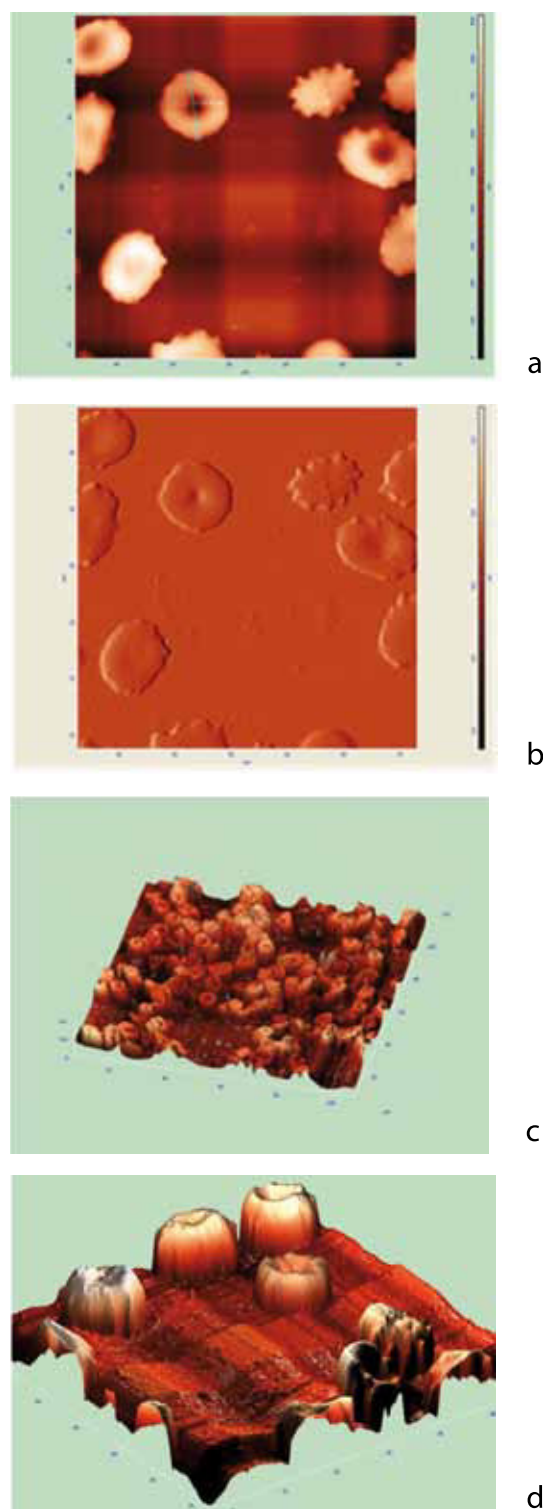


Fig. 4. Nanostructured organization of red blood cells under the influence of high glucose concentration (10.0 mmol/l); a, b — two-dimensional image of red blood cells obtained using AFM "Integra prima"; c, d — three-dimensional image of red blood cells obtained using AFM "Integra prima"

the number of discocytes, the ovalocytosis coefficient and the number of microcytes (Fig. 1).

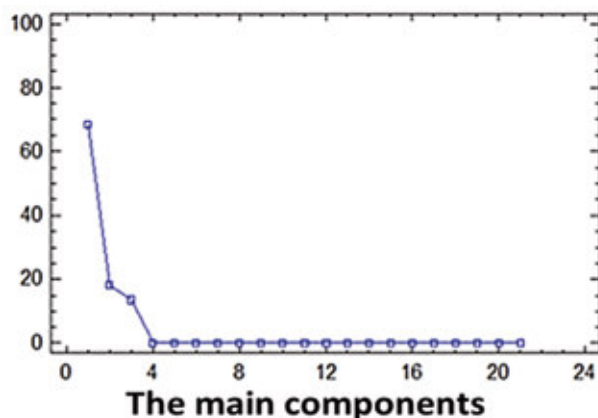


Fig. 1. The main components highlighted in the analysis of morphometric characteristics of er in the control blood sample

At a glucose concentration of 6.5 mmol/l, 2 main components were identified describing 100% of the variance of the analyzed features. The first main component describing and 76.4% of the variance, the largest value among the signs had a ratio of ovalocytosis, the number of discocytes and mikrocytos when the dispersion of the analyzed morphometric characters of er became predominant beshenkovichy period and the greatest weight among the signs had the number of discocytes (0,240), the coefficient of ovalocytosis (0,238) and the number of mikrocytos (0,228) (Table. 1.). In the second main component which describes 18.1% of the variance of the analyzed features, the largest changes were made by the data after 10 minutes of the experiment. Among them, the number of deformed irreversibly altered forms of er (0.327), codocytes (0.254) and microcytes (0.249) was dominant.

Analysis of a blood sample with a glucose concentration of 7.5 mmol/l also allowed us to identify 2 main components. In the first main component, which describes 58.3% of the variance of the analyzed morphofunctional parameters of er, the ovalocytosis coefficient, the number of microcytes and discocytes had the greatest informative significance among the features.

When performing the main component analysis, 2 main components were identified in a blood sample with a glucose concentration of 10.0 mmol/l. In the first main component, which describes 60.5% of the variance of the analyzed er features, the number of microcytes, spherocytes, and poikilocytosis were the most important among the features. The increase in the changes in the proportion of microcytes, in our opinion, is due to the influence of high glucose

concentration which causes acceleration of the aging process of the cell and, consequently, its shrinking and reduction in size [8].

According to the method of main components at a glucose concentration of 15.0 mmol/l, 2 main components were also isolated. In the first main component, which describes 59.2% of the variance of the analyzed er features, the indicators of anisochromia and anisocytosis as well as the number of echinocytes had the highest weight among the features.

Analyzing the contribution of each of the studied indicators to the marked changes, the dominance of anisochromia, anisocytosis, echinocytes, spherocytes, ovalocytosis coefficient and discocytes was revealed. At the same time, it turned out that the greatest variability is caused by such indicators as anisochromia and the number of spherocytes. The fact that the greatest shifts are observed 10 minutes after the start of the experiment (Fig. 2) fits well into the hypothesis about the influence of high concentrations of glucose on the morphometric parameters of er and reveals a similar picture with the concentration of glucose 10.0 mmol/l (Fig. 3).

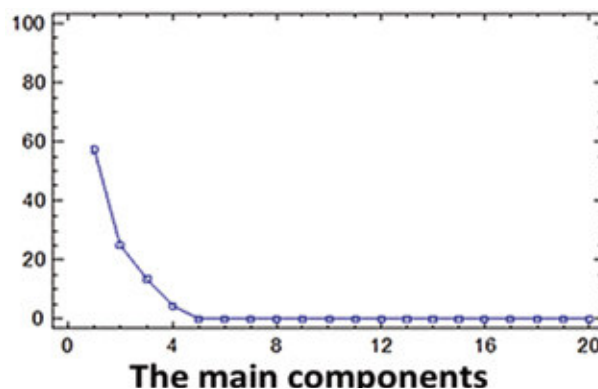


Fig. 2. The main components identified in the analysis of morphometric features of er after 10 minutes of the experiment

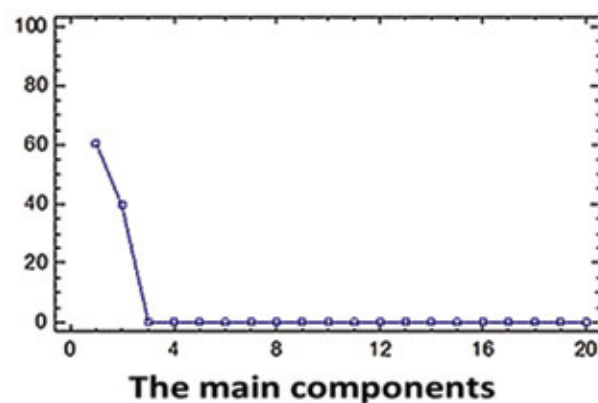


Fig. 3. The main components identified in the analysis of morphometric features of er with a glucose concentration of 10.0 mmol/l

Table 1. Weight of morphometric features of er in the control blood sample

The signs	The components		
	1	2	3
Microcytes	0,228	0,249	0,081
The normocytic	-0,224	-0,247	-0,128
Macrocytes	-0,183	-0,200	0,361
Deformed bodies	-0,200	0,327	-0,084
Discocytes	0,240	-0,204	0,063
Echinocytes	0,119	0,200	0,477
Elliptocytes	-0,249	-0,001	-0,198
Spherocytes	0,180	-0,332	0,202
Codocytes(target-shaped)	0,223	0,254	0,123
Pegmatite (bitten)	-0,110	-0,339	0,371
Dacryocytes (teardrop-shaped)	-0,221	0,202	0,227
The ratio of ovalocytosis	0,238	-0,034	0,255
Poikilocytosis	-0,250	0,157	-0,042
Anisocytosis	-0,251	0,041	0,179
Anisochromia	-0,248	0,003	0,201
Area of the object	-0,231	-0,242	0,069
Average diameter	-0,225	-0,264	0,045
Factor of the form	-0,262	-0,051	0,048
Polarization	-0,237	0,039	-0,257

This also explains the significance of the anisochromia index as one of the signs of the degree of cell aging and the course of pathological changes. The appearance of spherocytes seems to be associated with an increasing intoxication effect of glucose concentration which led to a violation of the stability of the membrane.

In addition, the combination of the appearance of spherocytes can be considered as a pre-hemolytic stage which is passed by echinocytes, stomatocytes with irreversible damage [9–18].

Analyzing the contribution of each of the studied indicators to the marked changes, the dominance of anisochromia, anisocytosis, echinocytes, spherocytes, ovalocytosis coefficient and discocytes was revealed. At the same time it turned out that the greatest variability is caused by such indicators as anisochromia and the number of spherocytes.

CONCLUSION

Thus, the erythrocyte system has a significant instability to the effects of high glucose concentrations i.e. there is no adaptive mechanisms and high hyperglycemia. The system ceases to be resistant to external effects of glucose at a concentration of 7.5 mmol/l. With a further increase in the concentration of glucose occurs as if its loosening which is shown by

significant shifts in the morphometric indicators of er from normal parameters. Consequently, during the entire experiment the greatest changes occurred in blood samples with high concentrations of glucose and more stable, respectively, were blood samples with normal glucose content and glucose concentration of 6.5 mmol/l. In addition, we confirmed the hypothesis that a concentration of 7.5 mmol/l destabilizes the red blood cell system.

Apparently, it is possible that staged changes in glucose supply from the incubation medium by means of passive and facilitated diffusion with its consequent anaerobic oxidation of er, which determines the level of phosphorylation of phosphoproteins in the cell cytoskeleton, functioning of the pump and receptor apparatus of the membrane. Therefore, by changing geometry of er we can judge the initial state of the erythrocyte membrane and the level of oxidative processes of er.

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COVID-ASSOCIATED PANIC ATTACKS: REGIONAL MANAGEMENT ASPECTS

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ABSTRACT — The modern coronavirus pandemic (COVID-19) poses a mortal threat to the populations of more than 210 countries and at the same time constitutes a real challenge to national governments. One of the pandemic problems is the fear of uncertainty, which may lead to development of panic attacks among the general population. It was established that at the national level in Ukraine, standards for provision of medical care to patients with panic attacks amid the COVID-19 pandemic have not been elaborated. The article analyses measures of regional authorities on creating an algorithm for providing the special care to patients with mental disorders during a pandemic on the basis of a specialized psychosomatic clinic.

KEYWORDS — mental disorders, COVID-19, medical care algorithm, health management.

INTRODUCTION

COVID-19 outbreak has started as a health section problem of one country. But too quickly, it becomes a global problem that, at an individual level, affects all areas of health — physical, social and mental health [5; 9].

MATERIALS AND RESEARCH METHODS

The study was conducted on the basis of the Center for Psychosomatic Pathology of the regional hospital named after I.I. Mechnikov (Dnipro, Ukraine). The investigation took place from 16 March 2020 till 30 April 2020. The investigation processed the data from the Center's medical statistics, as well as world statistics on coronavirus infections Worldometer [10]. In Ukraine, the prevalence of the COVID-19 has been registered in all its regions. As of April 30, 2020, 10 406 cases were registered in the country, 246 of them deaths, 1238 recoveries [2]. In addition, the study was the subject of government decisions and or-

ders on COVID-19 issued by the Ukrainian Ministry of Health.

RESULTS AND DISCUSSIONS

In addition to the real epidemic of the coronavirus [2], in Ukraine, as well as around the world a mental epidemic has arisen associated with the induction of the psyche by the media and society. The most powerful trigger mechanism for the panic attack associated with the Covid today is precisely the media. It is common for the human subconscious to react to danger, and the reaction of one person causes a chain reaction of others. A person with a rich imagination perceives information about the possibility of getting sick as a real threat to life, and he/she may have a reaction in the form of mental disorders, such as a panic attack, anxiety disorder, depression and others.

Even the most mentally stable person could have a panic attack due to news about the Coronavirus. It is proved that a mental state under stress affects the immune system — it reduces immunity, and panic could cause harm [4]. It should be noted that such a symptom as any difficulties of breathing is characteristic of both a panic attack and the COVID-19 [5], which increases anxiety and the frequency of panic attacks. Therefore, this fact requires distinction, which can be conducted only by a specialist.

At the primary level of management, such a specialist is a family doctor. The doctor will determine the presence or absence of somatic symptoms, including the symptoms of the Coronavirus, the presence of symptoms of a panic attack. At this moment in Ukraine, the algorithm for the diagnosis and treatment of the Covid-associated panic attacks has not been included in the structure of the national standard of medical care in the light of the COVID-19 pandemic [7].

For mild symptoms of anxiety and / or depression, the patient can be treated by a family doctor for 7–14 days. If there is no improvement, a family doctor issues a referral to a psychiatrist.

The Dnipropetrovsk region is the largest in Ukraine in terms of population. The regional government, namely the Dnipropetrovsk Regional Council set up a Center for Psychosomatic Pathology with 30 beds [1; 3]. This Center is a structural unit of the I.I. Mechnikov regional clinical hospital, which is defined

by the Government of Ukraine as the main hospital for inpatient treatment of the Covid infection [8]. The creation of the Center for Psychosomatic Pathology in the structure of the regional hospital is important for patients with somatic pathology, in whose onsets psychological pathogenic effects play an important role. The services of the Center of Psychosomatic Pathology have become especially popular in conditions of military conflict in the Eastern Ukraine from 2014 up to the present, which made it possible to provide highly qualified comprehensive assistance to the wounded and injured during the military conflict [6]. The demand for the Center is also high in the light of the Coronavirus infection pandemic in Ukraine.

For the period under study, the Center was contacted by 103 patients with various disorders. The subjects underwent their first treatment under the supervision of a family doctor (Table 1).

Table 1. *Characterization of pathologies, primarily treated at the level of outpatient general practice*

The main diagnosis	Specific gravity, %
Somatoform vegetative dysfunction	90
Cardiovascular disease	25
Gastrointestinal diseases	19
Endocrine diseases	15
Pulmonary disease	13
Other somatic diseases	10

Data of the Center for Psychosomatic Pathology. All patients are taken as 100%. One patient may have several diagnoses.

As it can be seen from the table, panic attacks and other mental disorders are disguised as somatic pathologies or remain unrecognized by general practitioners at the stage of outpatient treatment.

In the case of moderate symptoms of panic disorder, the patient is sent for specialized psychiatric care (Table 2).

As it can be seen from the table 2, the diagnosis of panic disorders is more widely carried out only at the stage of inpatient treatment.

Based on the Psychosomatic Center the algorithm for providing medical care to patients with panic attacks in the context of the COVID-19 pandemic was developed and implemented for a family doctor. The algorithm is sent to all primary care physicians in the Dnipropetrovsk region (1200 doctors).

Part I. General issues

- 1.1. Mental disorders in case of COVID-19 can develop at all stages of the infectious process, in any form and harm, have different clinical severity,

Table 2. *Description of pathologies most commonly encountered in specialized psychiatric care*

The main diagnosis	Specific gravity, %
Panic disorder	25%
General Anxiety Disorder	22%
Mixed anxiety and depressive disorder	20%
Alcohol addiction	8%
Depressive Disorder	9%
Hypochondriacal disorder	10%
Substance Abuse	5%
Bipolar Affective Disorder	1%
Severe mental disorders	2%

Data from the Center for Psychosomatic Pathology

prognosis, and the degree of danger to oneself and others.

- 1.2. Consultations of a psychiatrist on the diagnosis and treatment of mental and behavioral disorders amid COVID-19 can be carried out with a personal reception (examination) by a psychiatrist, by phone and by web call (for doctors in the region).
- 1.3. If you are a family doctor, then act on the psychosocial factors that are causing a person stress at the moment. Provide additional social support to patients. Teach a person how to deal with stress. Tell him/her about normal reactions to acute stress disorder. Reassure the person that these symptoms sometimes occur after severe stress, and this is hardly a serious medical problem. Prescribe treatment for concomitant diseases, if necessary — include special drugs. Always be in touch with such a patient, ask him/her to visit again within 10 days if the symptoms have not subsided, or at any time if the symptoms worsen.

If there is no proper effect after all of the above measures, proceed to part II.

Part II. Special issues (Table 3).

CONCLUSIONS

In the light of the COVID-19 pandemic, one of the most important challenges is the Covid-associated panic attacks. The algorithm for providing highly specialized aid is necessary for qualified medical care, which can improve the quality of life of patients amid the Coronavirus infection pandemic.

The co-authors declare that there is no conflict of interest in the scientific article submitted for publica-

Table 3. The algorithm for the family doctor's actions in providing medical care to patients with panic attacks in the context of the COVID-19 pandemic

Phase	Action content	Specialist
I.	COMPLAINTS: palpitations, chest pain, feeling of lack of air, dizziness, feeling of unreality; secondary fear of death, loss of self-control or going crazy; fear of developing the next panic attack	Family doctor
II.	SURVEY: clinical, paraclinical, psychological questionnaires	Family doctor
III.	Somatic DIAGNOSIS and concomitant syndromological diagnosis of mental disorder has been established	Family doctor
IV.	Method of treatment: general-acting drugs, tranquilizers, antipsychotics, antidepressants, anxiolytics, psychotherapy Treatment 7-14 days	Family doctor
V.	THERAPEUTIC EFFECT ACHIEVED	
	NO Examinations: clinical, psychopathological, clinical, pathopsychological, paraclinical (EEG, CT, MRI, ultrasound) Actions: inpatient and outpatient clinical observation for the differential diagnosis with anxiety-phobic F 40.0 - F40.2 and other anxiety disorders F41.1, F41.2, manifestations of anxiety included in the structure of some somatic diseases (for example, thyrotoxicosis, coronary heart disease, chronic renal failure, rheumatoid arthritis) F 54.0	Psychiatrist
	YES Treatment: continued treatment and follow-up	Family doctor
VI.	EXPECTED TREATMENT RESULTS ARE ACHIEVED	
	Panic disorder: the termination or a significant decrease in the frequency of panic attacks and related disorders, as well as a decrease in avoiding behavior. Significant improvement: no further monitoring and treatment needed Improvement: dynamic observation by a psychiatrist, psychotherapy, observation by a family doctor	Psychiatrist Family doctor Psychiatrist

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CONTRIBUTORS

S. Moroz, I. Khozhylo S. Ryzhenko — idea, research methodology, preparation of articles for publication, formulation of conclusions; R. Khaitov — analysis of primary documentation, generalization of materials, graphics; V. Semenikhina, N. Turishcheva — review of literature and legislation, S. Moroz — developing the algorithm.

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CHANGES IN MALE REPRODUCTIVE SYSTEM UNDER ADVERSE ENVIRONMENTAL CONDITIONS

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ABSTRACT — The article investigates effects of adverse environmental factors under experimental conditions on different units of male reproductive system. White male rats weighing 210 g were exposed to microwave radiation of low intensity and natural gas containing hydrogen sulfide. The level of malonic dialdehyde (MDA) and kinetic indexes of lipoperoxidation were determined in homogenates of mediobasal hypothalamus and testes. Testosterone and luteinizing hormone levels were determined in the blood serum by the enzyme immunoassay method. Both microwave radiation and natural gas leads to a surge in the MDA level in testicular tissue and hypothalamus. The exposure to natural gas triggered the suppression of testicular steroidogenesis. The long-term exposure to natural gas caused profound biochemical changes in testicular tissue and epididymis by the level of protein. In general, the exposure to natural gas caused more serious changes in morphofunctional state of rat testes.

KEYWORDS — malonic dialdehyde (MDA), luteinizing hormone, testosterone, oxidative stress, lipoperoxidation, Leydig's cells, testicular tissue.

Oxidative stress is a state of imbalance between the systemic manifestation of reactive oxygen species and the ability of biological systems to detoxify readily the reactive intermediates or to repair the resulting damage. Disturbances in the normal redox state of cells can cause toxic effects through the production of peroxides and free radicals that damage all components of the cell, including proteins, lipids, and DNA. Further, some reactive oxidative species act as cellular messengers in redox signalling. Thus, oxidative stress can cause disruptions in normal mechanisms of cellular signaling.

In humans, oxidative stress is thought to be involved in the development of many diseases or may exacerbate their symptoms [10]. These include cancer, Parkinson's disease, Alzheimer's disease, atherosclerosis, heart failure, myocardial infarction, vitiligo, and chronic fatigue syndrome [5]. Oxidative stress also

provokes infertility [1]. However, reactive oxygen species can be beneficial, as they are used by the immune system as a way to attack and kill pathogens [11]. Short-term oxidative stress may also be important in prevention of aging [3].

The stress concept considers stress to be physical and emotional [13]. At the same time stressing factors may be chemical agents (industrial toxicants, drugs) and food factors (disbalance in macro- and microelement content, deficiency in protein etc) [9]. In this connection we have studied the effects of physical stress (microwave radiation) and chemical stress (natural gas containing hydrogen sulfide) in comparison, which will allow us to find out the ways of stress development as well as to disclose possible adaptive mechanisms within the male reproductive system.

The purpose of the work

is to study the effects of adverse environmental factors under experimental conditions on different units of male reproductive system in comparison.

MATERIAL AND METHODS

The objects of the study were 80 white male rats weighing 200–220 g. The animals were subjected to the following stress conditions: 1) low intensity electromagnetic radiation; 2) natural gas containing hydrogen sulfide. The exposure with electromagnetic radiation was realized during 30 days for 30 minutes daily. To make electromagnetic field, the monochromatic electromagnetic wave generator was used («Yav-1-7.1», Russia; $\lambda = 7.1$ mm, frequency $f = 42.194$ GHz). To provoke chemical stress, the Astrakhanian natural gas was used. The natural gas exposure was carried out in concentration of 10 mg m^{-3} (by H_2S) during 30 and 120 days for 240 min daily. So, the following groups were formed: 1) Control group, 20 males; 2) experimental group 1 (E-1), 20 males (microwave radiation); 3) experimental group 2 (E-2), 20 males (gas exposure, 30 days); 4) experimental group 3 (E-3), 20 males (gas exposure, 120 days).

At the end of the experimental effects, the animals were decapitated under ether anesthesia in compliance with the Geneva Convention (1985). The level of malonic dialdehyde (MDA) and kinetic indexes of lipoperoxidation (spontaneous spLPO,

ascorbate-dependent asclPO) were determined in homogenates of mediobasal hypothalamus and testes [12]. Peroxide resistance of erythrocytes was measured in blood [8]. Testosterone and luteinizing hormone (LH) levels were determined in the blood serum by enzyme immunoassay method. The protein content and fractional distribution of proteoglycans in epididymis and testes extracts were determined by electrophoresis method at pH 5 [7]. Sections of testicular tissue of 7 μ m thick were made with the help of microtome "Microm HM-400" (Germany), and then stained with hematoxylineosin dye. The obtained preparations were studied using the universal microscope "Nu" (Germany) connected to the color television camera "Pixera" (USA). All the data obtained during the study were statistically processed using Student's criterion, the differences were considered significant at $p < 0.05$. The relationship between the studied parameters was estimated by calculating the Pearson correlation coefficient (r) [4].

RESULTS

Microwave radiation (group E-1) caused an increase in erythrocyte peroxide hemolysis by 20%, compared with the control ($p < 0.05$), which indicates an increase in free radical oxidation in the blood and testifies to the development of oxidative stress. In group E-1, an increase in the dynamics of free radical oxidation processes was also observed in the testicular tissue: the initial level of MDA increased by almost 38.5 % compared to control values ($p < 0.001$). In the hypothalamic tissue, the initial level of MDA exceeded the control value slightly. At the same time, the kinetic indexes of lipid peroxidation, especially ascorbate-dependent, did not differ practically from the corresponding control values (Table 1). This fact indicates an insignificant effect of low-intensity microwave radiation on the regulatory unit of male reproductive system [2].

At the same time, in group E-1, the levels of testosterone and LH in blood plasma did not differ significantly from the control indexes, although it was found that the level of testosterone tended to decrease (Table 2). Thus, microwave radiation did not have a noticeable effect on the testosterone-producing activity of the testes, nor on the gonadotropic function of the adenohypophysis [2].

Under the influence of microwave radiation, a random arrangement of spermatogenic epithelial cells, or its uneven height, was observed. In some cases, multiple tears of the basal membrane were observed. An increase in the total number of Leydig cells at the expense of average size cells was also noted. Their area, however, tended to decrease. These contradictions

explain the almost unchanged testosterone-producing activity of the testes under conditions of low-intensity microwave radiation (Fig. 1).

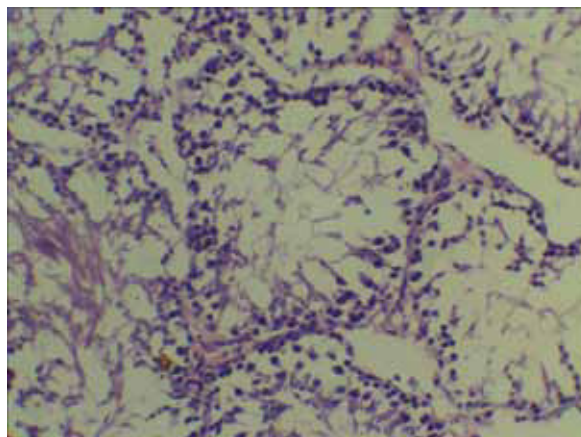


Fig. 1. The structure of testicular tissue in rats exposed to microwave radiation. Stained by hematoxylin-eosin. Magnification 200 $\times$

The exposure with natural gas during 30 days (group E-2) caused an increase in erythrocyte peroxide hemolysis by 23.1 %, compared with the control group ($p < 0.05$) which testifies to the oxidative stress development. When exposed to hydrogen sulfide-containing gas, an increase in lipoperoxidation (LPO) processes in testicular tissue was observed. The initial level of MDA increased by 1.5 times compared to the control values. The kinetic indexes of LPO under conditions of gas intoxication increased significantly also, especially ascorbate-dependent lipid peroxidation. Therefore, under conditions of natural gas exposure, the intensification of radical oxidation processes takes place in testicular tissue, which results in functional state disorders in this tissue. In hypothalamic tissue, a significant increase in free radical processes was noted also, which indicates an inhibition of its functional activity in general. This, in its turn, negatively affects the functional state of adenohypophysis (Table 1).

The exposure to natural gas (group E-2) led to a sharp decrease in the level of testosterone in blood plasma by 37.5% ($p < 0.001$) compared to the control indexes. The level of LH, however, did not change significantly, but tended to decrease. At the same time, the changes in testosterone and LH levels corresponded to a high coefficient of positive correlation $r = +0.808$ with a confidence of 95% (Table 2).

Under conditions of natural gas exposure the considerable decrease of diameters of seminal tubules and the increased quantity of interstitial tissue at the

Table 1. Changes in lipoperoxide indexes in rat testes and hypothalamus under adverse conditions

Experimental conditions	n	MDA, nmol/0,05 g	Kinetic indexes, nmol MDA h ⁻¹	
			spLPO	ascLPO
Testicular tissue				
Control	20	4,89 ± 0,151	45,97 ± 0,840	48,74 ± 0,702
Group E-1	20	*** 6,77 ± 0,272	* 48,32 ± 2,003	*** 55,21 ± 0,894
Group E-2	20	*** 7,42 ± 0,457	*** 65,36 ± 3,104	*** 76,48 ± 2,431
Hypothalamic tissue				
Control	20	5,45 ± 0,280	56,68 ± 1,145	62,95 ± 1,451
Group E-1	20	*** 7,94 ± 0,506	59,28 ± 1,101	63,52 ± 2,007
Group E-2	20	*** 10,44 ± 0,398	*** 82,07 ± 1,023	*** 102,44 ± 4,013

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$ compared with the control group

Table 2. Changes in testosterone and LH levels in blood plasma in rats

Experimental conditions	n	Testosterone, ng cm ⁻³	LH, mMU cm ⁻³	r	p (r) <
Control	20	2,829 ± 0,0731	0,425 ± 0,0538	+0,935	0,05
Group E-1	20	2,614 ± 0,1160	0,420 ± 0,0068	+0,634	0,05
Group E-2	20	*** 1,769 ± 0,0814	0,370 ± 0,0152	+0,808	0,05

*** $p < 0.001$ compared with the control group

expense of small Leydig's cells were observed. This may be considered as a compensatory reaction of endocrinocytes on the background of destructive changes in spermatogenic epithelium. At the same time the oedema of interstitial tissue and necrosis of spermatogenic cells took place. Seminal tubules were distantly located to each other. The chaotic distribution of spermatogenic epithelium cells and empty seminal tubules in a certain number of cases were observed. The height of spermatogenic epithelium was considerably decreased (Fig. 2).

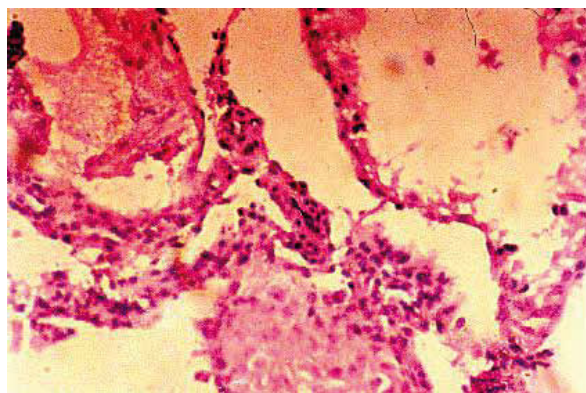


Fig. 2. The structure of testicular tissue in rat exposed to natural gas. Stained by hematoxylin-eosin. Magnification 200×

Therefore chronic intoxication with the natural gas containing hydrogen sulfide provokes testicular steroidogenesis depression that may be explained by radical formation processes as a result of oxidative stress development as well as endocrine changes in the system hypothalamus-pituitary [2].

In additional investigation (group E-3) we measured the average quantity of protein in proteoglycan samples from epididymis and testes. The average amount of protein in proteoglycan samples in the control group was $9.5 \pm 0.76 \mu\text{g mg}^{-1}$ (by the mass of the tissue). The exposure to natural gas during 30 days did not affect the concentration of protein significantly and the concentration seemed to be $9.8 \pm 0.85 \mu\text{g mg}^{-1}$. By the 120th day of exposure the amount of protein in proteoglycan fractions increased up to $7.4 \pm 0.35 \mu\text{g mg}^{-1}$ which indicates a decrease in protein biosynthesis in testes. The amount of sulfates was $3.6 \pm 0.3 \mu\text{g cm}^{-3}$ normally. The amount of sulfates in rats exposed to natural gas during 30 days did not differ from the control indexes. However, the level of sulfates began to increase only after long-term exposure, and by the 120th day of exposure to natural gas (group E-3) their level achieved to the value of $19.1 \pm 0.85 \mu\text{g cm}^{-3}$. This explains the increasing of the acidic proteoglycan fraction. Therefore, after three weeks' exposure with

natural gas profound biochemical changes occur in testicular tissue and epididymis.

CONCLUSIONS

Thus, the microwave radiation of low intensity provokes a damaging effect directly on spermatozoa, causing changes in the structure of spermatogenic epithelium. Under conditions of metabolic shifts caused by natural hydrogen sulfide-containing gas, reproductive dysfunctions are caused by both toxic effects of free radicals and inhibitory regulation from the hypothalamic-pituitary complex [2, 6]. The leading disturbances of morphofunctional state of testes under the influence of natural gas are spermatogenic epithelium necrosis, desquamation of germ spermatogenic cells in the lumen of the tubules, multiple ruptures of the basal membrane of seminiferous tubules on the background of compensatory growth of interstitial tissue.

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MICROWAVE RADIATION AND MALE REPRODUCTIVE FUNCTION

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ABSTRACT — The purpose of the paper is to study the effects of low intensity microwave radiation on morphofunctional state of testes in white rats. The intensification of lipid peroxidation was determined in testicular tissue, which correlated with worsening of morphofunctional state of epididymal spermatozoa. The leading disorders were broken and lost tails of spermatozoa. Therefore, microwave radiation of low intensity does not affect steroidogenesis considerably while it causes morphofunctional changes of spermatozoa.

KEYWORDS — microwave radiation, lipoperoxidation, spermatozoa.

Electromagnetic waves come in a very wide range of wavelengths: there are radio, microwave, infrared (heat), visible light, ultraviolet, X-ray, and γ -ray waves. All are used in medicine in one way or another. Microwave radiation is used in certain kinds of heat treatment, where the heat is generated in the target tissue (as in a microwave oven) [1, 2]. At the same time there is little information about the influence of microwave radiation on functional state of reproductive system. In this regard, we investigated how low intensity microwave radiation affect morphofunctional state of testes in white rats as well as some biochemical indexes of different units of reproductive system in animals.

The purpose of the paper

was to study the effects of low intensity microwave radiation on morphofunctional state of testes in white rats as well as some biochemical indexes of different units of reproductive system in animals.

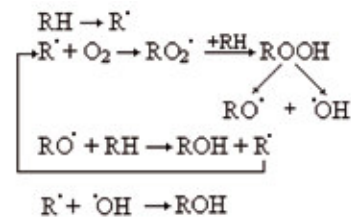
METHODS

White male rats of 215–240 g were subjected by microwave radiation with frequency of 42 GHz during 30 days for 30 min. daily. At the end of the experimental effects, the animals were decapitated under ether anesthesia in compliance with the Geneva Convention (1985). The level of lipoperoxidation in testicular and

hypothalamic tissues was determined [3]. Testosterone and luteinizing hormone levels in blood plasma were measured by enzyme immunoassay method. Morphofunctional state of epididymal spermatozoa and testicular tissue were studied. All the data obtained during the study were statistically processed using Student's criterion, the differences were considered significant at $p < 0.05$.

RESULTS

Under conditions of low intensity microwave radiation, peroxide haemolysis of erythrocytes has been found to increase that testifies to oxidative stress development. Unsaturated phospholipids RH are oxidized to produce hydroperoxides ROOH which, in their turn, break down to give rise to different oxygen-containing derivatives ROH and reactive oxygen species (ROS). Thus, oxidative stress development may be represented in the following way:



The hormone levels of testosterone and lutropin have been found not to differ trust-worthily from that of the control indexes. The relative weights of gonads and pituitary under experimental conditions were compared with the control group. The intensification of free radical oxidation processes was determined in testicular tissue, which correlated with the worsening of morphofunctional state of epididymal spermatozoa. The leading disorders were broken and lost tails of spermatozoa. Under the influence of microwave radiation, an increase in total number of Leydig's cells took place, which is likely to be a compensatory reaction of testes and may be connected with the resonance effect conditioned by microwave radiation.

CONCLUSIONS

Therefore, low intensity microwave radiation does not affect steroidogenesis considerably while it causes morphofunctional changes of spermatozoa.

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METHOD OF NEAR-FIELD DIELECTROMETRY OF BIOLOGICAL FLUID

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ABSTRACT — The purpose of the work was to study the possibilities of near-field microwave dielectrometry. It is established that the developed device, using the principle of near-field resonant microwave sensing, allows performing the dielectrometry of biological fluid (on the example of blood). With the use of this technology, approximate standards of the dielectric constant of whole blood were formed. The presence of age-related features of the parameter level was demonstrated in this study.

KEYWORDS — microwave dielectrometry, dielectric permittivity, blood.

Over the past 30 years, a certain amount of data has been accumulated describing the dielectric properties of biopolymers can be used for evaluating the functioning of biological objects [2, 4, 7], for screening diagnostics of neoplasms [3], diabetes mellitus [4] etc.

Several studies have measured the dielectric properties of erythrocytes and plasma in the range 10 kHz—250 MHz, temperature dependence of electrodynamic parameters of blood is installed in the range of 1 Hz÷40 GHz [1, 6, 7]. In addition, measurements of the dielectric characteristics of blood in a wide frequency range revealed numerous physical properties of macromolecules and their fragments [1, 5, 7]. On the other hand, the question of an unambiguous interpretation of these measurements and their relationship to the mechanisms of intracellular interaction remains open and questionable [6, 7]. According to modern concepts, many metabolic and functional changes in cells that accompany various pathological processes are determined by structural disorders of intra- and extracellular water [1, 5]. At the same time, laboratory and diagnostic prospects of equipment for assessing the dielectric characteristics of biological fluids have not been disclosed. In this

regard, the purpose of the work was to study the possibilities of near-field microwave dielectrometry.

MATERIAL AND METHODS

Our measuring system for studying the dielectric properties of blood is a high-quality microwave resonator made on a segment of a coaxial line with a fluoroplast filling. At one end of the resonator there is a magnetic frame, the other is connected to the load, which includes a probing near-field antenna. The experimental setup scheme is shown in Fig. 1.

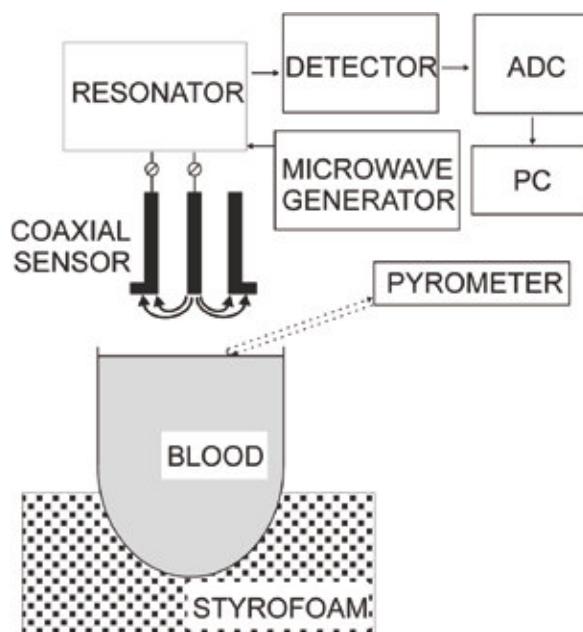


Fig. 1. Device for near-field microwave dielectrometry of liquids (principal scheme)

Due to the small transverse dimensions of the sensor, a relatively small volume of blood (50–100 µl) was used. The distance from the end of the sensor to the bottom and to the side walls of the cell was fixed (about 3 mm), which is obviously more than the distance between the internal and external conductors. In this regard, the inaccuracy of standing of the sensor in the cuvette led to insignificant errors (no more than 1–2%) in measuring the permittivity. The electrodynamic parameters of the biological fluid were restored in the near-field antenna region by shifting the

resonant frequency and decreasing the signal amplitude during resonance. Alcohol with a known complex permittivity was used as the calibration control. Temperature control was performed using a pyrometer.

The developed complex was tested on whole blood samples of 35 adults (age — 20–45 years) and 25 children (age — 10–14 years) who did not have acute or chronic pathology at the time of the study. The material was obtained with the informed consent of the patients or their legal representatives.

The results were processed using the Statistica 6.0 program.

RESULTS

Our research allowed us to demonstrate the possibility of evaluating the dielectric characteristics of biological fluid on the example of blood, as well as to form standards for the dielectric properties (permittivity and conductivity) of whole blood in children and adults (Fig. 2).

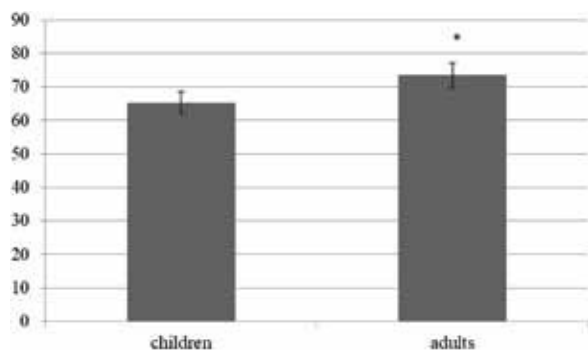


Fig. 2. The level of dielectric permittivity of the blood in children and adults, * — the statistical significance of differences $p < 0.05$

It was found that the dielectric permittivity of biofluid in humans is determined in the range of 40–75 units, and in healthy adults the parameter is detected at higher values ($p < 0.05$).

CONCLUSION

It was shown that the developed device, using the principle of near-field resonant microwave sensing, allows conducting dielectrometry of biological fluid (on the example of blood). With the use of this technology, we developed approximate standards of the dielectric constant of whole blood. The presence of age-related features of the parameter level was revealed in this study.

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INTERRELATION OF TRACE ELEMENTS AND THE STRUCTURAL ORGANIZATION OF LYMPH NODES AT YOUNG AND SENILE AGE

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ABSTRACT — The article deals with the study of interrelation of trace elements and morphology of lymph nodes at different localization and age-related changes. Lymph nodes of different localization at young and old animals were analyzed by a morphological method with definition of trace elements by roentgen fluorescent method and the use of synchrotron radiation. There are data on forming of the lymphoid-microelement association important for integrative assessment of the structural organization of lymph nodes. Structural modification of lymph nodes has certain patterns, proceeding from features of a microelement profile. The region-dependent morphological variant of lymph nodes corresponds to a certain content of trace elements and their correlation with compartments of lymph nodes. Trace elements deficiency and reduction of compartments of lymph nodes are considered as predictors of aging of lymphoid tissue. The results have practical significance to justify a higher trace-element content in anti-aging programs.

KEYWORDS — lymph nodes, trace elements, gerontology.

INTRODUCTION

Lymph nodes are peripheral organs of immune and lymphatic system representing difficult organized structures reacting to different exo- and endogenous factors [1, 2]. Lymph nodes functions together with trace elements. Many trace elements play an important role in maintenance of the optimum immune response, showing regulatory, structural and stabilizing functions [3, 4]. Trace elements take an active part in cofactors or catalysts of enzymes of free radical oxidation in cells of the immune system [4, 5]. Activity of enzymes and the immune system are closely related with change of a trace element homeostasis and,

finally, with change of the structure of peripheral lymphoid organs [1, 3]. Aging is connected with an immunogenesis problem that is defined by features of the structural organization of peripheral lymphoid organs according to the concept of the lymphatic region [1]. It does relevant studying morphological equivalents of the immune response of lymph nodes depending on a microelement profile and age.

The aim of the study is assessment the structural organization and trace elements of lymph nodes at young and senile age.

MATERIALS AND METHODS

The experiment was conducted on white Wistar rats with the natural rate of aging at the age of the 3rd month (young animals) and 1.5 years (old animals). Mesenteric, inguinal and tracheobronchial lymph nodes were analyzed by a morphological method.

Lymph nodes were fixed in 10% neutral formalin. After fixing we resorted to the classical scheme of washing, dehydration, imbibition with a xylol, paraffin and preparation histologic sections on the microtome. Histologic sections of lymph nodes painted hematoxylin and eosine, azure-II-eosine, trichromatic paint on Masson. The cross-section area of lymph nodes was standardized and taken for 100% that allowed to estimate and compare the structural organization of lymph nodes.

The content of trace elements (Se, Mn, Fe, Cu, Zn) in lymph nodes was defined by the roentgenfluorescent method with use of synchrotron radiation. The work was done at the shared research center SSTRC on the basis of the Novosibirsk FEL/VEPP-4 – VEPP-2000 complex at BINP SB RAS, using equipment supported by project RFMEFI62119X0022 [6].

The morphometric analysis of structures of a lymph node was carried out by means of a morphometric grid and the Image-Pro Plus 4.1 program. Statistical data processing was performed with licensed statistical software package StatPlus Pro 2009, AnalystSoft Inc. Data were expressed as average arithmetic with definition of a standard (mean square) error. Belonging to normal distribution was defined when calculating criterion of Kolmogorov-Smirnov and the

accompanying indicators. A P-value < 0.05 was considered statistically significant.

RESULTS

Lymph nodes reach the maximum development to three-months age of young rats of Wistar. It precedes involution of lymphoid tissue at the natural rate of aging. The structural and functional answer of a lymph node is optimum at this age and has rather high degree of correlation with the content of trace elements. Structural and functional zones occupy the different area in the standardized lymph nodes. Parameters of structures define a row: mesenteric — inguinal — tracheobronchial lymph nodes from the smallest to the greatest value. The structure and a microelement profile of lymph nodes differs in each lymphatic region.

The mesenteric lymph node has the cortical and medullary ratio equal 1.33 ± 0.14 in comparison with other lymph nodes. Such value of a cortical and medullary ratio determines the smaller area occupied by medullary cords ($18.25 \pm 0.82\%$) and lymphoid small follicles ($8.60 \pm 0.21\%$) and vice versa, high index of T- and B-zones ratio (1.24 ± 0.17) and also the area occupied by a sinus system ($11.89 \pm 0.41\%$). Construction features of the mesenteric lymph node are combined with the maximum content of Cu, Se, an average content of Fe, Zn, the minimum content of Mn (Table 1).

The tracheobronchial lymph node distinguishes the high cortical and medullary index (2.20 ± 0.13) and the lymph node has the big B-zone consisting of medullary cords ($24.26 \pm 0.54\%$) and lymphoid follicles ($11.46 \pm 0.28\%$). Low ratio of T- and B-zones (1.02 ± 0.09) and the small area, occupied by a medullary lymphatic sinus ($5.25 \pm 0.26\%$) in a lymph node is observed. Morphological variant of the tracheobronchial lymph node are combined with the smallest content of Fe, Cu, Zn, an average content of Mn, Se (Table 1).

The inguinal lymph node is characterized by average parameters of compartments at the size of cortical and medullary index equal 1.97 ± 0.10 and a ratio of T- and B-zones — 1.08 ± 0.13 in comparison with mesenteric and tracheobronchial lymph nodes. The inguinal lymph node has the maximum content of Mn, Fe, Zn, average content of Cu, minimum content of Se (Table 1)

It is obvious that trace elements are necessary for support of lymph nodes activity in young age. Microelements participate in a differentiation and proliferation of the immunocompetent cells forming compartments in lymph nodes [1–3]. This fact will be significant for the relationship between trace elements and compartments of a lymph node. Morphofunc-

tional the analysis showed prevalence of the immune response on cellular type in all lymph nodes at young age. The structure and a trace element profile of lymph nodes carry the region-dependent character, reflecting features of each lymphatic region.

There is a minimization of structurally functional compartments of lymph nodes to reduction of maintenance of microelements in process of aging by 1.5 years of rat life. The structure of lymph nodes changes when aging depending on features of the lymphatic region.

The mesenteric lymph node is characterized by low indexes of structure. The cortical and medullary ratio is 0.73 ± 0.07 , the ratio of T- and B-zones is 0.58 ± 0.11 . These values of indexes determine the smallest area of lymphoid structures of cortical substance at increase in the area of medullary substance (medullary cords are increased up to $41.68 \pm 1.08\%$ and lymphatic sinus are increased up to $9.46 \pm 0.43\%$). Change of structure of the mesenteric lymph node is combined with the maximum content of Se, an average content of Cu, Zn and the minimum content of Fe, Mn (Table 2).

The tracheobronchial lymph node distinguishes high value of structure indexes. The cortical and medullary ratio is 1.79 ± 0.12 , the ratio of T/B-zones is 1.28 ± 0.10 . These indexes define development of structures of cortical substance (the cortical plateau reaches $15.95 \pm 0.34\%$, the paracortex — $25.53 \pm 0.57\%$, lymphoid follicles — $3.22 \pm 0.19\%$) at the smallest area occupied by medullary cords ($24.48 \pm 0.58\%$) and a lymphatic sinus ($6.71 \pm 0.39\%$). Morphological variant of the tracheobronchial lymph node are combined with the maximum content of Cu, an average content of Se, Mn, Fe, the minimum content of Zn (Table 2).

The inguinal lymph node is characterized by average parameters (the cortical and medullary ratio is 1.11 ± 0.10 , a ratio of T- and B-zones is 0.91 ± 0.12) at the increased lymphatic sinus system ($12.24 \pm 0.44\%$) in comparison with mesenteric and tracheobronchial lymph nodes. The inguinal lymph node distinguishes the maximum content of Mn, Fe, Zn and minimum content of Se, Cu (Table 2).

There is forming of regional specifics of the structure and a microelement profile of lymph nodes when aging, according to the drained lymphatic region. The morphofunctional analysis showed prevalence of the immune response on humoral type in mesenteric and inguinal lymph nodes and saving the immune response on cellular type in a tracheobronchial lymph node at senile age.

We carried out the correlation analysis for confirmation of relationship between microelements and adenoid tissue. Microelements are necessary for proliferation and functioning of lymphoid (immune) cells

Table 1. The content of trace elements in lymph nodes of young animals, mkg/g

Trace elements	Young rats of Wistar (three-months age), lymph nodes		
	inguinal 1	mesenteric 2	tracheobronchial 3
Mn	4,12 ± 0,32	2,15 ± 0,13	2,54±0,15
Fe	672,5 ± 54,22	254,8 ± 20,66*	221,4±12,12*
Cu	6,45 ± 0,35	6,48 ± 0,47	5,27±0,17*°
Zn	75,6 ± 2,81	68,71 ± 2,52*	58,26±2,30*°
Se	0,96 ± 0,05	1,38 ± 0,05*	1,25±0,06*

Table 2. The content of trace elements in lymph nodes of old animals, mkg/g

Trace elements	Old rats of Wistar (age 1.5 years), lymph nodes		
	inguinal 1	mesenteric 2	tracheobronchial 3
Mn	4,40 ± 0,63	2,71 ± 0,14*	3,34±0,25*°
Fe	523,8 ± 71,91	182,5 ± 14,33*	226,4±14,64*
Cu	4,68 ± 0,27	5,29 ± 0,35	5,37±0,14*
Zn	61,5 ± 2,06	57,27 ± 1,72*	47,36±2,83*°
Se	0,73 ± 0,08	1,14 ± 0,06*	0,81±0,04°

The note to tables 1-2: * $P_{1-2,3} < 0,05$; ° $P_{2-3} < 0,05$ — the level of statistical significance of distinctions

[1–4, 7, 8]. Lymphoid follicles are the most important among other functional compartments of a lymph node. Lymphoid follicles are responsible for proliferation of lymphoid cells (lymphopoiesis).

Trace elements show medium-to-high correlation with lymphoid nodules in lymph nodes of young animals. Trace elements differ on structure in lymph nodes of different localization. There is a positive correlation of lymphoid follicles concerning Mn ($r=0.37$, $p < 0.05$), Cu ($r=0.70$, $p < 0.001$) in a tracheobronchial lymph node; negative correlation concerning Zn ($r=-0.51$, $p < 0.01$) in an inguinal lymph node; positive correlation concerning Cu ($r=0.52$, $p < 0.01$), Mn ($r=0.43$, $p < 0.05$), Fe ($r=0.69$, $p < 0.01$) and negative correlation concerning Zn ($r=-0.38$, $p < 0.05$) in a mesenteric lymph node. It is possible to assume emergence of lymphoid-microelement association for ensuring lymphopoietic function at young age. We obtained other data at old animals. The lack of microelements reduces activity of enzymes that, in turn, initiates decrease in proliferation of cells and a reduction of lymphoid follicles [1, 7–9]. There is a loss of lymphoid-microelement association because of easing or lack of correlation between trace elements

and lymphoid follicles. It leads to decrease of function of lymph nodes at senile age.

DISCUSSION

There are several reasons of close attention to a problem of interrelation of microelements and structures of lymph nodes. First, immune function is connected with development of compartments of a lymph node in the process of proliferation and a differentiation of immunocompetent cells [2–4, 7]; secondly, existence of direct or indirect connection between trace elements and enzymes participating in proliferation of lymphoid cells [8], thirdly, purposeful uses of trace elements for correction of the immune response [7, 9]. Trace elements have the modification properties concerning structure of lymph nodes, defining degree of cell-mediated and humoral immunity. Influence of trace elements on the immune response has ambiguous character and depends on localization of lymph nodes. Level of content of trace elements leads to structural reorganization in a lymph node.

We consider that sign of effectively operating compartments is their interaction with trace elements during the different periods of life. Forming of lymphoid-microelement association carries the region-dependent character and leads to forming of a certain morphological type of the structure of a lymph node. Trace elements deficiency causes disturbances in the immune system. [1, 4, 7, 8]. Aging is accompanied by disorganization of internal structure of lymph nodes depending on concentration of trace elements. The imbalance of structure and trace elements in a lymph node is the reason of decrease immune and drainage functions of lymph nodes at senile age. Trace elements prevent oxidant-dependent damage of tissue when aging, positively influencing an immunological homeostasis [4, 8]. It is possible to conclude that different concentration of microelements changes structures of a lymph node and forms cellular or humoral type of the immune response.

CONCLUSION

The obtained results show patterns of structural modification of lymph nodes, proceeding from age and features of a microelement profile. Forming of lymphoid-microelement association defines development of lymphoid tissue at young age. The indispensable condition of functioning of lymph nodes is optimum concentration of trace elements. Trace elements enter cofactors of enzymes and possess the regulatory and structural stabilizing function in lymph nodes. Easing and loss of lymphoid-microelement association is a predictor of aging of peripheral lymphoid organs. Destabilization of structure and a microelement pro-

file of lymph nodes deteriorates drainage and immune functions in the lymphatic region. It is supposed that prevention of microelements deficiency will allow to improve the structural organization and to increase function of lymph nodes that will slow down process of aging of lymphoid tissue.

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THE IMPACT OF OSTEOPLASTIC COMPOSITIONS ON REMODELING OF BONE TISSUE IN IMMUNODEFICIENT ANIMALS: EXPERIMENTAL STUDY

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ABSTRACT — Periodontitis often occurs on the background of pathology of various organs and systems, which doubtlessly affect the course and prognosis for inflammatory and destructive processes of the periodontium. The prevalence of periodontal diseases in diabetic patients has been up to 95%. This comorbid pathology is based on universal pathogenetic mechanisms (immunological disorders, metabolic changes, free radical oxidation). The structure of periodontal pathology in patients with diabetes mellitus is dominated by generalized periodontitis of moderate and severe degree, which features the development of deep periodontal pockets, progressing loss of bone tissue and a surgical treatment that would require implantation. Implantation materials based on bioceramics with hydroxyapatite are most commonly employed. Our experimental study assessed remodeling of bone tissue in immunodeficient animals while implanting various osteoplastic compositions.

KEYWORDS — periodontitis, diabetes mellitus, immunodeficiency, osteoplastic materials.

INTRODUCTION

Periodontitis is often accompanied by pathologies of organs and systems, and this, in turn, worsens the course, clinical manifestations, as well as the outcome and prognosis for destructive changes in periodontal tissues [1, 2]. Diabetes mellitus has already assumed a leading role as a comorbidity of periodontal disease, which can be explained by its enormous prevalence (422 million people all over the world suffer from diabetes nowadays), as well as it is known as a cause of disability and a high mortality (number 3 after cardiovascular disease and malignant tumors) [3–9]. Therefore it is not a merely medical issue but also a social one.

Major disturbances of periodontitis associated with diabetes suppress the immune response of the body and affect T cells of the immune system. Diabetes mellitus might be referred as an immune-related disease that combines an autoimmune nature and immune deficiency [10]. The literature suggests that there is an influence of the immune system on bone regeneration [11, 12]. Under inhibition of the immune system, the transition to certain morphological stages of bone regeneration is delayed with a reduction in the number of osteoblasts. The interaction between the immunity and osteogenesis supposes a principal possibility for its regulation with the help of immune stimulators [13].

Aim of the study

to study the processes of bone remodeling in animals with experimental immunodeficiency during implantation of various osteoplastic compositions.

MATERIALS AND METHODS

This study involved 60 nonlinear Wistar rats weighing 200–250 g. Osteoplastic agents containing hydroxyapatite were used as implantation materials (Table 1).

Experimental model reproduction method

General anesthesia with Zoletil-50 (Virbac, S. A., France; dosage — 0.5 mg/kg of body weight) was done prior to a skin incision (1.5 cm) on the rat's inner surface of the thigh. After the joint was exposed, trepanation was performed with hard-alloy spherical burr #9 in the medial part of the femur distal epiphysis to the depth of the burr head. In the experimental series, the trepanation hole was filled with the studied composition of hydroxyapatite-based osteoplastic material, while the wound was sutured layer by layer with PGA. The following method of local tactivin application was used: 0.3 ml of tactivin solution was applied on a strip of osteoplastic material. A strip fragment (about 2×2 mm in size) containing approximately 5 mcg of tactivin was inserted into the bone cavity of the femur distal epiphysis. The immunodeficiency in the experimental animals was modeled through subcutaneous injection of cyclophosphane diluted in saline (dosage

Table 1. Types of experimental invasion

Group	Invasion	Number of rats
1	The experimental model reproduction in intact animals	12
2	Reproduction of an experimental model in immunodeficient animals, with no osteoplastic materials used	12
3	Reproduction of an experimental model in immunodeficient animals and the use of hydroxyapatite-based osteoplastic materials	12
4	Reproduction of an experimental model in immunodeficient animals and using a combined osteoplastic material containing hydroxyapatite and the tactivin immunostimulator (bovine thymus extract)	12
5	Reproduction of an experimental model in immunodeficient animals and using a combined osteoplastic material containing hydroxyapatite and the immunostimulator tactivin with additional subcutaneous administration of tactivin at a dose of 100 mcg per 1 / kg of animal weight	12

— 50 mcg per 1 injection), first one injection for two days in an arrow, and then, to maintain the immunodeficiency status, at an interval of 10 days.

The hip defect was created on the 12th day against the developed immune pathology. The experiment duration was 60 days. The animals were decapitated under anesthesia on the 5th, 15th, 30th, and 60th day after the surgery. These terms reflect the major stages of reparative osteogenesis. The femoral bones were isolated and fixed in a 10% neutral formalin aqueous solution, dehydrated in alcohols, and encased in paraffin following the generally accepted method. 7–8 micron sections were made to be further stained with Ehrlich hematoxylin solution and water-alcohol eosin. The work on the laboratory animals was performed following the Helsinki Declaration (2000) on the humane treatment of animals.

RESULTS AND DISCUSSION

The morphological study outcomes suggest that the suppression of the immune system cells activity has a negative effect on the healing of experimentally reproduced bone defects.

Group 1. 5 days. In the proximal epiphysis, there is a bone defect embracing the cortical plate and spongiosa on $\frac{1}{2}$ of the bone perimeter. 15 days. Intensive development of periosteal bone callus registered, which has a trabecular structure. The periosteal bone callus descends into the defect at the level of the spongiosa, joining the bone regenerate moving from the endosteum. The regenerate has a trabecular structure. 30 days. The bone defect, almost completely to the level of the cortical plate, is a trabecular bone callus. The bone trabeculae in the central areas of the callus feature a broad-mesh structure. Closer to the cortical plate, the mesh structure gets finer. The bone structures are getting dense. 60 days. The periosteal bone reparation makes a uniform spongy mass of bone callus that fills the area of the traumatic destruction (Fig. 1).

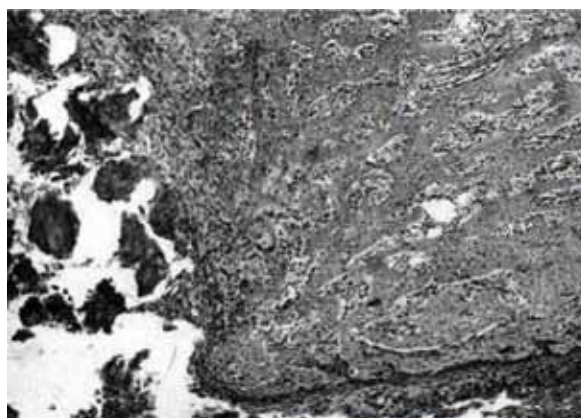


Fig.1. Group 1. 60 days into the experiment. A powerful periosteal callus merges with the distal bone reparation, embracing the bone defect and its contents. Hematoxylin and eosin. x 40.

Group 2. 5 days. The bone defect penetrates through the cortical plate to occupy part of the spongiosa, and partially reach the bone-marrow canal filled with destructured red bone marrow. The defect lumen show unstructured masses, lots of osteocyte-free bone fragments. The granulation tissue development as well as of connective tissue components of the preparation is poor. 15 days. A fall in the red bone marrow cells number, total death of the bone cambial elements. Absence of these cells in the growth zone. 30 days. The red bone marrow is atrophic. The structures of the epiphysis spongiosa are rarefied, while their bone substance reveals degenerative changes with the rarefaction sites. The growth area and the plate are absent. 60 days. Partial recovery of the red bone marrow. The cortical plate defect is filled with bone material. The periosteal bone reparation features poor development (Fig. 2).

Group 3. 5 days. The bone defect is filled with osteoplastic material, where granules from hydroxyapatite crystalline mass and the oxyphilic fibrous remains

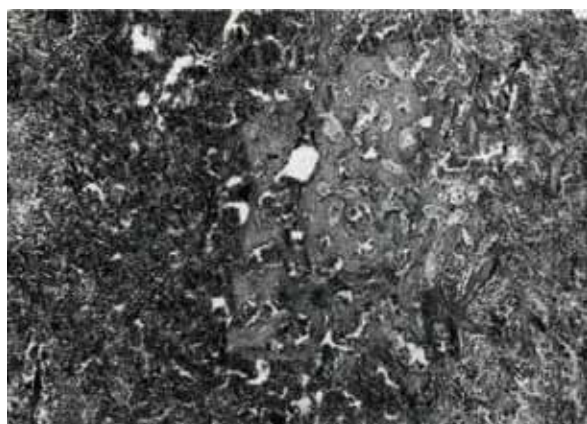


Fig. 2. Group 2. 60 days into the experiment. The endosteal callus (center and right) is build of defective osteoid beams. Bone marrow (left) features significant destruction. Hematoxylin and eosin. $\times 40$

of collagen can be identified. 15 days. The bone defect consists of loose connective tissue. There are rounded bodies of hydroxyapatite granules with a distinct crystal structure to be observed. Fibroblastic elements grow into the tubules that penetrate the granules. 30 days. The growth zone cartilage plate is narrow, while its structural arrangement is disturbed. The transition zone to bone structures is undeveloped. The area of injury still features a cortical plate defect. There is no periosteal bone callus. 60 days. The red bone marrow shows active regeneration process; the area of injury reveals complete closure of the cortical plate defect by the bone callus. The osteoplastic material is sealed into the mature trabecular bone tissue. Complete integration of the mineral with the bone tissue (Fig. 3).

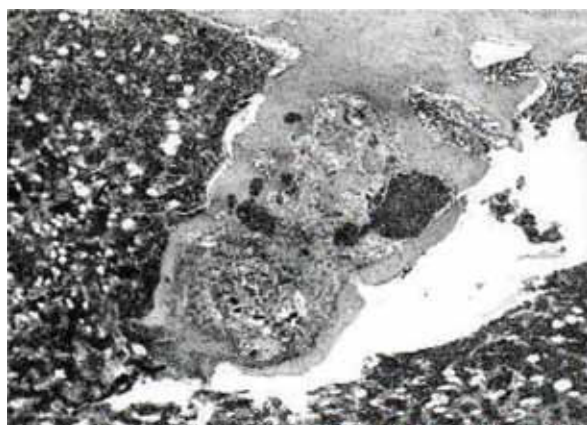


Fig. 3. Group 3. 60 days into the experiment. The area of injury features a bone callus (center) with granules of hydroxyapatite (dark color) sealed in. Hematoxylin and eosin. $\times 40$

Group 4. 5 days. The injury area contains a cortical plate defect, which penetrates the epiphysis thickness. The bone defect edges are smooth, with no osteocytes. 15 days. The red bone marrow is reduced through a significant length. The injury area presents a cortical plate defect with smooth edges. Regeneration can be observed from the endost part only. 30 days. Active regeneration is underway in the red bone marrow. The bone defect is filled with remnants of necrotic detritus of hydroxyapatite, cellular-fibrous and fibrous connective tissue. For a considerable length, the bone defect is replaced with a bone regenerate with a mature structure, which presents powerful bone beams, sometimes developed osteonic systems. 60 days. The red bone marrow is in a state of active functioning. The bone defect is preserved only at a small section of the cortical plate and epiphysis. It is filled with fibrous connective tissue surrounded with compacted bone callus (Fig. 4).

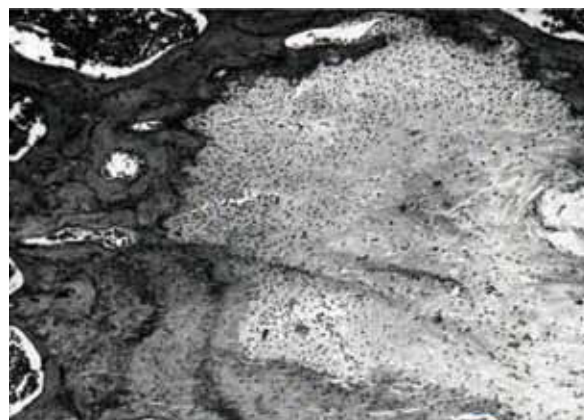


Fig. 4. Group 4. 60 days into the experiment. The bone defect is filled with fibrous connective tissue. Hematoxylin and eosin. $\times 63$

Group 5. 5 days. The area of injury reveals a bone defect at the level of the cortical plate with hydroxyapatite granules. 15 days. The bone defect is filled with regenerate tissue surrounding hydroxyapatite granules. 30 days. A bone defect in the injury area features intensive progress of soft tissue regenerate around the hydroxyapatite granules, the bone regenerate connects to the endostal bone callus, which is actively built along the defect edges. 60 days. Closure of the defect with a bone callus. Hydroxyapatite particles integration with the bone preparation structures is observed in the newly developed bone as well as their gradual replacement with bone matter (Fig. 5).

CONCLUSION

1. The obtained data suggest that remodelling of a condition of immunodeficiency is accompanied by suppression of the immunocompetent cellular elements.

2. Implantation of osteoplastic material with immunocorrecting properties improves the course of reparative osteogenesis.

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LINEAR FEATURES OF PLANUM SPHENOIDALE IN ADULTS AND THEIR COMMON VARIABILITY

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ABSTRACT — The aim of this study is to identify the linear variability of the planum sphenoidale in adults, depending on the skull base type. Stereotometry was used on 87 certified skulls to identify the basilar angle as well as to determine the base type; craniometry was employed to examine the linear planum sphenoidale parameters. The study outcomes revealed that a short and wide planum was typical for the plate-basilar craniotype; long and narrow planum pointed at the flexibasilar type; in case the planum was long and narrow at the anterior margin, and wide at the posterior area, it was attributed to mediobasilar type.

KEYWORDS — planum sphenoidale, sphenoid bone, craniotype, skull.

INTRODUCTION

The study of the morphology of the structure of the craniofacial complex is relevant for improving and developing new methods of diagnostics and surgical interventions on the maxillofacial region [1-5].

Currently, neurosurgery pays great attention to clinical anatomy issues focusing on developing proper surgical access to the brain lower surface and neurovascular formations, based on the variability of skull structures. One of such skull structures is the planum sphenoidale, which is part of the sphenoid upper wall, and which is involved in the development of the middle section of the anterior cranial fossa, located between the ethmoid bone cribriform plate and the sphenoid crest of the sphenoid bone [6, 7].

No clear boundaries have been developed so far, just like no algorithm has been designed for selecting

surgical tactics in terms of getting access to neoplasms localized at the planum sphenoidale of the anterior cranial fossa [8, 9], which is due to lack of detailed metric information concerning the morphostereotopic variability of the planum sphenoidale in people of different age, sex and the skull shape [10, 11]. Respective literature offers scattered descriptions of the morphometric variability of the skull base bones and their structures [12–21], yet there is no systematic data available on the general variability of the planum sphenoidale linear features, which serves rationale for this study.

Aim of study

To identify the variability of the planum sphenoidale linear features in adults, depending on the skull base type

MATERIAL AND METHODS

The study involved 87 certified skulls people of mature age (21–60 years old) obtained from the collection of the fundamental museum at the Department for Human Anatomy, Saratov State Medical University. Stereotopometry was used to identify the basilar angle between the craniometric points (*n-s-ba*) for each skull, with 3 types of the skull base distinguished: flexi-, plate- and mediobasilar. The craniometry method was employed to examine the width of the planum sphenoidale anterior border – at the level of the ethmoid bone cribriform plate posterior edge; the posterior border – in between the midpoints of the visual channels anterior walls; the planum length on both sides of the skull.

The statistical processing of the obtained data was carried out with the Statistica 10.0 software in the Windows. For all the examined parameters, variation & statistics elements were identified – M, m, σ , C ν %, P. The statistically meaningful difference between the average values was calculated through the Student criterion. The differences were considered statistically meaningful at P < 0.05.

RESULTS AND DISCUSSION

For the flexibasilar craniotype, the transverse size of the planum sphenoidale anterior border (10.8±0.2 mm) is 7.8 mm below that of the posterior

edge (18.6 ± 0.3 mm; $P < 0.01$). The planum longitudinal diameter on both sides of the skull has the same average value (15.6 ± 0.4 mm; $P > 0.05$).

In case of the mediobasilar craniotype, the transverse size of the planum sphenoidale anterior edge (11.0 ± 0.2 mm) is 8.6 mm smaller than that of the posterior border (19.6 ± 0.3 mm; $P < 0.01$). The average value of the planum longitudinal size on both sides of the skull revealed no statistical difference — $14.8\text{--}15.0 \pm 0.4$ mm ($P > 0.05$).

For the plate-basilar craniotype, the planum sphenoidale anterior edge transverse size (12.0 ± 0.4 mm) is by 7.8 mm exceeded by the posterior edge (19.8 ± 0.4 mm; $P < 0.01$). The longitudinal diameter of the planum sphenoidale on both sides of the skull showed no significant difference ($13.8\text{--}13.9 \pm 0.4$ mm; $P > 0.05$).

A comparative analysis of the planum linear parameters among the craniotypes showed that the transverse diameter of the planum sphenoidale anterior edge for the plate-basilar craniotype (12.0 ± 0.4 mm) exceeded by 1.0 mm the medio- (11.0 ± 0.2 mm; $P < 0.05$) and by 1.2 mm — the flexibasilar (10.8 ± 0.2 mm; $P < 0.05$) types. The planum posterior edge transverse size for the plate- and medio-basilar craniotypes (19.8 ± 0.4 mm and 19.6 ± 0.3 mm, respectively) turned to exceed by 1.2 mm and 1.0 mm, respectively, if compared with the flexibasilar type ($P < 0.05$).

The planum longitudinal size on both sides of the skull in the flexi- (15.6 ± 0.4 mm) and mediobasilar (15.0 ± 0.3 mm; 14.8 ± 0.4 mm) craniotypes showed a statistically significant prevalence (by 1.8–1.9 mm; 1.2–1.1 mm) compared with the similar parameters for the plate-basilar type (13.8 ± 0.3 mm; 13.7 ± 0.4 mm; $P < 0.05$, respectively).

The literature offers conflicting data on the effect that the type of the skull base has on the dimension-related features of the planum sphenoidale. Our study revealed the general variability of the planum sphenoidale linear features — in the plate-basilar skull type, the planum anterior and posterior edges are 1.1 times as wide compared to the medio- and flexibasilar types, while the planum is 1.1 times as long in case of the medio- and flexibasilar types compared to plate-basilar one. The planum posterior edge is wider than its anterior edge in each craniotype, whereas the average values of these parameters are dominant in the plate-basilar craniotype. However, there is no reliable way to compare the planum parameters variability, since the available literature contains no works focusing on the dimensional specifics of the planum sphenoidale and its variability that would allow detecting clear clinical diagnostic criteria for identifying the boundaries of

the radical removal of tumors found in the anterior and mid-cranial fossae [8, 9, 22, 23]. The respective literature offers only isolated data concerning lack of influence that the basilar angle has on the planum parameters variability; however, the authors hereto believe that the planum dimensional features should be taken into account when employing the transbasal approach to the resection area of the anterior cranial fossa middle section [24].

CONCLUSIONS

A short and wide planum sphenoidale is typical for the plate-basilar craniotype; long and narrow — for the flexibasilar type, while a planum that is long and narrow at the anterior edge, and wide at the posterior one typically belongs to the mediobasilar type. The obtained data can be used for morphological methods of clinical research, as well as it may be taken into account when planning surgical access to the neurovascular structures and the brain structures adjacent to the skull base bones.

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INFLUENCE OF A NEW PYRIMIDINE DERIVATIVE PIR-9 ON THE ACTIVITY OF VON WILLEBRAND FACTOR IN FOCAL CEREBRAL ISCHEMIA IN RATS

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ABSTRACT — A study was conducted to assess the effect of a new pyrimidine derivative PIR-9 (50 mg/kg) on the activity of von Willebrand factor in the conditions of focal brain ischemia in rats. It was confirmed that the studied compound PIR-9 contributes to a decrease in the activity of von Willebrand factor by 14,1% ($p < 0,05$) compared to the group of negative control rats. PIR-9 exceeds the comparison drug Cavinton by 10,9% in strength of effect ($p < 0,05$) comparable to sulodexide.

KEYWORDS — brain ischemia, cerebral ischemia, pyrimidine derivatives, von Willebrand factor, endothelial dysfunction.

INTRODUCTION

Disorders of cerebral hemodynamics currently remain one of the leading causes of death and disability in the working population [1], while vascular endothelium plays an important role in their development [2]. Von Willebrand factor (VWF) is a specific marker of endothelial dysfunction, an increase in the activity of which in combination with an increase in the aggregation ability of platelets indicates a violation of the functioning of the vascular endothelium [3]. Thus, agents that restore pathologically increased activity of von Willebrand factor in the post-ischemic period can be considered as potential cerebroprotectors. Previous studies indicate the presence of cerebrotropic properties in pyrimidine derivatives [4], which makes it interesting to study the effect of these compounds on VWF activity in conditions of acute cerebral circulation disorders.

Objective

To study the effect of a new pyrimidine derivative PIR-9 on the activity of von Willebrand factor in the conditions of 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 50 male Wistar rats ($m = 200\text{--}220$ g), divided into 5 groups ($n=10$). Rats were kept on a standard vivarium diet, with a natural succession of light and darkness. The first group — falsely operated animals (FO), the second — negative control group (NC), the third and fourth — rats who were administered the comparison drug Cavinton (3,2 mg/kg) and Sulodexide (30 URL/kg (units the release of lipoprotein lipase)), respectively [6, 7]. The fifth group of animals received the studied compound 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]. The studied objects were introduced immediately after the operation and then for 3 days. The activity of the von Willebrand factor (VWF) was determined by agglutination method using a set of reagents of the NGO "RENAM". 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

As can be seen from figure 1, the concentration of VWF in the group of animals with the simulated pathology that were not subjected to therapy was $133,5 \pm 2,3\%$, which was 37,87% ($p < 0,05$) significantly higher than that of false-operated rats ($96,83 \pm 2,46\%$). The introduction of Cavinton did not significantly

reduce the level of Willebrand factor relative to untreated rats, while another comparison drug — Sulodexide led to a decrease in the studied indicator by 19,9% ($p < 0,05$) (at the same time, significantly higher than the FO value of the rat group). It is worth noting that the level of VWF against the background of the introduction of the comparison drug sulodexide was also significantly lower than this value in the Cavinton group of rats by 16,9% ($p < 0,05$). Against the background of PIR-9 therapy, a decrease in VWF was also observed, so this indicator was $114,7 \pm 2,8\%$, which in turn differed by 14,1% ($p < 0,05$) from the identical value of the group of rats that did not receive pharmacological support and by 11% ($p < 0,05$) in comparison with the group of rats that were administered Cavinton. There were no statistically significant differences between the groups receiving the experimental substance PIR-9 and the comparison drug Sulodexide.

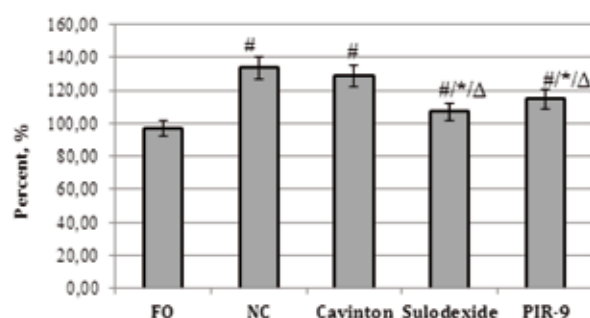


Fig. 1. Assessment of the effect of PIR-9 compound and reference drugs on the activity of von Willebrand factor under conditions of focal cerebral ischemia in rats

Note: FO — a group of false-operated rats; NC group of rats negative control; NC — negative control rats; Cavinton — a group rats treated with Cavinton; Sulodexide — a group rats treated with Sulodexide; 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

The introduction of a new pyrimidine derivative under the code PIR-9 (50 mg/kg) significantly reduced the pathologically overestimated activity of von Willebrand factor by 14,1% ($p < 0,05$) relative to the group of negative control rats and by 10,9% ($p < 0,05$) in comparison with animals receiving Cavinton, which may indicate a decrease in platelet adhesion against the background of receiving this compound by rats. By the strength of its effect, the PIR-9 compound surpassed the comparison drug Cavinton (3,2 mg/kg) and was comparable to sulodexide (30 URL/kg), this fact is an important link in the correction of endothelial

dysfunction resulting from acute cerebral circulation disorders. Thus, the pyrimidine derivative under the code PIR-9 is a promising object for further study and correction of ischemic brain injuries.

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REGENERATION EFFECT OF AN AQUEOUS EXTRACT OF CYMBOPOGON PROXIMUS ON INFECTED WOUNDS IN A RODENT MODEL OF STEROID HYPERGLYCEMIA

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ABSTRACT — We analyzed the processes of regeneration of an infected skin wound with *Streptococcus epidermidis* (*Streptococcus*) in 30 laboratory rats where a model of hyperglycemia was created by administration of dexamethasone. Further, these animals were divided into 3 equal groups: in the 1st group the wound was treated with an ointment containing *Cymbopogon proximus*; in the 2nd group an ointment containing sodium fusidate 2% was applied to the wound; in the 3rd group (control) — Vaseline was applied. The use of *Cymbopogon proximus* leads to an increase in the total number of white blood cells, an increase in the activity of lymphocytes (+383%) ($p = 0.03$), which leads to improved regeneration of the infected wound. Also, we noticed that the glucose level was restored to the initial values, in 5 days of oral intake of an aqueous extract of *Cymbopogon proximus*, in contrast to the other groups ($p = 0.001$). We found that the regeneration activity of an infected wound in rats with steroid hyperglycemia does not significantly differ in case of antimicrobial ointment and *Cymbopogon proximus* treatment.

KEYWORDS — Diabetic foot, infected wound, medicinal plants research, *Cymbopogon proximus*, regeneration, steroid hyperglycemia.

INTRODUCTION

There are many diseases that are accompanied by chronic pain syndrome [1, 2]. Corticosteroids are often used to relieve persistent pain [3]. Long-lasting use of corticosteroids is the main cause of hyperglycemia [4]. This makes some trouble, as the number of patients suffering from diabetes continues to increase. Chronic hyperglycemia in diabetes leads to the development of severe complications, such as atherosclerosis, heart and kidney failure, neuropathy, and immunodeficiency [5, 6, 7]. The most serious complication of diabetes is the development of a diabetic foot [8]. The dynamics of the frequency of detection of new cases of diabetic foot in adult patients in the Russian

Federation tends to increase annually [8]. It is known that diabetic foot often forms trophic ulcers, which are 50% infected [9]. Therefore, it is important to search for safe drugs with both hypoglycemic, antimicrobial and anti-inflammatory effects [5, 10].

Aim

To explore the regeneration processes of infected skin wounds in rats on the background of steroid hyperglycemia using *Cymbopogon proximus* (lemongrass) growing in Sudan.

METHODS

This was an experimental research that we carried out on 30 white rats weighing 200–250 g, which were obtained in the animal nursery laboratory *Andreevka* (Moscow region). All manipulations with animals were performed in accordance with the guidelines for the maintenance and use of laboratory animals [11]. First, we created a model of hyperglycemia in animals by intramuscular administration of dexamethasone 4% — 0.2 ml for 4 days. This rhythm of dexamethasone injections leads to the development of hyperglycemia, the glucose level in animals increases 6 times — from 5.08 ± 1.18 to 30.025 ± 16 mmol/l ($p < 0.001$). Next, we created a model of an infected skin wound in rats. To do this, we made an incision of 2.0 x 0.5 cm on the skin of the animal in sterile conditions, under local anesthesia. Then, we performed a double transfer of the exudate infused with *Streptococcus epidermidis* (which we took from a patient suffering from streptoderma) to the wound area. The next step was to divide all experimental animals in a randomized manner into 3 groups:

— Group 1 — treatment of wounds with an ointment based on vaseline and powder from plant *Cymbopogon proximus* in 1:2 dilution. In addition, these rats received daily 2 ml of water extract of *Cymbopogon proximus* orally for 5 days ($n = 10$).

— Group 2 — treatment with an ointment containing sodium fusidate 2% for 5 days ($n = 10$).

— Group 3 (control) — treatment of the wound with vaseline for 5 days ($n = 10$).

After 5 days of therapy, we visually assessed the wound condition on a five-point scale, where 5 points

were the maximum signs of wound inflammation, and 0 points were the absence of signs of inflammation. We also studied changes in the peripheral blood of animals on the hematological analyzer PCE-90Vet (USA). Statistical processing of the material was carried out using the program "STATISTICA 7.0". The reliability of differences between quantitative indicators was assessed using the Mann–Whitney test. The differences were considered significant at $p < 0.05$.

RESULTS

After stopping the administration of dexamethasone and before the end of the experiment, the glucose values in the second and third groups of the study were within the range of 10.4 ± 2.85 mmol/l. in animals of the first group, when using an aqueous extract of *Cymbopogon proximus*, the glucose level decreased to 5.4 ± 0.79 mmol/l ($p = 0.001$). Table 1 shows the analysis of infected wound regeneration in all groups of rats. We did not get significant differences between the effectiveness of antimicrobial ointment based on sodium fusidate 2% and *Cymbopogon proximus* ($p > 0.05$). At the same time, we observed marked wound regeneration on the background of *Cymbopogon proximus* compared to the control group ($p < 0.05$).

Accelerated regeneration of a wound, infected with *Streptococcus epidermidis*, when treated with *Cymbopogon proximus* extract, is associated with the effect of this herb on the cells of the immune system (Table 2).

The drug form based on *Cymbopogon proximus* prevents the development of leukopenia, leads to the growth of lymphocytes (+383%), which has a positive effect on the rate of wound regeneration. However, we recorded a decrease in the level of neutrophils in the first group of rats compared to other groups of animals. Perhaps this fact was associated with a faster exudation phase, which is characterized by the migration of neutrophils from the vascular lumen to the tissues for bacterial phagocytosis.

DISCUSSION

Currently, an active research is underway for effective and safe drugs that stimulate wound regeneration. Widely known are herbal preparations based on *Aloe vera*, *Calendula officinalis*, *Hypericum perforatum*, etc., which have antimicrobial, antiviral, anti-inflammatory, immunomodulatory properties due to the inhibition of cytokines and macrophages [10]. Selim SA. evaluated the antimicrobial and antioxidant properties of *Cymbopogon proximus* (oil and methanol extract) in vitro [12]. The results of the antimicrobial test showed that the methanol extract of *Cymbopogon proximus* has moderate antibacterial activity,

and the oil extract strongly suppresses the growth of the test bacteria, with the exception of yeast [12]. Our research shows that *cymbopogon proximus* extract has a positive effect on most components of the wound process: it reduces the severity of hyperemia, swelling, compaction, soreness and increases the intensity of regeneration. We did not find a significant difference in the rate of wound regeneration when treating with an ointment based on *cymbopogon proximus* extract and an ointment containing sodium fusidate ($p > 0.05$).

CONCLUSIONS

Therapy with an aqueous extract of *Cymbopogon proximus* has a reliable hypoglycemic effect, which allows using this herb for both prevention and correction of hyperglycemia. The effect of *Cymbopogon proximus* on the regeneration of an infected wound in conditions of hyperglycemia caused by dexamethasone did not differ from the effectiveness of antimicrobial ointment.

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Table 1. Regeneration indicators of an infected wound in white rats with steroid hyperglycemia during the treatment with various groups of drugs

The wound state	1 st group(therapy Cymbopogon proximus)	2 nd group (therapy sodium fusidate 2%)	3 rd group (control)
Hyperemia	+++	++	+++++
Edema	+	+	+++++
Painfulness	+	++	++++
Consolidation of the wound edges	+	++	++++
Regeneration activity	+++++	++++	+

Table 2. The level of immune blood cells in rats with an infected skin wound on the background of steroid hyperglycemia in the treatment of various groups of drugs

Blood Patient Groups	Indicators	Leukocytes (*10 ⁹ /n)	Neutrophils (%)	Lymphocytes (%)
1 st group (therapy Cymbopogon proximus)		2,9±0,2	16,46±5,82	87,05±2,8
2 nd group (therapy Sodium fusidate 2%)		0,92±0,15	39,07±6,66	31,25±12,25
3 rd group (Control)		2,42±0,26	24,43±8,06	74,65±11,19
p		< 0,05	< 0,05	= 0,03

* comparing the first group of animals with the second and third

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HISTOMORPHOLOGICAL CHANGES IN THE LUNGS IN ACUTE BACLOFEN POISONING

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ABSTRACT — *Baclofen is a myorelaxant, a derivative of gamma-aminobutyric acid. Due to its psychotropic effect the drug is often subject to abuse especially in young people. The article deals with histomorphological changes in the lungs in Baclofen poisoning.*

KEYWORDS — Baclofen, poisoning, lungs,
histomorphological changes.

INTRODUCTION

Baclofen is a beta-p-chlorophenyl derivative of one of the inhibitory neurotransmitters — gamma-aminobutyric acid [1, 2]. It is believed to work by agonizing GABA receptors (specifically the GABAB receptors) [3].

This drug is administrated orally or intrathecally (by delivery into the spinal canal) [3]. Oral Baclofen is indicated to patients with multiple sclerosis, muscular spasticity, some spinal cord diseases, such as tumors, infectious diseases, injuries, acute disorders of cerebral circulation, meningitis [4]. A number of studies have shown that Baclofen is effective in the treatment of alcohol addicts [5–10] and patients with cerebral palsy [11]. Adverse effects of Baclofen may include headache, drowsiness, dizziness, weakness, fatigue, nausea and vomiting, urinary retention, constipation [3].

This drug has a pronounced psychoactive effect and can be a subject to abuse in drug addicts, especially in young people [12]. Acute Baclofen poisoning, which is associated with high risk of death, can be resulted from an accidental overdose, criminal actions, or suicidal behavior. The pathogenesis of acute

Baclofen poisoning and thanatogenesis in such cases remains unclear.

One of the target organs in Baclofen poisoning is the lung. At the same time, the data on morphological changes in such poisoning is limited.

The objective of the study

was to assess histomorphological changes in the lungs in acute Baclofen poisoning 3 hours after its administration.

MATERIAL AND METHODS

Experimental studies were performed on 10 Wistar rats divided into 2 groups. The group of controls included 5 intact animals, experimental group was treated with Baclofen at a dosage of 85 mg/kg.

Keeping animals and working with them were carried out in accordance with the European Convention for the protection of vertebrates used for experiments or other scientific purposes (Strasbourg, 18.03.1986).

The lungs were fixed in 10% neutral formalin and immersed into paraffin. Histological sections were processed according to the standard method and stained with hematoxylin and eosin. The histological sections were examined by light microscopy using Nikon Eclipse E-400 microscope with a video system based on the Watec 221S camera (Japan) at 400× magnification.

The following signs were assessed: emphysema, atelectasis and dystelectasis, thickening of the interalveolar septi, WBC infiltration of the interalveolar septi, capillary and venous plethora, sludge, hemorrhages in the interalveolar septi and alveoli, the presence of secretion in the lumen of the bronchi.

In order to confirm the reliability of the appearance of a particular histological sign, we used the Fischer ratio. The presence of a histological sign was considered to be reliable if it did not appear in any cases in one group and appeared in 4 or 5 cases in the other.

RESULTS AND DISCUSSION

There were no pathological changes in the lungs of the controls. The alveoli were intact, airy. Small areas of subpleural dystelectasis were observed. There

were no signs of emphysema. There were no circulatory disorders (venous, capillary plethora, hemorrhages in the interalveolar septi and alveoli) either. The lumen of the bronchi was free.

In the lungs of animals treated with Baclofen at a dose of 85 mg/kg, plethora of venules and capillaries was observed. Sludge was observed in the pulmonary arteries. There was an expansion of the alveoli and pronounced emphysema (which was mainly subpleural). The interalveolar septi were thinned in the emphysema zone. There were subpleural atelectasis and dystelectasis. There were some areas of interalveolar septi thickening (due to edema). WBC infiltration of interalveolar septi was also detected. Macrophages were observed in the lumen of some alveoli.

The presence of plethora of venules and capillaries, sludge, emphysema, atelectasis and dystelectasis, and cellular reaction (WBC infiltration of the interalveolar partitions) can be considered reliable in this group.

According to literature, Baclofen does not have a direct toxic effect on the bronchi and lungs. However, it increases the presynaptic blockade of nerve impulses that are generated in the spinal cord. This leads to suppression of their transmission. As a result, muscular tone increases. Their excessive relaxation may lead to difficulty breathing and the development of hypoxia. The effects of GABA receptors stimulation on smooth muscles of the bronchi and on the lungs are also very important. GABAA receptor agonists are known to cause contraction of smooth muscles of the bronchi, bronchioles, which is accompanied by spasm and breathing difficulties [13, 14]. Although Baclofen is a selective agonist of GABAB receptors, in high doses it causes GABAA receptor stimulation as well. We observed this effect in the study group. Emphysema was observed in the lungs of the animals.

Under hypoxia vascular-tissue permeability increases. It was also shown that vascular-tissue permeability increased when GABA receptors were stimulated [15], which is also confirmed by the results of our experiments. Thickening of interalveolar partitions due to edema was observed in the experimental groups.

CONCLUSION

As a result of the study we identified a complex of pathological changes in the lungs of experimental animals in the early period after Baclofen administration, which included circulatory disorders in all the elements of the microcirculatory bed (plethora of capillaries, venules), emphysema, atelectasis and dystelectasis, WBC infiltration of intraalveolar septi and thickening of intraalveolar septi due to edema. In order to quantify the severity of histomorphological changes in the lungs a morphometric study is required.

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DEVELOPMENT OF CENTRAL DIABETES INSIPIDUS IN A FEMALE PATIENT AFTER SURGICAL TREATMENT OF PITUITARY ADENOMA

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ABSTRACT — The purpose of the article is to provide some insight into the current medical literature and relevant works on the issue of diabetes insipidus and clinically analyze the medical record of a female patient of the Endocrinology Department of Tver Regional Clinical Hospital who was operated for prolactin-secreting pituitary macroadenoma, with diabetes insipidus developed in the postoperative period.

There was a clear cause-effect relationship between the previous neurosurgical intervention in the hypothalamic-pituitary area and a developed clinical picture of diabetes insipidus. The diagnosis of diabetes insipidus was confirmed by laboratory and instrumental studies. Treatment with desmopressin has proved to be effective. The variety of causes and possible severe complications of diabetes insipidus require its accurate differential diagnosis in order to distinguish between its various forms and other causes of polyuria in the postoperative period, while ensuring the administration of a pathogenetically targeted and safe treatment. We assume that analyzing this clinical case will improve the awareness of doctors about this disorder for its identification and timely treatment.

KEYWORDS — diabetes insipidus, antidiuretic hormone, polyuria, polydipsia, transnasal adenomectomy.

INTRODUCTION

Diabetes insipidus (DI) is a group of diseases that are based on a defect in the synthesis, secretion or action of the antidiuretic hormone (ADH), which leads to the failure of the kidneys to reabsorb water and concentrate urine, and is manifested by excessive thirst and excretion of a large amount of diluted urine [1].

According to its etiology, DI is classified into central, nephrogenic, dipsogenic, and gestagenic [2]. Central diabetes insipidus (CDI) is the most common form, detected with a frequency of 1:25,000. Its prevalence varies from 0.004% to 0.01%. The disease can be detected at any age, but most often develops between 20 and 40 years [2, 3]. According to some researchers, the disease can be equally common in both men and

women, whereas others argue that women predominate with the ratio of 2.2:1 [3].

There has recently been a trend towards an increase in CDI due to a growing number of brain surgeries [1]. Acute CDI occurs in 13–30% of patients in the postoperative period after transsphenoid surgeries [2, 3]. For the manifestation of CDI, the secretory capacity of the neurohypophysis has to reduce by 85% [3, 4].

There are various options for the course of postoperative CDI such as a transient form, when acutely manifesting DI resolves on its own within 3–5 days [4], a permanent form associated with an acute onset, but does not go away within six months [5], a form with three-phase development, which occurs only in 3–5% of patients and can lead to either persistent permanent polyuria or recovery if there is a sufficient number of functioning neurons to adequately respond to changes in blood osmolality [2, 4, 5].

Prognostic factors for the development of CDI after removal of large formations in the hypothalamic-pituitary area include the size and nature of its growth, type of surgical access, age and gender of the patient [6]. The risk of permanent CDI is higher in young adults, men with a large weight of intracellular tumor, with intraoperative cerebrospinal fluid leaks, in individuals with preoperative DI, with repeated surgeries on the hypothalamic-pituitary area, as well as with a large resection of the contents of the Turkish saddle or with damage to suprasellar structures during surgery [4, 5, 7].

If the decrease in the total water content in the body with DI develops faster than the adaptive mechanisms of the brain can react, it gets dehydrated, shrinks, separates from the dura mater with vascular rupture and intracranial hemorrhages, increased intracranial pressure with compression injuries of the brain stem [10].

In the postoperative period, polyuria may be associated with hyperglycemia and glucosuria, with normal excretion of fluids administered in the perioperative period [11]. Given the variety of causes that lead to DI or just to polyuria in the postoperative period, it is important to clarify the etiology of the disease and correctly conduct a differential diagnosis, which allows administering pathogenetically correct and safe treatment.

Aim

to present a clinical analysis of a patient in the Endocrinology Department of Tver Regional Clinical Hospital with postoperative CDI.

Case Description

A 59-year-old female patient S. who lives in Tver was admitted to the Endocrinology Department of Tver Regional Clinical Hospital on July 4th, 2019 with complaints of severe dry mouth, thirst, especially at night, weakness, drowsiness, frequent urination up to 5–6 times during the night; increased blood pressure (BP) to 180/110 mm Hg accompanied by tremor, frequent urination.

According to the patient's history, from the age of 20, she had complained of heart palpitations, clubbed fingers, narrowed field of vision, *flies before the eyes*. In July of that year, she had a brain CT which revealed a 15×17×22 mm formation in the cavity of the Turkish saddle (pituitary adenoma with intra-suprasellar growth). The patient was referred to a neurosurgeon who administered more tests which revealed an increased blood prolactin level of 51.17 ng/ml (normally 4.79–29.9), while the levels of insulin-like growth factor 1, somatotrophic and adenocorticotrophic hormones were within the normal ranges. During the ophthalmological examination, angiopathy of the retina of both eyes was diagnosed. In the same month, the patient was hospitalized to the Endocrinology Department for further examination, more detailed assessment and treatment planning. Taking into account the presence of prolactin-secreting pituitary macroadenoma, absence of clinically significant changes in perimetry data, and high risk of surgical treatment, conservative treatment was administered.

The patient was re-admitted to the hospital in July 2017 with the diagnosis of hyperprolactinemia, prolactin-secreting pituitary macroadenoma with intra- and suprasellar growth. The new brain CT scan showed pituitary adenoma of the previous size (15×19×17 mm), and chiasmal compression was detected. Ophthalmological examination revealed edema of the optic disc in both eyes. The patient refused the proposed surgical treatment of adenoma. She was observed by an endocrinologist on an outpatient basis. The woman received treatment with cabergoline (an agonist of dopamine receptors with a prolonged action) – 0.25 mg 2 times a week.

The disease progressed and a transnasal transphenoid adenomectomy was performed in May 2019. In the early postoperative period, there was an improvement in vision, an increase in the volume of vision fields, but there was frequent urination and an episode of polyuria; and increased oral dryness was observed.

Those symptoms were regarded as the development of diabetes insipidus. The patient was administered 60 micrograms of desmopressin daily, but refused to take the drug. The above-mentioned symptoms of the disease worsened, and the patient was readmitted to the Endocrinology Department in order to clarify and confirm the diagnosis of postoperative hypopituitarism and select therapy.

On admission, the patient's condition was estimated as satisfactory. Normal constitution, height — 165 cm, weight — 144 kg. BMI — 52.9 kg/m² corresponding to Grade 3 obesity. Skin of normal color, normal moisture, dry on the elbows. Narrow whitish striae on the skin of the abdomen. Visible mucous membranes — pink. Thyroid enlargement (Degree 1), dense, heterogeneous, painless. Parathyroid glands — not palpable. Symptoms of thyrotoxicosis and tetany — negative. On lung auscultation: breath sounds — harsh, no rales revealed. Pulse — 76 BPM, rhythmic. BP — 135/90 mm Hg. Heart tones — muted, rhythmic, accent of tone II on the aorta. Tongue — moist with a white coating. Abdomen — soft and painless. Liver, spleen, and kidneys — not palpable. Costovertebral angle tenderness test — negative on both sides. Pulsation of the dorsal arteries of the foot — weakened on the right side. Skin of the feet — dry, peeling. Swelling of the shins and feet. Regular stools, smooth and soft. Diuresis — approximately 5.0 liters.

Blood biochemistry revealed hypercholesterolemia, hypertriglyceridemia (total cholesterol — 6.98 mmol/L, triglycerides — 3.90 mmol/L); bilirubin, transaminases, thymol turbidity test, total blood protein were within the normal ranges, urea — 5.0 mmol/L, creatinine — 90.6 mmol/L, GFR CKD-EPI — 60 ml/min/1.73 m², potassium — 4.4 mmol/L, calcium — 2.5 mmol/L, sodium — 123 mmol/L. Fasting and postprandial blood glucose levels did not exceed the normal ranges. Prolactin, somatotrophic, thyroid-stimulating and free T4 levels and the diurnal rhythm of cortisol secretion were normal.

The patient's urinalysis showed low specific gravity, urinary sediment without pathology, and no glucose. To assess the kidney concentration capacity, the Zimnitsky urine test (renal osmoregulation function study) was done. According to its findings, the total diuresis was 6,500 ml, which was regarded as polyuria. Day diuresis was equal to night diuresis and amounted to 3,250 ml, there was nocturia. Fluctuations in specific gravity were from 1,003 g/L to 1,004 g/L, which was regarded as decreased kidney concentration capacity of hypostenuria type.

The complete blood count revealed an increased ESR to 55 mm/h, it later decreased to 20 mm/h.

Based on the data obtained, the patient was diagnosed with central diabetes insipidus, the state after transnasal transsphenoidal adenomectomy on prolactinomas of the pituitary gland.

In accordance with the diagnosis, desmopressin was administered: 0.1 mg at 8 a.m. and 0.2 mg at 10 p.m. The treatment resulted in a positive dynamics in the patient's condition: the frequency and volume of urination decreased, and during the night the frequency of urination decreased to 1–2 times.

Upon discharge, a repeated renal osmoregulation function study (Zimnitsky test) was performed. The total diuresis was 1,980 ml, the day diuresis was 810 ml, and the night diuresis was 1,170 ml. Fluctuations in the urine specific gravity ranged from 1,006 to 1,014. Consequently, the treatment was effective, polyuria was stopped, and the concentration capacity of the kidneys improved.

The patient was discharged with recommendations to continue the treatment started on an outpatient basis. Since our patient is still at a high risk of remission of postoperative CDI, which usually occurs 3–6 months after surgery, it is recommended to instruct the patient about the symptoms of water intoxication and measures for its prevention and treatment.

DISCUSSION

In this clinical case, there is a clear cause-effect relationship between the previous neurosurgical intervention in the hypothalamic-pituitary area for prolactin-secreting pituitary macroadenoma, when the manifestations of diabetes insipidus developed immediately after the operation (dry mouth, polyuria), and the effectiveness of administered therapy with a synthetic analog of vasopressin. These facts combined with laboratory and instrumental findings confirm the central type of diabetes insipidus.

It can be assumed that the analysis of this clinical case will improve the awareness of doctors about this pathology and will allow them to recognize and start treatment of CDI in a timely manner.

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VEGETATIVE SYMPTOMS AND ARTERIAL STIFFNESS IN PATIENTS WITH HYPERTENSION-ASSOCIATED CEREBROVASCULAR DYSFUNCTION DEPENDING ON PLASMA TOTAL CHOLESTEROL

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ABSTRACT — 129 general practice patients with stages II and III arterial hypertension (AH) were enrolled in a study aimed to assess the severity of cerebral disorders, rigidity of the vascular wall and the manifestation of vegetative symptoms. It was found that in AH patients with hypercholesterolemia, the manifestations of cerebrovascular dysfunction intensified. There were significant changes in the elastic properties of the vascular wall accompanied by vegetative symptoms, which should be taken into account when designing an individual treatment plan.

KEYWORDS — arterial hypertension, vascular wall stiffness, cerebrovascular disorders, vegetative symptoms.

INTRODUCTION

A special in its importance place among cerebrovascular diseases is occupied by chronic cerebral ischemia, developing as a result of slowly progressive cerebral circulation insufficiency most often against the background of atherosclerosis, arterial hypertension or their combinations [1–5]. The importance of solving problems of early diagnosis, prevention and therapy of chronic cerebral ischemia is due to the high prevalence of the disease among the population, and its importance as a risk factor for stroke [6]. Not only neurological, cognitive, but also vegetative disorders are present in the clinical picture of chronic cerebral ischemia. A close relationship between cerebrovascular pathology and functioning of vegetative nervous system is known [7, 8]. At the same time, the peculiarities of vegetative regulation of cardiac rhythm and its relationship with cerebral hemodynamics in patients with chronic cerebral ischemia with hypercholesterolemia are not sufficiently studied.

MATERIALS AND METHODS

129 patients (men — 34, women — 95; mean age 55, 2 ± 11.3 years) of stage II and III AH, which were on dispensary observation with a general practitioner and received combined hypotensive therapy. In accordance with the GFCF National Clinical Recommendations for the diagnosis and correction of lipid metabolism disorders (2017), patients were divided into 2 groups depending on the level of total cholesterol in blood plasma: the 1st (control) group comprised 68 patients with optimal (< 5.0 ; 4.3 ± 0.5 mmol/l) level; 2–61 patients with increased (≥ 5.0 ; 6.1 ± 0.9 mmol/l) blood plasma total cholesterol level.

The criteria of exclusion were: symptomatic AH, signs of heart failure, endocrine, infectious, mental diseases. At the time of the study, all subjects received routine hypotensive therapy (calcium channel blockers, angiotensin-converting enzyme inhibitors) according to the severity of the disease.

All patients were subjected to a clinical examination, and the neurological status of the patients was assessed. An A.M. Vane questionnaire was used to detect vegetative dystonia syndrome (SVD), which was filled in by patients. In the mathematical processing of the results of the questionnaire, the total sum of points obtained from the evaluation of the questionnaire should not exceed 15 points in healthy people, whereas in case of excess it is possible to talk about the presence of SVD.

The vegetative tone was evaluated by the Kerdo index (IR) as follows: $IR = (1 - ADD/HR) \cdot 100\%$, where ADD is diastolic AD blood in mm Hg. HR — frequency of total reductions per 1 minute. At full vegetative weight (eitonía), the Kerdo index is zero; If the coefficient was negative, the sympathetic tone dominated; parasympathetic tone is increased in case of high coefficient.

The rigidity of the vascular wall was studied by photoplethysmographic method using the apparatus *Angioskan-01 Professional* (Russia) in the morning hours in a quiet and darkened room, strictly fasting; before the procedure, patients did not smoke or consume tea, coffee. The following indicators were

calculated on the basis of the planimetric analysis of a pulse wave: the index of rigidity (SI, m/s), the index of augmentation (Alp 75, %) normalized for pulse rate (beats/min ChP=75), the index of reflection (RI, %). For assessment of endothelial dysfunction carried out test with jet hyperaemia with definition of the index of occlusion on amplitude (IOA, conv. units) and shift of phases (SF, ms) between channels [1]. The obtained data were accumulated in Table Excel 2003, and statistical processing was carried out using the statistical package Statistica 10. The normality of the sample distribution was determined by the Kolmogorsk-Smirnov criterion. The arithmetic mean of the standard deviation ($M \pm SD$) was calculated in the data processing for quantitative characteristics. The difference between the fractions was estimated using the χ^2 criterion in the 2×2 conjugation tables, Fisher's exact criterion. Comparison of the two groups on quantitative scales was based on the non-parametric Mann-Whitney. Correlation analysis was performed using the Pearson linear correlation coefficient to determine the dependencies between the parameters studied. The level of statistical significance was recorded at 0.05.

RESULTS

in patients of the 1st group, the level of blood pressure was $134,2 \pm 13,6 / 83,5 \pm 10,6$ mm Hg.st.; the level of total plasma cholesterol is $4,3 \pm 0,5$ mmol/l. The initial manifestations of cerebrovascular insufficiency were recorded in 22 (32,4%), chronic cerebral ischemia I and II stages — in 46 (67,6%). When assessing the clinical signs of cerebral disorders, dizziness was detected in 43 (63,2%), headache in 54 (79,4%), noise and tinnitus in 35 (51,5%), decreased memory and attention in 51 (75,0%), sleep disturbance — in 45 (66,2%), increased fatigue — in 45 (66,2%) patients. When assessing the neurological status, there were irregularities in the performance of coordination tests (Romberg test, finger test) in 46 (67,6%) patients.

During the contour analysis of the pulse wave, an increase in RI ($38,2 \pm 15,1\%$) was observed, which indicated an increase in the tone of small resistance vessels, the SI level was $7,9 \pm 0,1$ m/s, Alp 75 ($10,3 \pm 15,3\%$). When conducting an occlusion test, IOA — $1,9 \pm 0,7$ conv. units, SF — minus $6,6 \pm 4,6$ ms, which indicated the presence of endothelial dysfunction.

Hyperventilation syndrome was detected in 26 (38,2%), thermoregulatory syndrome in 36 (52,9%), neurogastric syndrome in 37 (54,4%), sweating disorders in 45 (66,2%), asthenic in 31 (45,6%), cardiovascular — in 34 (50,0%) patients. The Kerdo index was minus $17,9 \pm 20,6$ points. According to the Wayne scale, 50 (73,5%) of the examined had signs of autonomic dystonia ($28,2 \pm 13,9$ points).

When conducting a correlation analysis in the absence of hypercholesterolemia, there was a statistically significant inverse correlation between a very weak force between the level of total blood plasma cholesterol and IOA $r = -0,252$ ($p < 0,01$), and the total score on the Wayne scale $r = -0,272$ ($p < 0,01$); very weak strength between the Kerdo index and Alp 75 $r = -0,245$ ($p < 0,01$), weak strength between the Kerdo index and IOA $r = -0,348$ ($p < 0,01$).

In patients of group 2, the level of blood pressure was $138,9 \pm 17,6 / 82,1 \pm 9,9$ mm Hg. st.; the level of total plasma cholesterol was $6,1 \pm 0,9$ mmol/l. The initial manifestations of cerebral insufficiency were recorded in 6 (13,1%), chronic cerebral ischemia stage I and stage II - in 53 (86,9%; $p < 0,01$, test χ^2). An increase in cerebral complaints was noted. So, headache was detected in 50 (82,0%), noise and tinnitus in 46 (75,4%; $p < 0,005$, test χ^2), reduced memory and attention in 52 (85,2%), dizziness — in 40 (65,6%), increased fatigue - in 46 (75,4%), sleep disturbance — in 48 (78,7%) patients. According to a neurological examination, impaired coordination tests (Romberg test, finger test) were found in 53 (86,9%; $p < 0,010$, test χ^2) patients.

When conducting a contour analysis of the pulse wave in patients of this group, an increase in Alp 75 ($19,7 \pm 11,8\%$, $p < 0,0001$), RI ($47,3 \pm 19,6\%$, $p < 0,007$) was observed, indicating a more pronounced violation of the elastic properties of the vascular wall; SI level was $7,9 \pm 0,7$ m/s. During an occlusal test, a decrease in IOA ($1,7 \pm 0,5$ conv. units) and SF (minus $5,5 \pm 6,1$ ms, $p < 0,040$) was recorded, which indicated a more pronounced endothelial dysfunction.

Hyperventilation syndrome was detected in 32 (52,5%; $p < 0,010$, test χ^2), thermoregulatory syndrome — in 35 (57,4%), neurogastric — in 34 (55,7%), asthenic — in 38 (62,3%; $p < 0,029$, test χ^2), cardiovascular syndrome — in 31 (50,8%), sweating disorders — in 40 (65,6%) patients. The Kerdo index was minus $18,6 \pm 23,1$ points. According to the Wayne scale, there were signs of autonomic dystonia ($33,5 \pm 13,9$ points, $p < 0,034$) in 48 (78,7%) examined.

When conducting a correlation analysis for hypercholesterolemia, there was a statistically significant direct correlation between the weak strength between total blood plasma cholesterol and Alp 75 $r = 0,351$ ($p < 0,01$), and RI $r = 0,303$ ($p < 0,05$); weak strength between the Kerdo index and Alp 75 $r = -0,315$ ($p < 0,01$).

DISCUSSION

In the examined AH patients with hypercholesterolemia, cerebrovascular disorders in the form of stage I and II chronic cerebral ischemia are more common, which are combined with increased rigidity

of the vascular wall and pronounced endothelial dysfunction. The frequency of vegetative disorders with the prevalence of parasympathetic tone among AH patients is registered equally regardless of the level of total cholesterol of blood plasma, while the expression of vegetative symptoms increases in the progression of cerebrovascular disorders. In patients with hypercholesterolemia, a direct correlation between blood plasma total cholesterol level and Alp 75, and RI, the Kerdo index and Alp 75 was revealed.

CONCLUSIONS

The combination of arterial hypertension with hypercholesterolemia is characterized by the presence of pronounced cerebrovascular disorders, significant disorders of the elastic properties of the vascular wall and endothelial dysfunction accompanied by vegetative disorders. This challenge should be considered when developing individualized plans for treatment and rehabilitation.

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CLINICAL CASE OF A FEMALE PATIENT WITH MULTIPLE MYELOMA

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ABSTRACT — The article presents a clinical case of a female patient with multiple myeloma. This bone malignancy occurring with increasing frequency in older adults is common in hematological practice, late diagnosed and poorly managed, with a high level of mortality.

KEYWORDS — multiple myeloma, plasma cell myeloma, incidence, chemotherapy, bortezomib.

Multiple myeloma (MM) is β -cell malignant tumor whose morphological substrate is plasma cells producing monoclonal immunoglobulin. According to the latest WHO classification, in 2017 the term *multiple myeloma* was replaced with *plasma cell myeloma*, a disease characterized by multifocal proliferation of neoplastic plasma cells associated with monoclonal immunoglobulin secretion [1].

MM represents approximately 1% of all malignant tumors, and accounts for 13% of all hematopoietic neoplasms. MM occurs with increasing frequency in older people, the median age at diagnosis being 63.7 years [2]. The prevalence of the disease among the population younger than 40 years does not exceed 2%. In Russia in 2017, the incidence of MM was 2.78 per 100,000 persons, with 4,075 new cases diagnosed. 2,587 patients died [3].

The duration of the disease before the onset of the first clinical symptoms can range from several months to 2–3 years [1]. The MM clinical manifestations are extremely diverse, but they are largely determined by infiltration of the bone marrow by the plasma cells (PCs) and organ damage. MM often presents with bone injuries, hypercalcemia, renal failure, amyloidosis, infiltration of the bone marrow by the myeloma cells, a decreased level of normal immunoglobulins, cryoglobulinemia, and hyperviscosity syndrome [4].

The purpose of our study was to present a clinical case of a patient with MM since it accounts for 60% mortality rate in Russia due to its multiple clinical manifestations and the diagnostic complexity.

Case description

A 69-year-old female patient M. who lives in the Tver Region presented to the Hematology Department of Tver Regional Clinical Hospital on January 2nd, 2019, with complaints of moderate general weakness, moderate pain in the lower extremities, ribs, left clavicle increasing with movement and palpation, a cranial bone growth.

According to the patient's history, for several years the woman had had minor bone pain for which she was not examined. In January 2018, she consulted her district physician about the painless growth in the left frontal area, increased bone pain, and general weakness. The initial examination and lab tests revealed mild anemia (Hb — 102 g/l), accelerated ESR (108 mm/h), and moderate proteinuria (2.15 g/l). The patient was referred to a series of X-ray bone tissue examinations. The 2-projection skull radiographs (July 16th, 2018) showed multiple foci of bone destruction; the shoulder radiographs revealed multiple foci of bone destruction of both clavicles, shoulder blades, and visible parts of the ribs. There was a deformity of the 6th right rib and swelling of the acromial end of the left clavicle. The radiographs of the thoracic and lumbar spine and pelvis showed multiple foci of bone destruction, signs of bilateral peritrochanteritis, and pathological Th 5 and Th12 fractures. Given the total pronounced changes in the bone structures of flat bones associated with an evident pain syndrome, the district physician suspected MM, and the patient was referred to a hematologist.

During the examination, the immunochemical assay (ICA) was performed, as well as radiography of the upper extremities. The findings of the ICA (September 18th, 2018) revealed paraprotein represented by M-gradient, 20.5 g/l, Bence-Jones protein secretion. The urine M-gradient was 0.91 g/day. The X-ray of the upper extremities and clavicles (October 2nd, 2018) showed a fused fracture of the acromial end of the clavicle with a massive bone callus on the right, as well as multiple foci of destruction in the examined areas.

In order to clarify the diagnosis and start proper therapy, on October 10th, 2018, the patient was referred to the Hematology Department of the Tver Regional Clinical Hospital, where MM was diagnosed and the 1st bortezomib-based VCD chemotherapy cycle was started on October 11th, 2018. The patient responded to the therapy well and was discharged in

satisfactory condition. The next hospitalization was from December 10th to December 22nd, 2018, during which the 2nd bortezomib-based chemotherapy cycle was performed. The patient's response to the regimen was positive, she showed some improvement, the bone pain decreased, the patient became more active, and became independent with her ADLs.

The next hospitalization for the 3rd chemotherapy cycle was from January 2nd to January 14th, 2019.

On admission, the patient's condition was estimated as satisfactory without any signs of mental confusion. The body temperature was 36.6 °C. The patient walked using a walker, and was active in bed. There were multiple dense growths on the skull, the skin over them was not changed, painless on palpation, the maximum size in the frontal left area was up to 6×3 cm. On palpation, the left clavicle, sternum, and ribs on the anterior surface were moderately painful. The patient had normal constitution, height — 160 cm, weight — 70 kg. The body mass index was 27.34 kg/m² corresponding to being overweight. The skin was pale pink, of normal moisture, no swelling. The shape of the chest was correct, normosthenic, the respiratory rate was 16/min. The BP was 120/70 mm Hg, the heart rate was 76 BPM, the borders of the heart were expanded to the left by 1.5 cm, the heart tones were rhythmic, muted. No abnormalities were detected in the other organs and organ systems.

The examination showed mild anemia (RBCs — $3.2 \cdot 10^{12}/L$, Hg — 103 g/l). Blood biochemistry revealed no deviations from normal parameters. Urinary Protein Excretion Estimation was negative. An ECG was also performed, which showed signs of incomplete left bundle branch block.

Clinical diagnosis

C90.0 Multiple myeloma, M-gradient in blood serum, with Bens-Jones proteinuria, osteodestructive process, anemia, soft tissue growths in the skull, stage IIA, ISS stage III. Condition after 3 VCD cycles.

Associated complications

Severe osteoporosis. Thinning of the cortical layer of the humerus. The acromial end of the clavicle is swollen.

The 3rd bortezomib-based chemotherapy cycle was performed: days 1, 4, 8, 11 — 1.3 mg/m² — 0.9 ml sub-Q. The treatment regimen included: dexamethasone 40 mg IV drip per 200 ml of normal saline on the days of bortezomib administration, Endoxan 400 mg IV drip per 200 ml of normal saline on days 1 and 8. In order to exclude the development of gastropathy, the therapy was supplemented with omeprazole 20 mg 2 times daily 30 minutes before meals on the days

of dexamethasone administration. For pain, Ketorol 3% solution was administered — 2.0 ml IV given over a constant infusion rate. On January 13th, 2019, for the purpose of osteoclast hyperactivation zoledronic acid was administered IV drip as a single 4 mg dose in 200.0 ml of normal saline. The patient responded to the therapy well, without complications, with improvement. Upon discharge, the patient's Hb was 111 g/l, RBCs — $3.7 \cdot 10^{12}/L$, WBCs — $9.60 \cdot 10^9/L$, PTLs — $172 \cdot 10^9/L$. The patient was discharged with recommended follow-up by the district physician and hematologist. The next hospitalization was due in 3 weeks for the 4th cycle of bortezomib-based chemotherapy.

Maintenance therapy of bortezomib-based increases the rate of complete remission, progression-free survival, and survival to progression. Since there is no conclusive evidence of an increase in overall survival, according to ESMO recommendations, maintenance therapy in elderly patients is not recommended [5].

DISCUSSION

The main negative prognostic factors for MM include high levels of $\beta 2$ -microglobulin, decreased serum albumin, elevated LDH, cytogenetic abnormalities: t(4;14), t(14;16), del17p13, del13q, 1q amplification, 13q deletion. Initial prognostic signs allow predicting the life expectancy of patients and their response to therapy, but they do not determine the choice of adequate treatment tactics for MM patients [2]. In our clinical case, there were no such factors. The timely MM therapy using the VCD regimen, as well as the absence of complications, made it possible to improve the patient's condition after the 3rd cycle (the bone pain reduced, the patient became more active) and slow down the disease progression. It is undoubtedly necessary to continue the therapy until complete remission has been achieved. The positive effect of the therapy has led to an increase in the patient's quality of life and, it can be assumed, the complete remission, when achieved, will increase its duration.

Thus, medical awareness of more frequent and characteristic clinical and laboratory manifestations of MM will allow detecting this disease at an early stage and timely start polychemotherapy thereby reducing the MM-related mortality rate.

Contributors

Elmira Aliyeva and Angela Asedova — literature review, clinical case description, submission for publication. Olga Poselyugina — clinical case selection, patient supervision, provision of data for the article. All the authors took equal part in writing the article. All the authors made an equal contribution to the

conception, design, and interpretation of the reported study. All the authors have equal rights.

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POST-TRAUMATIC DAMAGE OF BRACHIAL PLEXUS: CLINICAL CASE STUDY

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ABSTRACT — The article presents a clinical case of a post-traumatic injury of brachial plexus. As a result of head-on car collision the driver suffered an injury of left brachial plexus and its branches, multiple rib fractures, a broken left collarbone. Formation of posttraumatic edema ultimately led to interruption of venous and lymphatic drainage from the left axillary basin. A posttraumatic keloid and unremoved bone pieces aggravated the manifestations of edema, which persisted 6 months. This strongly challenged the rehabilitation aimed to restore nerve conduction.

KEYWORDS — brachial plexus injury, lymphedema, tissue hypoxia, lipid peroxidation.

INTRODUCTION

A brachial plexus injury is one of the most common peripheral nerve injuries. Specific features of preganglionic traumatic injury allow prediction of low likelihood of spontaneous recovery, and the need for surgical intervention tends to be high [1]. Such injuries usually result in disordered motor function, compromised sensitive impulse conductivity, cause severe disability and dramatic decrease of quality of life [3, 4]. Progressing hypoxia also hinders the normal recovery process. Post-traumatic pain shock, blood supply, lymph efflux and venous drainage disturbance contribute to worsening of existing tissue and circulatory hypoxia with subsequent oxidative stress development, accompanied by accumulation of lipid peroxidation products and damage of cellular membrane structures [5].

Clinical Case History

Patient, female, 48 years old, with the history of road traffic accident in September 2013 resulting in the severe brain contusion (post-traumatic encephalopathy with diffuse atrophy in the parietal lobe), multiple fractures of 1–4 ribs, fracture of the clavicle, compression

spinal fracture with D3, D5 disk injury, brachial plexus rupture (monoplegia of left arm with complete loss of any sensitivity), detachment of nerve roots C5–6, C6–7, C7–Th1, Th1–2 on the left and C5–6, C6–7 on the right, subscapularis tendon injury and traumatic injury of musculus deltoideus fibers. The third upper phantom limb caused severe pain syndrome.

In April 2014, the patient underwent revision surgery and neurolysis of primary and secondary stems, including distal branches of the right brachial plexus. Use of intercostal nerves for restoration of nerve conductivity in the injured extremity was not feasible due to the injury-related intercostal nerve structural changes. During post-surgery period, the patient suffered from persistent edema of injured site that contributed to the local negative impact on the peripheral nerves. Treatment administered for edema was inefficient, which further adversely affected restoration of the nerve impulse conductivity. During the early post-surgical period, the patient was administered with treatment including pharmacological and physical therapies at the present day, due to total loss of motor function and sensitivity of the left upper extremity and progressing lateral curvature of vertebral spine caused by additional load on this area, it is recommended to amputate non-functional extremity.

WORK-UP RESULTS

MRI Results over Time

The first MRI scan made in 1 month after injury.

The second MRI scan made in 2 months after injury.

The third MRI scan made in 6 months after injury.

Blood Tests Results over Time

Interpretation of results if blood tests made immediately on the day of injury revealed no changes in the red blood cell count, hemoglobin (Hb) concentration, and blood urea nitrogen concentration beyond normal range. At the same time, the creatinine concentration exceeded the upper normal limit by 7%, which was explained by the tissue damage as a result of traffic accident. ESR also increased and exceeded the upper normal limit by 36%.



Fig. 1. The injured site exhibits reduced blood supply along the major branches of the left subclavian artery (in the interscalene space) and the axillary artery. The scan shows the area of edema with compression of C5–Th2 roots. The signs of subclavian lymph vessels of 2–3 orders, the signs of bone fragments and colloid scars are also observed. In addition, the features of left lung upper lobe compression (S1–2, S3) are demonstrated

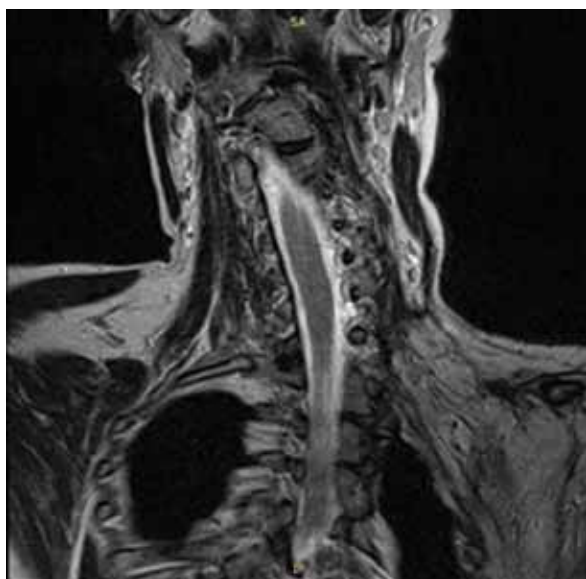


Fig. 2. The scan shows growing edema resulting from pressure on major blood vessels and their branches. The scar at the injured site exhibits no changes over time

Blood tests made in 2 months after the accident showed reduction of the white blood cell count to the normal level and ESR reduction to the level slightly

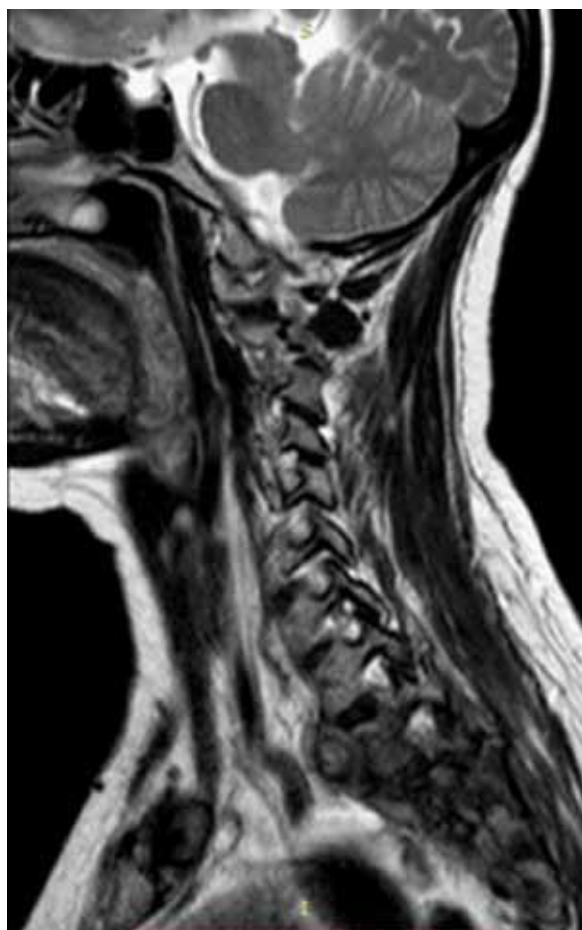


Fig. 3. The scan shows persistent edema and lymphatic ducts obstruction, compression of regional lymph nodes and vessels at the injured site, which contributes to the development of hypoxia and severe hemoglobinemia

above the normal range. Hb concentration and red blood cell count decreased by 5% as compared to the blood test results as of the accident date. The blood urea nitrogen showed significant increase (by 38%), which might result from activation of anaerobic glycolysis processes due to elevated glycogen depot consumption and inefficient aerobic glycolysis.

In 6 months after the injury, red blood cell count and ESR were within the normal range. The blood tests results revealed leukocytopenia (decrease by 6% beyond the lower normal level) probably caused by administration of high doses of antibiotics. Creatinine and urea concentrations remained high and exceeded upper normal level by 25% and 13% respectively, while Hb concentration showed no appreciable change as compared to the blood tests results as of the second month after injury. These results were most probably due to intensification of tissue hypoxia as a result of

failure to eliminate the reasons for its development: persistence of the coarse structural changes at the injured site, bone fragments, formation of colloid scars, post-traumatic anatomic asymmetry, which is confirmed by MRI data.

The persistent tissue hypoxia developed after the injury resulted in depletion of antioxidant pool, which led to enhancement of lipid peroxidation with accumulation of above reaction products at the injured site and subsequent cellular membrane destruction — in this particular case, trophic damage of the peripheral nerve tissue, preconditioned by failure to achieve nerve conductivity restoration (negative functional dynamics, decreased amplitude of injured extremity, worsening of pain syndrome and development of third limb phantom).

Taking into account the fact that the time-frames for nerve tissue restoration are usually within 3 months, in the first days after the injury it was imperative to direct the best possible efforts to efficiently combat the post-traumatic tissue edema, restore lymph efflux and adequate blood supply of this area and prevent formation of lipid peroxides.

CONCLUSIONS

It is important to note that the first medical aid for patients with brachial plexus injury should be directed to restore (preserve) anatomical structures at the damages site. It is necessary to start immediate anti-edema treatment in order to avoid hypoxia. During a surgery, it is important to prevent development of post-traumatic scars leading to blood supply, venous drainage and lymph drainage disruption [6,7]. In the early post-surgery period, it is crucial to achieve functional restoration of the injured site, which also contributes to reduction of hypoxia in the damaged area. It should be noted that this type of injuries mandates further more detailed research by morpho-physiologists in order to determine the pattern of nerve structures damage at the cellular level and ensure possibility for complete restoration.

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ACCURACY OF PULSE OXIMETRY FOR EARLY DETECTION OF CRITICAL CONGENITAL HEART DISEASE IN VOLGOGRAD REGION (RUSSIA)

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ABSTRACT — A retrospective diagnostic trial for early detection of critical congenital heart diseases (CCHD) was conducted in asymptomatic newborn infants with employment of a pulse oximetry screening (POS) regional protocol. The sensitivity of POS for CCHD detection was 75%, the specificity — 99.9%, the diagnostic test efficiency — 99.9%.

KEYWORDS — pulse oximetry screening (POS), critical congenital heart disease (CCHD), newborns.

INTRODUCTION

The preservation and promotion of children's health is one of the most pressing problems of world health. The solution of this problem has a high social significance and is among the priority tasks, since the health of the younger generation is the fundamental basis for the formation of the reproductive and labor potential of any state [1–5]. Early detection of CCHD improves patient outcomes in relation to both morbidity and mortality. Key screening tests for CCHD identification include prenatal ultrasonography and postnatal clinical examination of neonates. Although, both of these methods are available, CCHD is not detected in a significant proportion of children. Infants with cardiovascular malformations are usually asymptomatic at birth and some of them were recognized in 25% of living infants after discharge [10]. Currently, measuring the difference in blood oxygen saturation (SpO_2) in zones of blood supply above and below the open arterial duct has been proposed for early diagnosis of asymptomatic CCHD. The POS is approved and recommended to CCHD detection in Europe and USA [7]. A systematic review of 21 RCTs ($n = 457202$) showed high specificity and moderate sensitivity of the POS method for screening diagnosis of CCHD with a very low false positive rate [8]. The

screening in study performed by Hamilçikan Ş., & Can E. (2018) identified infants with other important pathologies, this forms an added value as an assessment tool for newborn infants [6]. Pulse oximetry is highly specific for detection of critical congenital heart defects with moderate sensitivity, that meets criteria for universal screening [9].

Purpose of the study

was to evaluate the POS regional protocol diagnostic capacity as a screening method for CCHD identification in asymptomatic newborns.

METHODS

The design of our retrospective diagnostic trial was approved by the Local Ethic Committee. Parents of enrolling children signed special ICF before any diagnostic procedure. POS regional protocol manipulations were performed in 86,8% (20,527/23,651) newborns from January to December 2017 in 13 obstetric hospitals in the Volgograd region. The gestational age of children were from 34 to 42 weeks (Me 37 (35–40) weeks). In accordance with the regional protocol, POS was measured at 24–48 hours of life in all children on their right arm and any leg, during at least 3 minutes (if no artefacts). Positive POS test criteria's followed by echo-cardiography (ECHO-CG) and cardiac surgeon consultation were: a) $SpO_2 < 90\%$ on the right arm and/or any leg, b) $SpO_2 = 90\%$ or $< 95\%$ on the right arm and/or leg or c) $(SpO_{2,arm} - SpO_{2,leg})$ gradient $> 3\%$.

RESULTS AND DISCUSSION

509 cases of congenital heart disease (2,2% of live births) were identified: antenatally — 124 (20,3%), postnatally — 385 (79,7%). All cases of congenital heart diseases were symptomatic.

6 positive POS results (0,03%) were reported in asymptomatic group of newborns ($N=20527$). There were next CCHD: transpositions of the main arteries ($N=2$), aortic coarctation ($N=2$), pulmonary artery atresia with intact interventricular septum ($N=1$) and tetralogy of Fallot ($N=1$). False negative POS results were obtained in 2 cases (0,01%) — interruption of the aortic arch and aortic coarctation, which is consistent with the data of several authors indicating a low specificity of POS for these types of CHD [5]. False

positive POS results were in 12 cases (0,06%). The sensitivity of POS for CCHD detection was 75%, the specificity — 99.9%, the diagnostic test efficiency — 99.9%.

Our results do not conflict with the results of Plana M. N. et al (Cochrane Systematic Review, 2017), which conclude that pulse oximetry (N=457,202 participants) is a highly specific (99,9%) and a moderately sensitive (76,3%) test for detection of CCHD with very low false-positive rates (0,14%). The current evidence supports the introduction of routine screening for CCHD in asymptomatic newborns before discharge from a well-baby nursery.

CONCLUSION

The regional program of pulse oximetry neonatal screening has shown itself to be a useful method for early detection of CCHD. At the same time, we have to use POS protocol standardization, as well as clinical examination of newborns to ensure diagnostic accuracy of pulse oximetry screening.

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RHEOVASOGRAPHIC ASSESSMENT OF THE MICROCIRCULATION IN CHILDREN WITH FLAT FEET: EXPERIMENTAL RESEARCH

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ABSTRACT — The aim of this work is to study the regional blood circulation in schoolchildren, taking into account the musculoskeletal system. Indicators of microcirculation in healthy children correspond to the *norm* relative to the standards. To assess arterial and venous blood flow in the vessels of the lower extremities in the feet, we used rheovasography performed with rheographic complex *REO-spectrum*. If there is a deviation of the mutual position of the bones of the feet and the configuration of the joints, the presence of changes in the microcirculation of the lower extremities preceding the initial stages of the formation of flat feet is established. There was a disruption of local hemodynamics in children over 12 years, including the decrease of pulse blood filling and maximum blood flow through the arteries at 24–55% in the lower leg and at 60–71% — in the foot with an increase of arterial tone by 1.2–1.5 times to the healthy level.

KEYWORDS — children, microcirculation, rheovasography, flat feet.

In modern society there has been a tendency to increase the prevalence of chronic pathology, including dystrophic diseases of the musculoskeletal system. This trend is fully observed in children, most clearly manifested in schoolchildren [1, 3, 5]. A large number of studies have been devoted to the diagnosis and treatment of musculoskeletal disorders in children [3–5]. At the same time, the main attention is paid to the study of the etiology, pathomorphology of deformities, development and improvement of techniques for correction of scoliosis and flat feet of 3–4 degrees [1, 5]. On the other hand, there is almost no information about the features of regional blood flow of the lower extremities in flat feet of the first degree.

The aim of this work

is to study the regional blood circulation in schoolchildren, taking into account the state of the musculoskeletal system.

MATERIAL AND METHODS

A group of children with flat feet ($n=175$) was examined. The second group included 242 healthy schoolchildren of the same age. The level of physical development of schoolchildren was determined by a standard set of anthropometric tools that passed metric control. To assess arterial and venous blood flow in the vessels of the lower extremities (lower leg-foot) in flat feet, we used the rheovasography of lower extremities performed on the rheographic complex *REO-spectrum* with subsequent computer processing of data [2]. The following rheographic characteristics were used for quantitative assessment of arterial blood filling of extremities, arterial tone, venous outflow and collateral circulation: rheographic index (RI, rel. ed.), maximum speed of blood filling of large-caliber arteries (V_{max} , Om/s), dicrotic index (DIK, %), diastolic index (DIA, %), pulse wave propagation time ($Q-x$, sec.) [2]. All patients (his parents) signed an information letters for inclusion in this study.

The data were processed in the software package Statistica 6.1 for Windows.

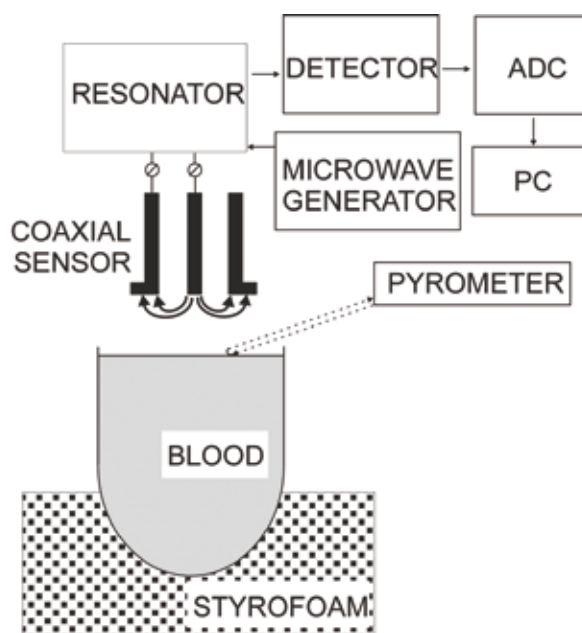


Fig. 1.

Table 1. Dynamics of rheovasography in healthy children and in flat feet

			RI, rel. un. (norm for leg - 0,65-1,0; norm for foot - 0,9-1,5)		Vmax, Om/s (norm - 1,3-2,3)		Q-x, sec. (norm - 0,25-0,33)	
			Right	Left	Right	Left	Right	Left
7-8 years old	Leg	1	2,1±0,04	2,1±0,04	2,3±0,02	2,4±0,02	0,18±0,05	0,18±0,04
		2	1,87±0,04	2,3±0,02	2,39±0,01	2,47±0,02	0,21±0,04	0,2±0,04
	Foot	1	0,7±0,03	0,8±0,03	1,07±0,02	1,35±0,01	0,21±0,06	0,21±0,06
		2	0,9±0,03	1,42±0,02*	1,08±0,02	1,74±0,01	0,22±0,05	0,21±0,01
9 years old	Leg	1	2,0±0,04	1,9±0,01	2,4±0,01	2,39±0,04	0,23±0,03	0,24±0,03
		2	1,8±0,01	1,9±0,02	2,4±0,01	2,47±0,01	0,21±0,04	0,21±0,04*
	Foot	1	0,82±0,03	0,82±0,03	0,97±0,04	1,0±0,05	0,26±0,05	0,26±0,02
		2	0,93±0,04	0,86±0,05	1,0±0,03	1,19±0,07	0,25±0,05	0,23±0,03
10 years old	Leg	1	1,82±0,02	1,73±0,02	2,27±0,01	1,96±0,02	0,23±0,03	0,19±0,01
		2	1,79±0,03	1,84±0,03	2,3±0,04	2,24±0,05	0,22±0,03	0,21±0,02
	Foot	1	0,99±0,03	0,64±0,02	1,3±0,01	0,75±0,02	0,22±0,01	0,21±0,01
		2	0,78±0,02	0,97±0,01	0,82±0,03	1,13±0,01	0,22±0,01	0,20±0,02
11 years old	Leg	1	1,89±0,02	1,8±0,01	2,5±0,01	2,25±0,03	0,21±0,03	0,20±0,03
		2	1,53±0,04	1,9±0,07	1,9±0,04	1,96±0,09	0,18±0,04	0,22±0,04
	Foot	1	1,0±0,03	1,24±0,01	1,1±0,05	1,5±0,02	0,25±0,05	0,20±0,01
		2	0,79±0,04	0,85±0,04	0,84±0,02	1,09±0,01	0,21±0,05	0,23±0,01
12 years old	Leg	1	3,26±0,03	2,8±0,03	2,6±0,05	2,5±0,04	0,18±0,07	0,18±0,01
		2	1,45±0,05*	1,44±0,03*	1,9±0,06*	1,89±0,05*	0,25±0,02*	0,26±0,02*
	Foot	1	2,16±0,03	1,76±0,08	2,34±0,02	2,04±0,01	0,18±0,07	0,18±0,04
		2	0,62±0,02*	0,45±0,02*	0,78±0,03*	0,63±0,01*	0,24±0,03*	0,22±0,02*
13 years old	Leg	1	2,6±0,02	2,48±0,02	3,4±0,03	2,2±0,02	0,24±0,06	0,23±0,04
		2	1,6±0,03*	1,74±0,01*	1,97±0,06*	1,7±0,02	0,22±0,04	0,19±0,06
	Foot	1	2,4±0,05	0,56±0,03	2,3±0,02	1,8±0,02	0,25±0,04	0,24±0,05
		2	1,3±0,04*	0,9±0,02*	1,38±0,07*	0,99±0,03	0,22±0,05	0,20±0,08
14 years old	Leg	1	2,03±0,03	1,4±0,01	2,37±0,06	1,58±0,05	0,26±0,03	0,26±0,06
		2	1,3±0,02	1,1±0,02	1,89±0,05	1,39±0,04	0,20±0,05	0,26±0,04
	Foot	1	1,14±0,01	1,08±0,01	1,75±0,02	1,17±0,07	0,25±0,03	0,24±0,05
		2	1,03±0,01	0,9±0,03	1,38±0,04	0,88±0,06	0,19±0,04	0,28±0,06
15 years old	Leg	1	1,53±0,02	0,97±0,01	1,37±0,02	1,3±0,04	0,23±0,01	0,23±0,02
		2	1,43±0,03	1,63±0,06*	1,97±0,02*	2,10±0,02*	0,21±0,06	0,24±0,03
	Foot	1	1,02±0,01	0,81±0,04	1,3±0,01	1,51±0,02	0,23±0,05	0,27±0,02
		2	1,1±0,01	0,85±0,05	1,5±0,05	1,43±0,04	0,18±0,03*	0,17±0,01*

Note: RI — rheographic index, Vmax — maximal speed of filling of large arteries, Q-x — pulse wave propagation time. Groups indication: 1 — healthy children, 2 — children with flat feet. * — statistical differences between groups are significant, $p < 0.05$

RESULTS

We registered that the severity of regional muscular circulatory abnormalities in children with flat feet is directly related to the age, while no gender differences were found. A number of indicators of rheovasography (such as wave propagation time or dicrotic index) in schoolchildren of 7–11 years old change slightly and do not differ in healthy children and children with

flat feet. High correlation of the dicrotic index with the respiratory component of the spectrum in the feet ($r=0.8$) was revealed in 8-year-old children. Full picture of age dynamics of rheographic parameters is shown in table. Based on these data, it can be concluded that the most active functional rearrangements of the micro-circulatory bed in children occur at the age of 12–13 years. This is implemented for all the main parameters

of reovasography (rheographic index, maximal speed of filling of large arteries and pulse wave propagation time).

CONCLUSION

It was stated, the parameters of microcirculation in most healthy children correspond to the age norm, and only some of them exceed this level. If there is deformation of the mutual position of feet bones and joints reconfiguration, the presence of changes in the microcirculation of the lower extremities preceding the initial stages of the formation of flat feet is established. We identified a disruption of local hemodynamics in children over 12, including the decrease of pulse blood filling and maximum blood flow through the arteries at 24–55% in the lower leg and at 60–71% — in the foot with an increase of arterial tone by 1.2–1.5 times to the healthy level.

CONTRIBUTORS

SBM and IVB collected, analyzed, and interpreted data and made the figures. AKM did the literature review, analyzed and interpreted data and collected data. LRD and YaVK collected data and made the figures. AKM, SBM, LRD, IVB and YaVK prepared the manuscript for submission.

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EFFECT OF BSMI (283 G>A) POLYMORPHISM OF THE VDR GENE ON THE COURSE OF CHRONIC LUNG DISEASES IN CHILDREN

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ABSTRACT — The study was aimed to evaluate the effect of BSMI (283 G>A) polymorphism of the VDR gene on the course of the chronic nonspecific pulmonary diseases in children. In this study, it was proved that the A/A genotype is associated with the development of primary and secondary chronic lung diseases in children, has a predisposing effect on the development of secondary chronic bronchopulmonary conditions in males, is a preemptive genotype for the development of severe exacerbation in children with CNSLD and correlates with the chronic gram-negative infections in patients.

KEYWORDS — chronic nonspecific pulmonary diseases, children, BSMI polymorphism, VDR gene.

INTRODUCTION

In recent years, multiple studies on the genetic origin of lung diseases in children have confirmed the role of hereditary factors in the disease pathogenesis. [1]. A number of vitamin D receptor gene polymorphisms, particularly BSMI (283 G>A) polymorphism were identified by using bioinformatics methods as a result of the search for single-nuclear polymorphisms with the expected phenotypic effect [2]. The VDR gene regulates the activity of genes for mineral metabolism and parathyroid hormone secretion, thus controlling the homeostasis of calcium and phosphorus. At the same time, there is a similarity between sequences with steroid and thyroid hormone receptors. Upcoming targets of this nuclear hormone receptor are involved in the regulation of both immune response and metabolic processes [2, 3].

MATERIALS AND METHODS

In this study, 98 patients with non-allergic chronic lung diseases were examined. Patients were divided into 2 subgroups: the first (42 children) was

consisted of children with chronic diseases formed on the initially intact lung (chronic bronchitis, obliterative bronchiolitis), the second was consisted of patients with genetically determined lung disease (cystic fibrosis, primary immunodeficiencies) and bronchopulmonary malformations. The control group was represented by conditionally healthy children (85 people). The molecular genetic study of the BSMI (283 G>A) polymorphism of the VDR gene was performed by polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP). The following parameters of patients with various alleles and genotypes were analyzed: gender, frequency and severity of exacerbations, microbiota pattern, variations in lung function, frequency and pattern of comorbid conditions, morphological changes according to CT lung screening. Statistical analysis of the obtained data was performed using the Data Studio software, STATISTICA 6.0 application package.

RESULTS AND DISCUSSION

Statistically significant differences were found in the frequency of occurrence of the G\G, G\A and A\A genotypes ($\chi^2 = 18.556$ $p < 0.001$ $df = 4$) between patients and controls. According to the data, the genotype including the minor A allele in the homozygous condition was significantly more frequent in patients of the first and the second subgroups than in control group ($\chi^2 = 7.889$ $p = 0.020$ $df = 2$ and $\chi^2 = 18.028$ $p < 0.001$ $df = 2$) (Table 1, 2). Moreover, in our study, the assessment of the risk ratio revealed a positive association of the homozygous minor genotype with the development of chronic lung diseases in children in both groups (OR = 3.850 (CI 1.432–10.352 and OR = 5.347 (CI 2.151–13.290), respectively.

In the study, we analyzed the possibility of association of the effect of this polymorphism on the gender in various forms of chronic lung diseases in children. It was revealed that the A/A genotype of the BSMI polymorphism (283 G>A) of the VDR gene in patients of the second subgroup is significantly more frequent in males ($\chi^2 = 11.400$ $p = 0.004$, $df = 2$. OR = 5.347 (CI 2.151–13.290)).

When analyzing the severity of exacerbations with the focus on the Bsm1 VST7 G>A polymorphism of the VDR gene statistically significant differ-

Table 1. Distribution of genotypes and variant alleles of BSM1 polymorphism (283 G>A) of the VDR gene in the first subgroup and control group

genotypes	control group (n=85)	first subgroup (n=42)	χ^2 ; p
G\G	28 (32,9%)	12 (23,8%)	$\chi^2 = 7,889$ $p=0,020$ $df=2$
G\A	49 (57,6%)	18 (42,8%)	
A\A	8 (9,5%)	12 (28,6%)	
alleles	n=134	n=60	
G	77 (57,4%)	30 (50,0%)	$\chi^2 = 0,933$ $p=0,335$ $df=1$
A	57 (42,6%)	30 (50,0%)	

Table 2. Distribution of genotypes and variant alleles of BSM1 polymorphism (283 G>A) of the VDR gene in the second subgroup and control group

genotypes	control group (n=85)	second subgroup (n=56)	χ^2 ; p
G\G	28 (32,9%)	20 (35,7%)	$\chi^2 = 18,028$ $p<0,001$ $df=2$
G\A	49 (57,6%)	16 (28,6%)	
A\A	8 (9,5%)	20 (35,7%)	
alleles	n=134	n=72	
G	77 (57,4%)	36 (50,0%)	$\chi^2 = 1,053$ $p=0,305$ $df=1$
A	57 (42,6%)	36 (50,0%)	

Table 3. Distribution of genotypes and variant alleles of BSM1 polymorphism (283 G>A) of the VDR gene according to the severity of exacerbation in children with CNSLD

genotypes	first subgroup (n=42)			second subgroup (n=56)		
	moderate exacerbation (n=32)	severe exacerbation (n=10)	χ^2 ; p	moderate exacerbation (n=40)	severe exacerbation (n=16)	χ^2 ; p
G\G	16 (50,0%) OR = 0,250 (CI 0,046-1,365)	2 (20,0%)	$\chi^2 = 6,475$ $p=0,040$ $df=2$	20 (50,0%) OR = 0,143 (CI 0,029-0,712)	2 (12,5%)	$\chi^2 = 6,771$ $p=0,034$ $df=2$
A\G	10 (31,25%)	2 (20,0%)		8 (20,0%)	6 (37,25%)	
A\A	6 (18,75%)	6 (60,0%) OR = 6,500 (CI 1,386-30,488)		12 (30,0%)	8 (50,0%) OR = 2,333 (CI 1,709-7,675)	
alleles	n=42	n=12		n=48	n=22	
G	24 (66,7%)	8 (40,0%)	$\chi^2 = 2,724$ $p=0,099$ $df=1$	16 (61,5%)	18 (39,1%)	$\chi^2 = 3,347$ $p=0,068$ $df=1$
A	12 (33,3%)	12 (60,0%)		10 (38,5%)	28 (60,9%)	

ences were revealed between the genotypes in patients with primary and secondary chronic lung diseases (Table 3). It was proved that the A\A genotype is a predisposing factor for the development of severe exacerbation, while the G\G genotype is associated with moderate set of symptoms in both patients of the first and second subgroups.

Significant differences in the G\G, G\A and A\A genotypes, the types of respiratory failure ($\chi^2 = 3,792$; $p = 0,435$ and $\chi^2 = 6,942$; $p = 0,140$) and the frequency of exacerbations ($\chi^2 = 2,792$; $p = 0,673$ and $\chi^2 = 5,984$; $p = 0,240$) in patients of 1 and 2 subgroups were not found in our study.

When analyzing the influence of the studied genetic polymorphism, associations were revealed between the microbiota pattern of the respiratory tract in the examined patients of the second subgroups with variant genotypes for the BMSI VST7 G>A polymorphism of the VDR gene ($\chi^2 = 10,376$; $p = 0,035$; $df = 4$). At the same time, a correlation was found between the A allele and the infection of gram bacteria in patients with cystic fibrosis ($\chi^2 = 7,000$; $p = 0,031$; $df = 2$). According to statistics, the mutant A\A genotype is predisposing to chronic culturing of pathogenic flora in patients with chronic lung diseases (Table 4).

CONCLUSION

Our study has proved that the A/A genotype is associated with the development of primary and secondary chronic lung diseases in children, has a predisposing effect on the development of secondary chronic bronchopulmonary pathology in males, is a preemptive genotype for the development of severe exacerbation in children with CNSLD and correlates

with the presence of chronic gram-negative infection in patients. The results can be useful for predicting the course of CNSLD in children, studying the influence of molecular genetic factors on pathology, and also be used as the basis for a personalized approach to prescribing vitamin D in this category of patients.

Table 4. Distribution of genotypes and variant alleles of BSMI polymorphism (283 G>A) of the VDR gene according to the duration of culturing pathogenic microflora in children with CNSLD

genotypes	first subgroup (n=42)			second subgroup (n=56)		
	intermittent infection (n=26)	chronic culturing (n=16)	χ^2 ; p	intermittent infection (n=20)	chronic culturing (n=36)	χ^2 ; p
G\G	14 (53,8%)	4 (25,0%)	$\chi^2 = 9,908$ p=0,008 df=2	10 (50,0%)	8 (22,2%)	$\chi^2 = 6,054$ p=0.049 df=2
A\G	10 (38,5%)	4 (25,0%)		6 (30,0%)	10 (33,3%)	
A\A	2 (7,7%)	8 (50,0%)		4 (20,0%)	18 (44,4%)	
alleles	n=36	n=20		n=26	n=46	
G	24 (66,7%)	8 (40,0%)	$\chi^2 = 2,724$ p=0.099 df=1	16 (61,5%)	18 (39,1%)	$\chi^2 = 3,347$ p=0.068 df=1
A	12 (33,3%)	12 (60,0%)		10 (38,5%)	28 (60,9%)	

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ROLE OF MODELLING IN CONTROL OF ASTHMA IN CHILDREN

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ABSTRACT — The study included 172 children of both sexes, aged 3 to 17 years with atopic bronchial asthma. The influence of various factors on the level of asthma control was analyzed by using a regression model. The following parameters were analysed: duration of disease, FEV1, IgE level, age. The best constructed logistic regression model revealed a sensitivity of 73.8 and specificity of 71.2. Distribution analysis and modelling confirmed that the regression model has a limited application for the construction of asthma control models due to nonlinear effects.

KEYWORDS — asthma, FEV1, IgE, children, regression model, control.

BACKGROUND

The problem of asthma control is multifaceted and difficult to solve despite being well studied. Modern advances in pharmacotherapy and monitoring of asthma still do not completely help in controlling the disease. The assessment can be carried out after several months of controller treatment and if possible after an attempt to reduce intensity of treatment in order to determine its minimum effective level for each patient. Since the course of asthma is extremely variable, severity of the disease can vary over months and years [1, 2, 3, 4].

Unfavorable prognosis in terms of development of bronchial asthma in patients with obstructive bronchitis is indicated by the following signs: family history of allergy, patients with chronic infection-allergic diseases, complication of pregnancy, artificial feeding from the first days of life, increased IgE. [5, 6].

MATERIALS AND METHODS

The study comprised of 172 children of both sexes with atopic bronchial asthma. The severity of

the disease was different. In all examined children, the diagnosis of the disease was determined and verified on the basis of diagnostic criteria and the current classification of the disease in accordance with the provisions of the National Program *Asthma in Children. Treatment strategy and prevention*, Moscow, revised 2017 [1].

First of all, the statistical interaction of each factor with the control level (three-level / two-level) was separately examined using the criterion χ^2 and the Fischer's Exact Test for both qualitative and categoric measurement, and with the Mann-Whitney Test criterion (Wilcoxon Rank Sum Test With Continuity Correction) for the continuous variables. The criterion values and p-value are shown in Chart 1.

The effect of various factors on the level of asthma control was analysed using regression model. The following parameters were included in the analysis: duration of disease, FEV1, level of IgE, age.

The sequential selection method was used to build the logistic regression model adjusted for all factors.

All obtained coefficients and model parameters are shown in Table 1. The P-value for the model coefficients was calculated by the Wald test.

The probability of asthma control can be calculated using the formulas:

$$Y = a_1 \cdot x_1 + a_2 \cdot x_2 + \dots + a_n \cdot x_n + a_0$$

$$P = \frac{1}{1 + e^{-Y}} \text{ logistic function.}$$

where a_i is the coefficients for the corresponding values of the factors x_i , a_0 is a constant term, e is the base of the natural logarithm.

RESULTS AND DISCUSSION

The analysis of clinical and anamnestic parameters and their influence on disease control was carried out.

According to the data in Table 1 asthma severity plays a key role in achieving control of the disease. Age and FEV1 (in model 1) have insignificant coefficients; these factors have a non-linear nature of the relationship with the control factor.

The disease duration coefficient is positive, which means that the longer the duration is, the more often disease control is achieved. The total IgE level, conversely, has a negative coefficient: the larger it is, the less likely it is to control the disease.

Table 1. Interaction between the factors and the control over bronchial asthma

Factor	Criterion value and p-value for two-level and three-level control classification
Sex	$\chi^2 = 0,35$, p-value = 0,84 $\chi^2 = 0,185$, p-value = 0,67
Age*	0-1: W = 1638, p-value = 0,35 0-2: W = 1132, p-value = 0,12 1-2: W = 1445, p-value = 0,006 W = 2577, p-value = 0,009
BA severity	Fisher's Exact Test, p-value = 1,4e-05 $\chi^2 = 24,017$, p-value = 6,0e-06
Onset age*	0-1: W = 1604,5, p-value = 0,47 0-2: W = 1561, p-value = 0,22 1-2: W = 2125,5, p-value = 0,58 W = 3686,5, p-value = 0,33
Genetic background	$\chi^2 = 0,82843$, p-value = 0,66 $\chi^2 = 0,14649$, p-value = 0,7
Illness duration*	0-1: W = 1381, p-value = 0,53 0-2: W = 929,5, p-value = 0,0045 1-2: W = 1456, p-value = 0,007 W = 2385,5, p-value = 0,0013

Table 2. Value of the coefficients of logistic regression and parameters of models

Factors*/Parameters	Model 1	Model 2	Model 3
Disease duration	0.18746 (0.01)	0.18355 (0.0002)	0.13633 (0.0013)
Asthma severity	-1.54523 (4.9E-06)	-1.62231 (1.0E-06)	-
Total IgE	-0.00236 (0.044)	-0.00236 (0.04)	-
Age	-0.004 (0.96)	-	-
FEV ₁	0.02208 (0.8)	-	0.03047 (0.0097)
Constant term	0.60668	2.3427	-3.62426
χ^2	48.195	44.960	17.566
p-value	3.2E-09	9.4E-10	0.00015
R ²	0.215	0.201	0.079
Sensitivity	72.9	73.8	65.6
Specificity	75.4	71.2	65.8

Thus, we suggested that in this system of factors there are nonlinear relationships which were confirmed by further modelling. In particular, the decision tree model was also built based on these factors which had sensitivity of 92.79 and specificity of 81.96.

CONCLUSION

The best model of the constructed logistic regression models gives specificity of 71.2 and sensitivity of 73.8. Distribution analysis and modelling show the limited application of the regression for the construction of asthma control models due to the nonlinear effects.

Thus, the modelling method allows to evaluate the role of various factors and their effect on the course of the disease and to predict the control effectiveness.

Elaboration of predictive markers for development of bronchial asthma in children will help improve the effectiveness of its diagnosis; timely initiation of preventive and therapeutic measures, which, in due course, may prevent disability in this group of patients.

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ALGEBRAIC MODEL OF KNEE JOINT STATUS: EXPERIMENTAL STUDY

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ABSTRACT — The rationale behind this paper relies on the fact that the effectiveness of any treatment procedure depends on the reliability of the operational and prognostic medical measurement experiment, which, in turn, relies on the metrological level of all the elements that are part of the instrumental resource.

Given the conditions, relevant is the issue of developing a methodology for selecting measuring tools, which would allow taking into account the cost, the reliability, the metrological as well as other features and indicators of the resource in question.

The purpose of the article is to assess the technical needs for solving problems set in the field of meaningfully defined objects – medical & biological systems (MBS). The solution to this problem can be found only on the basis of formalizing all the components that match the MBS description.

The research value implies the introduction of formal definitions for the anatomical (AnS), physiological (PhysS) and information-energy (IES) situations of a biological object (BO) and assignment of a diagnostic status of BO as a function of AnS, PhysS and IES. In addition, we have defined the principle of identifying the features of the instrumental base on following the basis of assessing the reliability of the physiological system status.

The pragmatic value of the data presented here implies the possibility of obtaining a numerical estimate of an acceptable reliability level that an instrumental resource can offer depending on the assessment of a physiological object sufficient reliability.

The innovation value of this item is related to the introduction of reliability scales for the BO diagnostic status as well as the reliability coming from the instrumental resource in medical measurements.

KEYWORDS — diagnostic situation, physiological system status reliability, set-theoretic model.

INTRODUCTION

Modern personificative medicine uses a high technological method of diagnostics; the treatment is based on using the results of fundamental sciences including constitutional anatomy [1–10].

The effectiveness of any treatment procedure is known [11–14] to be undeniably determined by the reliability of the operational and prognostic medical measurement experiment, which, in turn, is determined by the metrological level of all the elements within the instrumental resource. Besides, the instrumental resource includes equipment that features a significant variety of complexity — from large measurement and calculation complexes to simple one-dimension measuring devices.

In view of that, it is very important to create a methodology for selecting measuring instruments, which would allow taking into account the cost, the reliability, the metrological as well as other features and indicators of the instrumental resource.

Then, there is a need to assess technical needs in order to solve problems that have been set in the field of meaningfully defined objects — medical & biological systems (MBS). Such problems can be solved only on the basis of the formalizing all components that match the MBS description.

Also, it is a known fact [15] that any treatment technology can be described with a potential (required) error [16] to ensure high reliability of diagnosis. At the same time, by the *diagnostic error*, we can take the difference between the achieved value of assessing an individual body organ status or the body as a whole through the measurement process and a hypothetical assessment value that is taken as the average value known for a healthy organ or body. It is obvious that the maximum acceptable error in establishing a diagnosis for an accepted medical technology can be viewed as a *potential diagnostic error*.

An extremely important element in the description of MBS is the MBS status, which is the basis for comprehending a particular diagnostic situation.

Then, the *diagnostic situation* (DS) $M_{diag\ sit}$ of a biological (biomedical) object is a complex (set) of the anatomical $M_{an\ sit}$, physiological M_{phs} and information-energy states M_{ies} of this object:

$$M_{diag\ sit} = M_{an\ sit} \cup M_{phs} \cup M_{ies} \quad (1)$$

The definiteness of the DS assessment is most reasonable when based on the formalization of all its components.

MATERIALS AND METHODS

The model of the anatomical situation $M_{an\ sit}$ is a class that looks the following way:

$$M_{an\ sit} = \{M_{an\ syst}, M_{dr\ an\ syst}, M_{an\ phc}, M_{fc\ an}, M_{sp\ an}\}, \quad (2)$$

where $M_{an\ syst}$ is the category model of the anatomical system; $M_{dr\ an\ syst}$ is the definition range of the anatomical system; $M_{an\ phc}$ is the anatomical system physical constant set; $M_{fc\ an}$ is the set of the functioning conditions for the anatomical system; $M_{sp\ an}$ is the anatomical system parameters model.

At the same time, the anatomical situation model $M_{an\ syst}$ is either a graph or a category set. Subject to the definition for a graph (G) [17], its definition range M_{dr} is sets of X elements and a set transformation of G_X , i.e. in this case we are talking about the knee joint elements (KJ) — bones, tendons, and ligaments. The KJ elements attachment points, or fixations stand as the set transformation. The physical constants model $M_{an\ phc}$ are biomechanical indicators of KJ, which offer the description for elasticity, strength, flexibility, etc. The physical constants set model $M_{aph\ an}$ are a combination of anatomical limitations on the mutual position angles for the KJ bone elements, based on KJ bone elements relative motion, on various ligaments deformities. The model of anatomical system parameters $M_{sp\ an}$ is a Cartesian product [7] of KJ parameters that make up the joint function image, i.e. $M_{an\ sit}$.

Physiological situation model M_{phs} is a class of the following type:

$$M_{phs} = \{M_{fs\ ph}, M_{dr\ ph}, M_{phc\ ph}, M_{fcs\ ph}, M_{sp\ ph}\}, \quad (3)$$

where $M_{fs\ ph}$ is the category model of the functional physiological system; $M_{dr\ ph}$ is the model of the physiological system definition range; $M_{phc\ ph}$ is a set of physiological system's physical constants; $M_{fcs\ ph}$ is a set of physiological system's functioning conditions; $M_{sp\ ph}$ is the model of the physiological system's systemic parameter.

When detailing the physiological situation, note to be made that the category model [18] of the functional physiological system $M_{fs\ ph}$ is a combination of KJ elements interaction function under external (regarding the KJ) factors. $M_{dr\ ph}$ is a combination of definition ranges for each function of the functional physiological system. $M_{phc\ ph}$ develops from a number of coefficients, indicators, physical constants (that are part of the set), which describe the functions $M_{fs\ ph}$. $M_{fcs\ ph}$ is a limitations combination of function

domain, which enter $M_{fs\ ph}$. The physiological system parameter model $M_{sp\ ph}$ develops by the combination of the $M_{fs\ ph}$ function domain.

The information-energy situation model $M_{ie\ s}$ is a class of the following type:

$$M_{ie\ s} = \{M_{ie\ syst}, M_{dr\ ie\ syst}, M_{pc\ ie\ syst}, M_{fc\ ie\ syst}, M_{sp\ ie\ syst}\}, \quad (4)$$

where $M_{ie\ syst}$ is the category model of the information-energy system; $M_{dr\ ie\ syst}$ is the information-energy system definition range; $M_{pc\ ie\ syst}$ is a set of the information-energy system parameter constants; $M_{fc\ ie\ syst}$ is a set of the information-energy system functioning conditions; $M_{sp\ ie\ syst}$ is the analytical model of the information-energy system parameter.

Detailing of the information-energy situation model $M_{ie\ s}$ comes from analyzing the category representation. The information-energy situation model $M_{ie\ s}$ is to be expressed in the following way:

$$M_{ie\ s} = \{G_{SN} — sciatic nerve category; G_{TBN} — tibial nerve category; G_{FN} — femoral nerve category\} \rightarrow (CNS, SN) \leftrightarrow G_{SN}; \{G_{TB} = (CNS, TBN); G_{FN} = (CNS, FN)\}; \{\text{humoral categories}\}.$$

In view of the above, the complete algebraic model of the knee joint diagnostic status is to be presented as follows:

$$\begin{aligned} M_{diag\ sit} = & \{M_{an\ syst}, M_{dr\ an\ syst}, M_{an\ phc}, M_{fc\ an}, M_{sp\ an}\} \cup \\ & \cup \{M_{fs\ ph}, M_{dr\ ph}, M_{phc\ ph}, M_{fcs\ ph}, M_{sp\ ph}\} \cup \\ & \cup \{M_{ie\ syst}, M_{dr\ ie\ syst}, M_{pc\ ie\ syst}, M_{fc\ ie\ syst}, M_{sp\ ie\ syst}\}. \end{aligned} \quad (5)$$

RESULTS AND DISCUSSION

The algebraic model (15) serves as a formal basis to develop a set complex for assessing the reliability of the shaped diagnosis of the status. Note to be made that the status formulas include certain objects (the elements of the physiological component of the common organic system), the relations among them (or interactions), the constants and the conditions for interaction. All the participants in this structure are dimensional and feature a definable error. Then it is possible to find the maximum errors admissible in general assessment of the statuses, known from expert practice. Subject to the methods described in [19], for instance. In this case, we can argue that the maximum permissible errors of the instrumental

tools should be no worse than the general status assessment [20]:

$$AK_{exp}(\Delta_{FS}\lambda_{exp}^*) \rightarrow \theta_{ach}^*[\Delta\lambda_{FS}^*] \leftarrow AK_{instr}(\Delta_{FS}\lambda_{instr}^*) \quad (6)$$

where $AK_{exp}(\Delta_{FS}\lambda_{exp}^*)$ is the general assessment of the FS status obtained through expert evaluation employing a priori knowledge (AK) concerning this FS activity features; $AK_{instr}(\Delta_{FS}\lambda_{instr}^*)$ is the general evaluation of the FS status, which are to be obtained using a priori knowledge (AK), regarding measuring units specifics, and which may be employed through the FS monitoring; $\theta_{ach}^*[\Delta\lambda_{FS}^*]$ is the general assessment of the difference between the desired (potential) error that has been defined by experts, and the error that is maximum achievable through the measuring devices. Moreover, in the descriptions of situations, all the models may contain specific features, indicators, and parameters that have numerical values obtained through earlier studies and may contain some error. At the same time, all functional models are also obtained using approximations with nonideal and imperfect dependencies.

Similarly to [21], AK_{exp} may be presented in the following way:

$$AK_{exp}(\Delta_{FS}\lambda_{exp}^*) = \{ \lambda_{exp}^* = F_{exp}(\bar{\gamma}_{exp}), \bar{\gamma}_{exp} = [\gamma_{min exp}(t) \div \gamma_{max exp}(t)], M_{c exp}, L_{exp} = R_{m exp} \dots R_{1 exp}, \{R_{i exp}\}_{i=1}^m, \bar{w}_{exp}(t) \}. \quad (7)$$

Where λ_{exp}^* is the observed value that describes the physical functional system's behavior, which is base on expert evaluation; F_{exp} is the expert function of the FS comprehensive accepted classical behavior; $\bar{\gamma}_{exp}$ is the vector of expert impact of the FS for defining the response taken by the system; $[\gamma_{min exp}(t) \div \gamma_{max exp}(t)]$ is the change interval that the expert impact has on the FS that is being examined; $M_{c exp}$ is the set of external conditions within which the expert study is to be carried out; L_{exp} is the FS expert study methodology; $R_{i exp}$ is the i^{th} step within the FS behavior expert study methodology; $\bar{w}_{exp}(t)$ is the probability density for the distribution of comprehensive probabilistic characteristics of the expert study outcomes.

In a similar way we could present $AK_{instr}(\Delta_{FS}\lambda_{instr}^*)$:

$$AK_{instr}(\Delta_{FS}\lambda_{instr}^*) = \{ \lambda_{instr}^* = F_{instr}(\bar{\gamma}_{instr}), \bar{\gamma}_{instr} = [\gamma_{min instr}(t) \div \gamma_{max instr}(t)], M_{c instr}, L_{instr} = R_{m instr} \dots R_{1 instr}, \{R_{i instr}\}_{i=1}^m, \bar{w}_{instr}(t) \}. \quad (8)$$

$$[\gamma_{min instr}(t) \div \gamma_{max instr}(t)], M_{c instr}, L_{instr} = R_{m instr} \dots R_{1 instr}, \{R_{i instr}\}_{i=1}^m, \bar{w}_{instr}(t) \}.$$

Here AK_{instr} stands for a priori knowledge which concerns the actual FS status and which develops base on special measuring experiment using the selected instrumental tools; $\lambda_{instr}^*(t)$ is a measurable value that is adequate to the system parameter of this particular FS; F_{instr} is the calibration curve that approximates the function $\lambda(t) = f(\gamma(t))$, used for establishing the ideal adequate link between the measurement outcome and the standard impact within the medical experiment; $\bar{\gamma}_{instr}$ is the system parameter accepted for the medical experiment involving measuring tools; $M_{c instr}$ is the set of conditions for the medical measuring experiment; L_{instr} is the instrumental measuring procedure implemented via the conventional tool; $\{R_{i instr}\}_{i=1}^m$ is the i^{th} instrumental measuring transformation within the procedure L_{instr} ; $\{R_{nji instr}\}_{j=1}^m$ is the j^{th} instrumental module that is part of the measuring tool, which implements the procedure L_{instr} adequate to the scaling transformation of F_{instr} ; $\bar{w}_{instr}(t) = \{w_{1 instr}, \dots, w_{m instr}\}$ is the probability density for the distribution of the probabilistic characteristics combination, adequate to the accepted measuring tool.

CONCLUSION

As noted above, the effectiveness of any treatment procedure depends exclusively on the reliability of the operational and prognostic medical measurement experiment, which, in turn, is determined by the metrological level of the instrumental resource's elements. The proposed algebraic model for the knee joint status allows defining a method for obtaining formal estimates expressed as the required potential accuracy of the diagnosing assessment for the biomedical object status, to be performed through metric identification algorithms, which allows identifying the borderline errors for the instrumental resource, which, finally, creates the basis for metrological synthesis of medical measuring techniques.

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EFFICACY OF OZONE THERAPY IN TREATMENT OF EROSION AND ULCERATIVE LESIONS OF ORAL MUCOSA

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ABSTRACT — Ozone therapy has been widely used as an effective non-drug method for treatment of dental diseases. It has a pronounced therapeutic activity, ease of use, good tolerability, enables reducing the drug load and facilitates recovery processes. The work investigates antibacterial efficacy of ozone therapy in comparison with two alternative antibiotic medications for erosive and ulcerative lesions in the oral cavity. The study was carried out using the method of clinical and CITO-bacterioscopic research. The results of the CITO-bacterioscopic study showed effective antibacterial and antifungal activities of all three therapies. In 14 days, the inflammation was subdued and the total populations of coccal flora and *Candida albicans* were decreased. Moreover, the results of the clinical examination demonstrated higher efficacy of the therapy with ozonated olive oil. Already on the second day, relief of pain and improvement of the condition were observed. The obtained data confirmed the antibacterial activity of ozone therapy for treatment of oral mucosal erosions and ulcers. These benefits suggest its use for geriatric patients. However, further study with a focus on antioxidant properties of medical ozone in a reparative process is required.

KEYWORDS — ozone therapy, erosive and ulcerative lesions of oral mucosa, cytobacterioscopic studies.

INTRODUCTION

The choice of laboratory and clinical methods for assessing the dental status of a patient is determined by the nosological form of the disease, as well as by the relationship with the level of his somatic health. Along with the use of traditional laboratory and clinical research methods, the doctor also uses other modern informative methods and tests to identify the disease and make a final diagnosis [1–11].

The problem of treatment of erosive and ulcerative lesions of the oral cavity is relevant for dentists of all directions due to the chronization of the process [12, 13]. The treatment should have an etiopathoge-

netic orientation. Geriatric dental disorders may be caused by infectious, autoimmune processes, trauma, allergic reactions, irrational orthopedic treatment. Besides, questions of etiology and pathogenesis still cause scientific disagreement among scientists [14]. In addition, due to the anatomical features of the oral cavity, any erosion of this area is in constant contact with 300 or more types of microbes. Hence, the most commonly prescribed drugs are antibacterial [15]. However, this therapy in many cases entails consequences in the form of dysbiosis and the development of fungal infection, the emergence of resistance of microorganisms, sensitization of the body [16, 17]. Among other medical areas, medical ozone has become particularly popular as an antibacterial agent.

Ozone kills all kinds of bacteria, viruses, fungi and protozoa. The antiseptic effect of pure ozone is three hundred times stronger than that of chlorine. Ozone has no destructive and irritating effect on tissues. Therapeutic doses of ozone have an antihypoxic, immunocorrective effect, potentiate the action of antibiotics, improve the rheological properties of blood and enhance microcirculation [18–22].

Ozone therapy increases the delivery of oxygen to tissues, inhibits lipid peroxidation, and activates the antioxidant system in the lesion [23–25]. One of the important properties of ozone is its antibacterial effect, and the absence of a selective effect for antibiotic-resistant strains, as well as the absence of other consequences of traditional drug antibiotic therapy [26–29]. There are few studies that confirm the effectiveness of these properties of ozone in the treatment of diseases of the oral mucosa, which encourages further research of the use of this method in the oral cavity.

MATERIAL AND METHODS

On the basis of VOXP in the city of Volgograd, 43 patients with erosive and ulcerative lesions in the oral cavity due to trauma were examined and treated. 30 patients were affected due to sharp edges of their teeth, failed fillings and substandard orthopedic structures. All patients were divided into 3 groups. At the end of the examination, the patients of all three groups underwent oral sanitation, professional hygiene, elimination of traumatic factors (replacement of fillings, grinding of sharp edges of teeth, replace-

ment of orthopedic devices). In the first group, therapy included applications of ozonated olive oil at a concentration of 5 mg/l lasting 15 minutes for 2 weeks. In the second group, patients were assigned to oxygen–ozone irrigation of the lesion for 10 minutes daily for 2 weeks. And in the third group, patients were assigned to apply Metrogil Denta gel for 15–20 minutes twice a day for a course of 7 days (traditional treatment). To assess the quality of treatment, we used: a clinical examination, including a survey, clarification of complaints, and a visual examination. For a more detailed study, a CITO-bacterioscopic study was used.

Statistical processing of the obtained results was carried out using the Statistica 10 application software package using Student t-test. Differences were considered significant at $p < 0.05$. To assess the relationship between different indicators, Pearson's linear correlation coefficient was used, the level of statistical significance of which began with $p < 0.05$.

RESULTS

The effectiveness of the treatment was evaluated on day 7 and 14 days later. When compared with traditional dental treatment, the advantage of using ozonated olive oil was noted. Already on the second day after the treatment, patients reported a decrease in pain. Less effective was the method of oxygen–ozone irrigation. The subjects of the third group, who were treated with Metrogil Denta applications, showed the worst results, and clinical improvement was noted on 6–7 days after treatment. Erosive and ulcerative lesions were fully epithelized in all patients within 14 days. Evaluating CITO-bacterioscopic indicators, we can draw the following conclusions: absence of macrophages, in the first and second groups and absence of coccal flora, in all three groups, as well as a decrease in the number of lymphocytes on the 7th day and after 14 days up to the minimum value of 1 that signals the resolution of inflammation. Quantitative evaluation of lymphocytes and coccal forms have a direct correlation. The reduction of the coccal flora index to zero indicates the effectiveness of antibacterial activity of all three treatment methods. High values of the *Candida* (fungus) population before treatment indicate an acute period, and a gradual decrease during treatment occurred due to the restoration of homeostasis of the affected area and normalization of the species composition of the microflora (Table 1).

CONCLUSION

As a result of the conducted clinical study, the advantage of ozone therapy compared to both conventional methods has been proved, and the statistical significance of differences was noted between the comparison groups at all periods of ablation. At the

same time, this method is more promising due to the absence of subsequent complications typically occurring during the use of dosage forms. Also, based on the data of CITO-bacterioscopic indicators, the process of inflammation was better and faster stopped in groups with the use of ozone, which can be explained by its other properties (antioxidant effect, restoration of microcirculation, etc.). The most effective method was a combination of ozone and olive oil, which can be explained by the additional keratoplastic effect of the oil, and the clinical reduction of pain symptoms was achieved due to the analgesic properties of ozone therapy. For laboratory confirmation of the findings, further study of ozone in comparison with anti-inflammatory drugs is necessary.

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Table 1. Dynamics of cytobacterioscopic indicators in patients with erosive and ulcerative lesions of the oral mucosa at different times after treatment, M=m (number in the field of view)

Indicator	Ozonated olive oil			Oxygen-ozone irrigation			Gel Metrogyl Denta		
	Before treatment	7 days	14 days	Before treatment	7 days	14 days	Before treatment	7 days	14 days
Macrophages	2,5±0,4	0,5±0,2*	0	2,3±0,1	0,9±0,3	0	2,6±0,3	1,5±0,1*	0,8±0,4
Neutrophils	17,9±1,7	4,5±0,3*	3,6±0,2*	17,4±2,4	5,5±1,8	4,2±0,6	16,5±1,5	6,8±0,4*	5,4±0,4*
Lymphocytes	4,3±0,3	1,2±0,4	0,5±0,1*	4,8±0,4	1,4±0,2	0,9±0,1	3,5±0,6	1,7±0,4	1,5±0,1*
Fungi of the genus Candida	10,4±1,3	4,2±0,1*	2,9±0,1*	10,6±1,7	5,6±1,2	3,5±1,2	11,1±1,5	6,1±0,4*	4,8±0,3*
Cocca flora	2,1±0,5	0,2±0,1	0	1,9±0,4	0,5±0,1	0	2,0±0,7	0,9±0,1	0

* — The statistical significance of differences between comparison groups, with $p < 0.05$

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EFFECT OF MAXILLARY ANTERIOR BRIDGEWORK ON PHONETIC ADJUSTMENT

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ABSTRACT — The paper presents results of prosthetic reconstruction in patients with anterior maxillary defects using sound analyzer software. The research was carried out involving spectrograms and sonograms acquired from patients prior to, and after the treatment. The data obtained by instrumental acoustic analysis of the spectrograms and sonograms conducted with our computer technology will help orthopedic dentists in planning and conducting respective orthopedic treatment and it will also help them avoid possible complications, thus increasing significantly the effectiveness of orthopedic treatment of the defects in the anterior dentition.

KEYWORDS — sound analyzer software, sonography, spectrography, acoustic analysis, permanent denture.

INTRODUCTION

The relevance of modern diagnostic methods in applied dentistry is determined by the high prevalence and intensity of dental diseases. The knowledge of diagnostic approaches, the principles of constructing and making a diagnosis is of great importance for medical practice, since the formulated diagnosis is the rationale for the tactics of therapeutic and preventive measures.

Loss of teeth is associated with various factors — complicated caries, trauma, severe periodontitis, removal of the *trouble* tooth through the inflammation (periostitis, osteomyelitis), etc. However, the effect is only one — a dentition defect development. The issues arising at treating such defects with prosthetics depend on the cause behind the loss of teeth; the time after their removal; the TMJ structural features [1, 7, 8], as well as other specifics of the body [2, 3]. In case of a lateral defect development, patients tend to take such issues in a more tolerant fashion, and treatment with

prosthetics can be delayed indefinitely, which is not the case with a defect in the anterior dentition, which requires immediate replacement.

While restoring a single tooth typically will pose no trouble, dealing with defects of medium length can raise a number of questions, one of which is identifying the inclination angle of the maxillary anterior teeth palatal surfaces, thus, apart from aesthetics, to recover the speech function hence facilitating the patient's adjustment to the prosthesis [4, 5, 9]. Answers to these questions allow the orthopedic dentist and dental technician to obtain fundamental basic information concerning the ratios within the patient's dentofacial system, which is needed to make high-quality orthopedic prostheses featuring proper functional and aesthetic specifics.

The methods for phonetic quality control in prosthetics that are available from respective literature, focus on improving the pronunciation of speech sounds while using removable dentures [6, 10]. Searching through literature, we failed to find any sufficiently reliable methods and criteria for assessing the quality of prosthetics with a fixed structure. At the same time, more and more attention is paid to the improving the quality of dental treatment.

Aim of study:

to increase prosthetics effectiveness for patients with anterior maxilla dentition defects.

MATERIALS AND METHODS

Depending on the anterior dental arch status, we identified 3 groups of patients. Group 1 — 30 people with intact dentition, orthognathic bite and with no articulation issues, which made up the control group. Group 2 — patients with restored defects of the anterior dentition who had bridgework installed previously and who complained of diction issues — the comparison group. Group 3 — patients who underwent examination and orthopedic treatment in view of the upper jaw morphometric features — the main group.

To identify the relationship between the palatal vault configuration and the anterior teeth palate surface inclination angle in case of articulation issues, we developed a measuring device (Patent RU 53141 U1), as well as a method for identifying the palatal vault angles and the anterior teeth palate surface inclination angles (Patent RU 2314060 C1). The measurements were

done based on graphic displays of the palatal vault and teeth curved sections in the sagittal plane with respect to the horizontal plane. The length of the palatal vault was measured from the interdental papilla (at the central incisors approximal surfaces) to the line formed by the intersection of the median palatine suture with a line drawn at the level of the alveolar processes apex between the second premolars and the first molars (the depth of the palatal vault). This length was divided into three equal parts: alveolar, middle and palatal.

RESULTS AND DISCUSSION

Through the study, we found that the inclination angle of the anterior teeth palatal facings varied from 34° to 55° with an average of 45.6°, while the inclination angle of the anterior palatal vault middle third was equal to the inclination angle of the palatal facings of the anterior teeth with an accuracy of 84%, to range between 32–57°, whose average value was 45.1°.

Therefore, in 84% of the cases, the inclination angle of the anterior palatal vault middle third was equal to the inclination angle of the anterior teeth palatal facings. To obtain an objective assessment of the phonetic adjustment to the installed bridgework, we opted for spectrographic and sonographic analysis of the speech produced by patients (software — sound analyzers Steinberg Wavelab V5.01b, and Algorithmix renovator 2.1). The nature of the deficient pronunciation changed depending on the upper anterior teeth palatal facings inclination angle, and on the inclination angle of the palatal vault middle third.

In case of the upper front teeth retrusion, when the cutting edge can touch the inside lower lip rather low, we observe an additional overtone and a linkage sounding close to the German [pf] pronunciation (affricate). This is to be observed clearly on the spectrogram of the Russian word transcribed as [ˈflanets] uttered by a patient wearing a prosthesis installed previously in an outpatient setting. This overtone lies within a range of 3 to 10 kHz, which is perceived by a common ear as German [pf].

Similar issues lie behind the vowel overtone appearing through transition from the dorsal [ɹ] / [d] to the non-dorsal [də], so instead of pronouncing it like [dɔɹ], we would get something like [dəwɔɹ], or [təɹɔs] rather than [trɔs], etc.

In patients who had the palatal vault inclination angle of the prosthesis significantly below the inclination angle of the anterior palatal vault middle third, up to 15°, with the upper front teeth protrusion, the pronunciation of [z] / [s] was perceived as flat-aperture, as if hissing.

The spectrogram of the word [trɔs] pronounced by a patient with a bridgework made in an outpatient

clinic shows clearly that the sound [s] takes a frequency of 0.5 through 10 kHz, which is more typical of the sound [ʃ] (-sh-). The orthopedic treatment helped eliminate the defect, and the control spectrogram shows a narrowing spectrum of the sound [s], as well as its shift towards higher frequencies, which corresponds to the pronunciation norm.

CONCLUSION

In view of the above, the instrumental acoustic analysis data obtained by sound analyzer software confirms significant improvements in the pronunciation of sounds whose development is associated with the anterior upper dentition. Spectrogram and sonogram acoustic analysis done via computer technology will help orthopedic dentists in orthopedic treatment, as well as may help them avoid possible complications, which will contribute significantly to the effectiveness of orthopedic treatment offered for anterior upper dentition defects.

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DENTAL STATUS OF GERIATRIC PATIENTS WITH PRE-EXISTING CONDITION

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ABSTRACT — This study was conducted with the aim of a dental examination of elderly patients and investigation of the relationship between dental and somatic diseases. 70 geriatric patients aged 60–89 years underwent dental examination and their dental status was determined (by conducting a standard oral examination, which consists of taking the anamnesis, check-up, evaluation of the hygienic condition, the intensity and prevalence of caries and non-carious lesions) and identification of a somatic disease. As a result, a relationship between diseases of the hard dental tissues, periodontium and oral mucosa and pre-existing condition was detected. Absolutely all respondents needed individualized routine hygiene and dental treatments followed by orthopedic treatment to restore adequate chewing function. The study showed that the relationship between a somatic pathology and the condition of the oral cavity reflects the comorbidity of diseases. To choose treatment tactics, it is necessary to take into account not only the severity and course of the underlying disease, but also the presence of concomitant pathology of different body systems. Therefore, the treatment of geriatric patients should be carried out in collaboration with a general practitioner for a unified approach for monitoring such patients.

KEYWORDS — geriatric patients, dental examination, pathology of the hard dental tissues, somatic diseases.

INTRODUCTION

In accordance with the requirements of the World Health Organization, in the process of examining a dental patient, a certain diagnostic sequence must be followed with the planning and use of various laboratory and clinical research methods [1–11]. The past decades have been characterized by demographic processes leading to an increase in the proportion of elderly population, which is common for most countries of the world, including Russia. Dental examination of these patients is difficult due to their low mobility, high disability and social disorientation [12]. The high prevalence of dental diseases in elderly

populations can be accounted first of all by the fact that the maxillofacial region becomes susceptible for age-related morphological and physiological changes. At the same time old age implies the presence of one or more concomitant diseases, which not only aggravates a dental problem, but also impedes its treatment [13]. However, at the moment, the choice of tactics for the treatment of oral diseases does not take into account the relationship with systemic disharmony of the body.

The aim of the study

is to conduct a dental examination of geriatric patients with accompanying pathology and to investigate the relationship of dental diseases to systemic illness.

MATERIALS AND METHODS

A dental examination was conducted in 70 elderly patients aged 60–89 years, WHO-classified elderly (60–74 years) and senile (75–89 years). The comprehensive examination included the use of basic and complementary methods of examination: collection of anamnesis, oral examination, determination of caries indicators of prevalence, non-caries lesions, caries intensity — index of KPU, hygienic composition of the oral cavity IS (ONI-simplified index) Green-Vermillion examination, periodontal condition with the Russell's periodontal index was carried out. X-ray examination was performed if necessary. As a result, treatment needs of the patients were identified, as well as the relationship of somatic pathology with oral diseases was investigated.

RESULTS AND DISCUSSION

As a result of the examination, we identified 100% need for dental integrated treatment of the elderly patients. At the same time 68 people (97.1%) revealed pathology of hard tissues of teeth. Mainly, caries and their complications (59 people — 86.7%) were detected in patients, 13.3% were non-carious lesions. However, we have found that the localization of lesions correlates with concomitant diseases. When located on chewing and drug surfaces, patients indicated the presence of gastrointestinal pathology. The presence of lesions in the cervical region indicated endocrine pathology, predominantly diabetes mellitus and thyroid diseases. A high degree of caries intensity was determined in all patients. So KPU was 21, 8 ± 1.2 , which is probably due to the presence of somatic pathology. At

the same time, there is no consensus in the domestic and foreign literature, which is the root factor in the development of somatic or dental pathology.

67 patients (95.7%) showed poor oral hygiene. Index Green-Vermillion (OHI-S) was $4, 7 \pm 0.22$. This is probably due to two factors: on the one hand - insufficient oral care, on the other — hyposalivation of the examined persons, and saliva does not perform its main functions (trophic, cleaning, protective). In addition, patients also complained about oral dryness. Apparently xerostomy is due to physiological atrophy of salivary glands. Accompanying pathology exacerbates this process. We observed the greatest dryness of oral mucosa in patients with thyroid diseases and type 2 diabetes mellitus. At the same time, in this category of persons there were multiple non-caries caused by saliva deficiency, as saliva, performing in full trophic function, is a source of phosphorus, zinc, calcium.

Periodontal diseases have been detected in 100% of cases. Among them, moderate and severe periodontitis prevails — 65 people (92.8%). The Russell periodontal index (PI) was $5, 8 \pm 0.33$, corresponding to stage III of the disease. In this category of people, endocrine diseases, atherosclerotic vascular lesions, kidney diseases were noted as a concomitant pathology. Also, the above-mentioned pathologies were often of a combined nature. A 5 person (7.2%) was diagnosed with periodontitis complicated by moderate periodontitis in remission. When filling an anquet as a concomitant pathology, patients noted thyroid hypofunction. We did not observe idiopathic periodontal diseases in this study. It should be noted that in the oral cavity of the examined persons there was an increased erasability of hard tissues of teeth. In view of the above, all patients examined needed orthopedic treatment to restore dental integrity and adequate chewing function.

However, in addition to the pathology of dental hard tissues and periodontal diseases, we also observed lesions of the mucous membrane of the oral cavity. In patients with the expressed symptom of *dry mouth*, the prints of tooth crowns on the mucous membrane of the cheeks, *bubble-vascular* syndrome in arterial hypertension, inflammatory diseases of the mucosa of the oral cavity and lips: chronic recurrent aphthous stomatitis, angular cheilitis, etc. — in diseases of digestive tract. Language cover and swelling were present in 35 people (50%), of whom 87% have digestive tract pathology, 82% — endocrine pathology.

CONCLUSION

Geriatric patients are a population that requires increased attention from a dentist. In 100% of cases, a dental pathology has been detected. At the same

time according to the localization of caries in most cases it is in the neck area, which is connected with both hyposalivation and periodontal pathology. In case of disruption of trophic function of saliva, in case of accumulation of food residues favorable conditions for development of caries and its complications are formed. When choosing treatment tactics, it is necessary to take into account not only the degree of severity and course of the main disease, but also the presence of accompanying pathology of different systems of the body. The study showed that the relationship between somatic pathology and oral condition reflects the comorbidity of diseases. Therefore, the treatment of geriatric patients should be carried out in a comprehensive manner with a general physician for a single approach to the observation of such patients. Thus, it has been established that dental diseases and their degree of expression are directly dependent on the presence of a pre-existing condition and the severity of its manifestations. However, the identification of the primary cause and elaborating a comprehensive, differentiated approach to the therapy and prevention of dental diseases demand a long-term careful attitude, which provides justification for further research.

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METHOD FOR QUANTITATIVE ASSESSMENT OF DENTOFACIAL ANOMALIES IN CHILD AND ADOLESCENT ORTHODONTICS

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ABSTRACT — The paper deals with the practical application of the AMORF method for quantitative assessment of dentofacial anomalies. The proposed method allows quantifying such signs of dentofacial issues as facial aesthetics, morphology of the skull facial part, occlusion, periodontal bone tissue resorption in the sagittal, vertical, and transverse planes, as well as functional issues, close position of the teeth, their retention, root resorption and adentia. The applied focus of the AMORF method for quantitative assessment of dentofacial anomalies allows enables to select appropriate therapeutic options, and, judging the severity of the signs at the final stages of treatment, its effectiveness can be evaluated.

KEYWORDS — quantitative assessment of dentofacial anomalies, close teeth, retention, resorption adentia, sagittal plane, vertical plane, transversal plane, orthodontic treatment of children/adolescents.

INTRODUCTION

Orthodontic treatment for children and adolescents is a serious issue since it is most often associated with active growth, while cooperation and oral hygiene issues in some cases turn a stumbling block coupling with the patient's lack of motivation. Given that, the treatment plan may have to be altered through the course more often compared to the treatment of adult patients. The authors have offered convincing proof showing an increase in the role played in clinical dentistry by morphological, anthropometric, and functional research methods [1–10].

Orthodontists, therefore, often have to answer

questions like *What is the treatment tactics if based on the severity of dentofacial anomalies?, How did the signs of dentofacial anomalies change through the treatment?, Is the treatment outcome to be seen as positive or negative?*

Maxillofacial anomalies are associated with morphological, aesthetic and occlusal signs, periodontal bone resorption, close tooth position, their retention and adentia, root resorption, as well as functional disorders. The severity of these signs can vary significantly, and a change in one of them will not necessarily lead to a proportional change in the others. Facial aesthetic features, for instance, are above all influenced by the bone structures that determine their relief. These include the upper and the lower jaws, the asymmetry of which causes the contours deformation in the middle and lower face. However, soft tissue compensation must be taken into account, too. In some clinical situations, they can mask disturbances affecting occlusion and the structure of the skull facial part, while significant occlusal disorders can come combined with significant changes in facial aesthetics [11–12].

There is an obvious need for a quantitative assessment of dentofacial anomalies as the same qualitative diagnosis may imply treatment plans that are different in the scope, timing, cost, and long-term results [13–16].

The listed signs of dentofacial anomalies should be considered in the sagittal, vertical and transverse planes [17, 18].

Quantitative methods include the DAI Aesthetic Index (Dental Aesthetic Index; Cons N. et al., 1986) and the index for assessing the need to correct dentofacial anomalies, and the ICON index (Index of Complexity, Outcome & Need; Daniels C., Richmond S., 2000). However, note to be made that they only allow assessing occlusal signs, leaving out the rest of them, which offers an incomplete image of the dentofacial anomalies [19, 20].

In view of the above, we have developed and tested (involving over 5,000 patients with dentofacial anomalies) the AMORF method for quantitative assessment (A — Aesthetics, M — Morphology, O — Occlusion, R — Resorption, F — Function), which allows distinguishing 3 degrees of severity in the aesthetic, morphological, and occlusal disorders, as well as evaluating the resorption of periodontal bone

tissue in the sagittal, vertical, and transverse planes; 3 degrees of functional disorders; close position of the teeth, their retention, root resorption, and 2 degrees of adentia.

Practical application

The severity of each dentofacial anomaly symptom is identified subject to the AMORF quantitative assessment method, with all the data entered in Table 1. Next, the total numerical indicators by blocks are identified, before treatment and at the end of that, while the final conclusion regarding the treatment effectiveness is done based on the proportion where the total numerical indicator before treatment is taken as 100%, and the total numerical indicator at the end of treatment, expressed per cent, is an indicator of the treatment effectiveness, which is interpreted as follows: up to 25)% — significant improvement; [25–45)% — largely improved; [45–65)% — mildly improved; [65–85)% — minimal improvement; [85% and above — not improved or worsened, where square brackets mean *including*, round brackets — *value is not included in the numerical range*.

from a medical history thus demonstrating the potential of the AMORF method practical application.

Patient T, 12 y.o.; self-referred; came to the clinic complaining of the upper teeth uneven position; obstructed nasal breathing and speech production. The diagnosis was: upper and lower retrognathia; anterior inclination of the lower jaw; upper and lower incisors retrusion; narrowing of the upper and lower jaws; cross bite; close position of the teeth. Table 2 shows that before treatment the major disorders included aesthetics in the sagittal and vertical planes, as well as the teeth close position — they corresponded to Degrees 2 and 3 of severity, respectively. Functional disorders were obstructed nasal breathing and speech production, which corresponded to Degree 2 of severity.

Based on the diagnostic examination and recommendations on the choice of treatment tactics, the following plan was proposed to correct the maxillofacial anomaly: 1. The palate expander on the upper jaw and at the same time the labial bumper on the lower one, in order to improve the nasal breathing as well as to correct the close position of the teeth. 2. Braces on the

Table 1. AMORF-based quantitative assessment of dentofacial anomaly signs prior to/after treatment

PLANE	A	M	O	R	F
sagittal	before/after	before/after	before/after	before/after	before/after
vertical	before/after	before/after	before/after	before/after	
transverse	before/after	before/after	before/after	before/after	
SIGN	Degree 1		Degree 2		Degree 3
close position	before/after		before/after		before/after
retention	before/after		before/after		before/after
root resorption	before/after		before/after		before/after
adentia	before/after		before/after		

Note. From here on, ordinary font is used to show the common degree of the dentofacial anomaly signs prior to the treatment; bold font is used for signs after the treatment

The AMORF quantitative assessment method allows a comprehensive assessment of morphological, aesthetic, occlusal signs, periodontal bone resorption in the sagittal, vertical and sagittal planes, as well as it offers a way to assess close position of teeth, their retention, root resorption and adentia. The proposed method, if applied in clinical practice, allows, based on the severity of certain signs, understanding the etiology and pathogenesis of the dentofacial anomaly; selecting the right treatment tactics, as well as judging its effectiveness based on the change in the severity after the treatment. Here below we are offering an excerpt

upper jaw and an occlusal splint on the lower jaw until complete inclusion of teeth 1.2 and 2.2 in the dentition. 3. Fixed braces on the lower jaw, creating multiple fissure-tubercular contacts. 4. Removing the braces; retention period and observation. The main stages of orthodontic treatment can be seen in figures 1–8.

Treatment effectiveness assessment in Patient T (Table 2) based on the AMORF quantitative assessment method: A4M2O2R0F2+3 → A2M1O1R0F0+0

Before treatment: 13 — 100%

After treatment: 4 — 30.77%

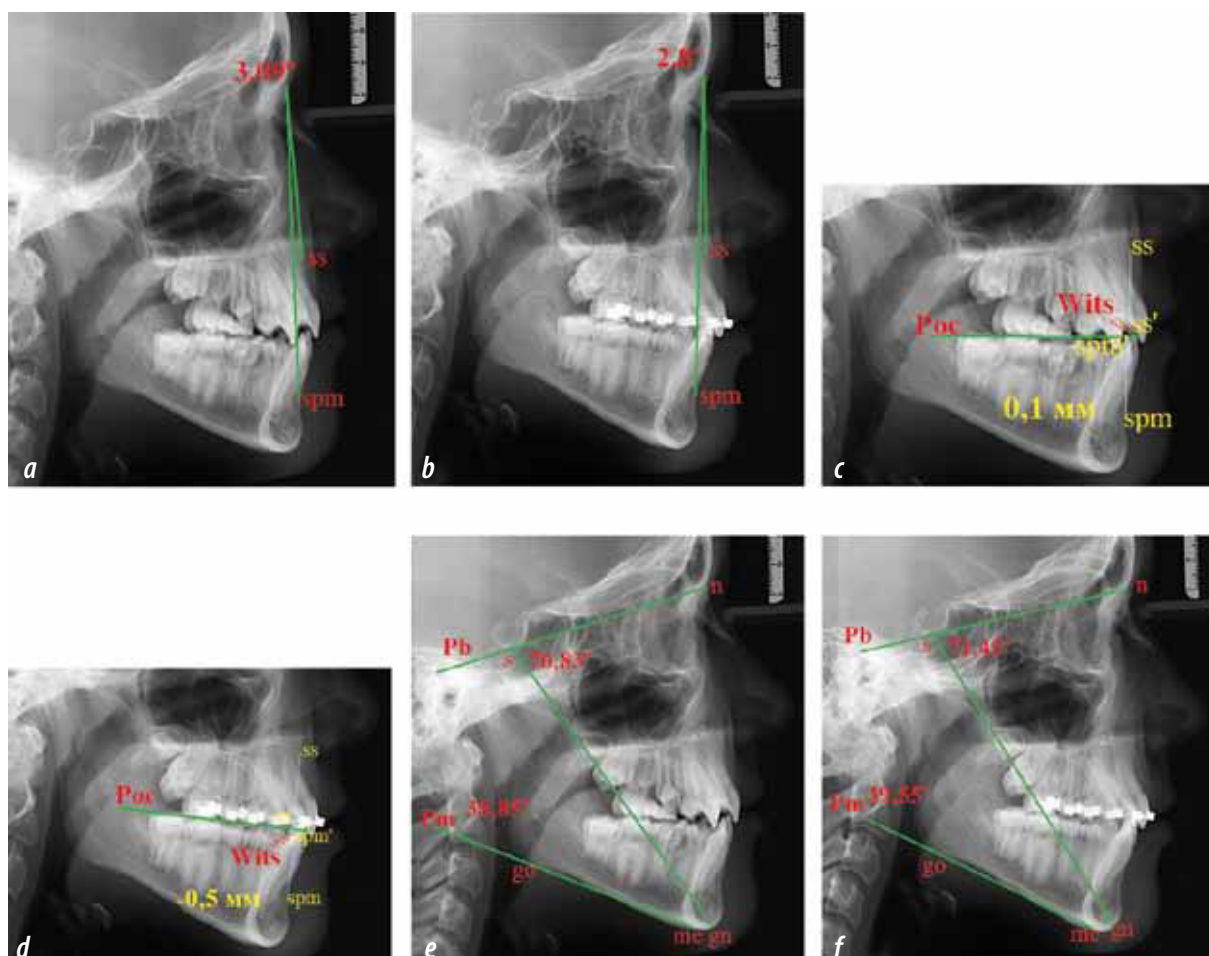


Fig. 1. Patient T's skull lateral telerradiographies, before (a, c, e) and after (b, d, f) treatment — the ss-n-spm angle value corresponds to Degree 1 of morphological disorders severity in the sagittal plane before treatment (a), and within norm — at the end of it (b); the Wits parameter values correspond to the norm before (c) and after treatment (d); the values of the n-s-gn and Pm / Pb parameters correspond to Degree 1 of morphological disorders severity in the vertical plane before treatment (e) and at its end (f)

The treatment effectiveness is interpreted here as largely improved.

CONCLUSIONS

1. In order to assess face structure disturbances, as well as treatment outcomes, it is reasonable to employ quantitative assessment methods. The proposed AMORF quantitative assessment method may be a good option.

2. Using the AMORF method of quantitative assessment for dentofacial anomalies allows choosing the orthodontic treatment tactics and, if needed, to find grounds for the treatment adjustment, as well as judging the effectiveness of the treatment upon completion.

3. Quantitative assessment of dentofacial anomalies allows demonstrating to patients and their parents the positive effect of the joint efforts taken by the doctor and the patient through the orthodontic treatment. This is especially important for growing patients, when orthodontic treatment takes long, including active growth periods of the facial part of the skull, and requires cooperation on the part of the patient when it comes to the use of intra- and extraoral devices.

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Fig. 2. Photographs of patient T's face before (a, c, e) and after (b, d, f) treatment: the Kn-sn-Kspm and Kn-prn-Kspm values correspond to Degree 2 of facial aesthetics severity in the sagittal plane before treatment (a) and 1 — upon its completion (b); the values of the gl'-sn' / sn'-Kme relationship correspond to Degree 2 of facial aesthetics severity in the vertical plane before (c) and 1 — after treatment (d); Kgn' — (Kn-sn) values correspond to the norm (e, f)

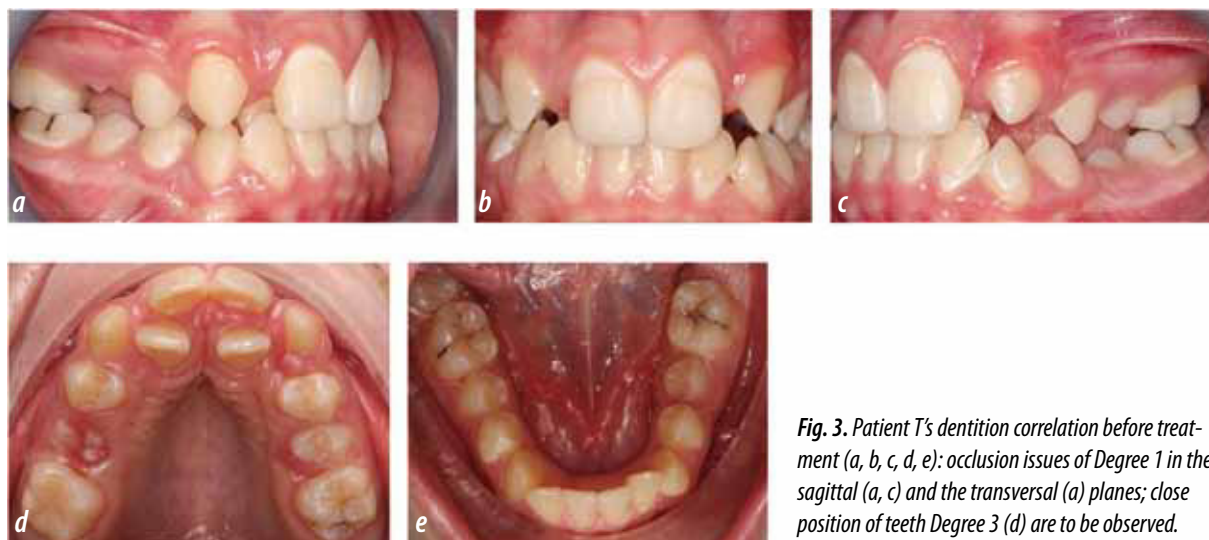


Fig. 3. Patient T's dentition correlation before treatment (a, b, c, d, e): occlusion issues of Degree 1 in the sagittal (a, c) and the transversal (a) planes; close position of teeth Degree 3 (d) are to be observed.

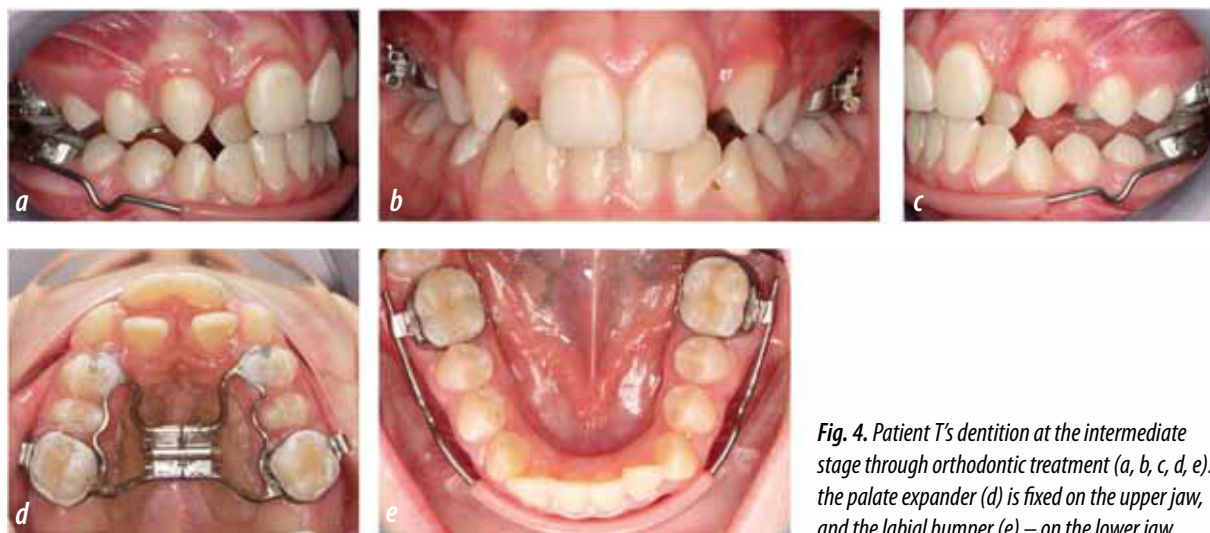


Fig. 4. Patient T's dentition at the intermediate stage through orthodontic treatment (a, b, c, d, e): the palate expander (d) is fixed on the upper jaw, and the labial bumper (e) – on the lower jaw



Fig. 5. Patient T's dentition at the intermediate stage through orthodontic treatment: braces (a, b, d, e, f) installed on the upper jaw, and an occlusal splint — on the lower (c)

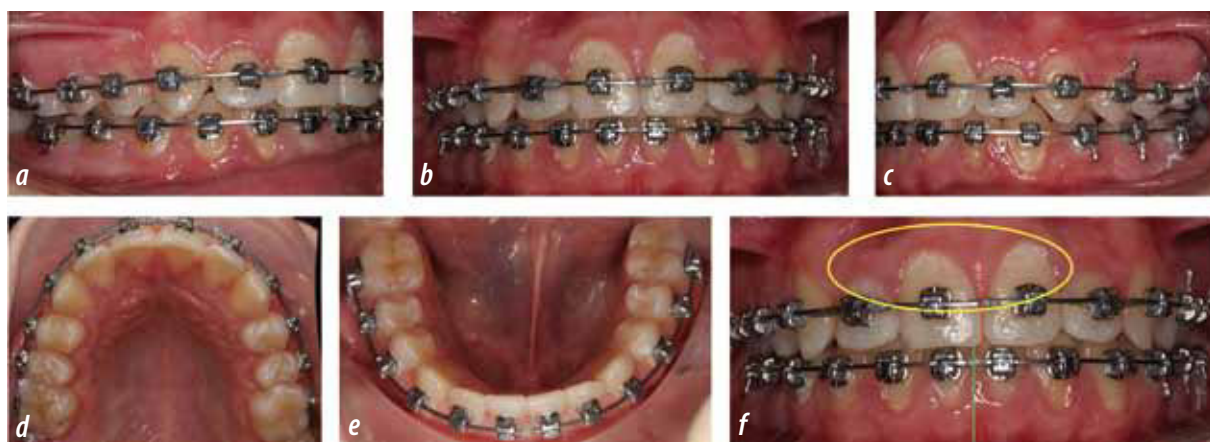


Fig. 6. Patient T's dentition before removing the braces: a slight discrepancy between the center lines of the upper and lower dentition (f) along with satisfactory fissure-tubercular contacts (a, b, c). Poor oral hygiene (f) in this case was an indication for premature removal of the device

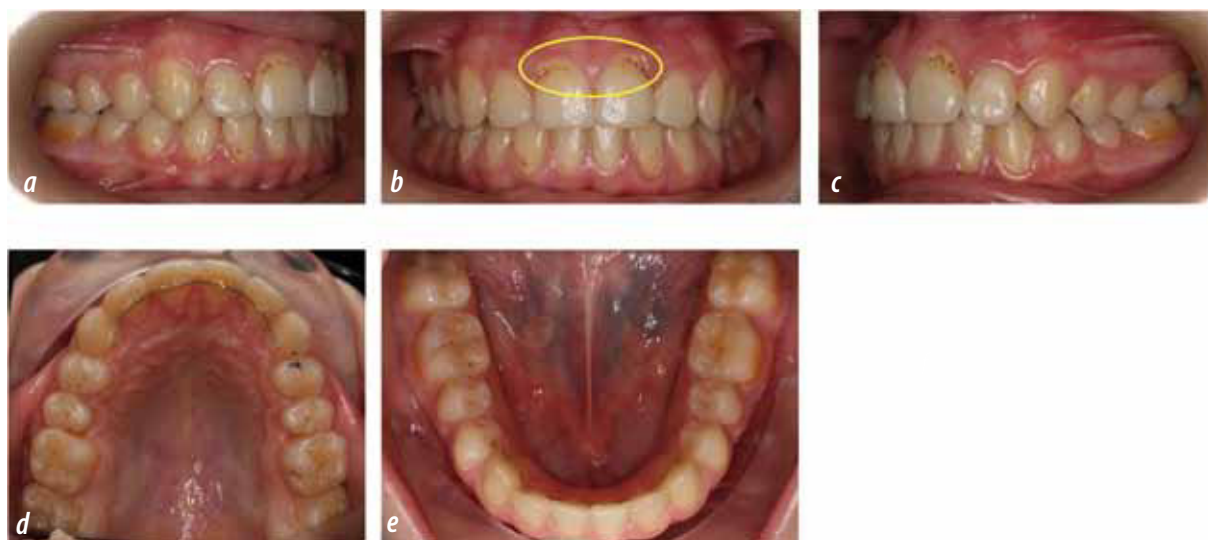


Fig. 7. Patient T's dentition one year after orthodontic treatment (a, b, c, d, e): oral hygiene got worse (b), while the dentition occlusion is stable

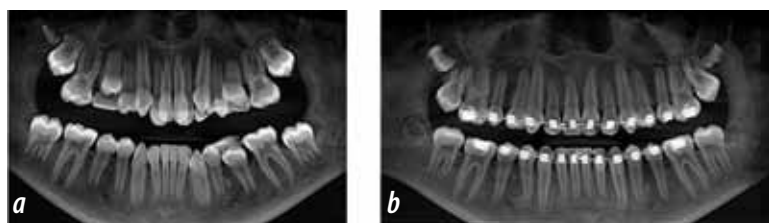


Fig. 8. Patient T's dentition CT section before treatment (a) and before the device removal (b)

Table 2. AMORF-based quantitative assessment of dentofacial anomaly signs prior to/after treatment

PLANE	A	M	O	R	F
sagittal	2/1	1/0	1/0	0/0	2/0
vertical	2/1	1/1	0/0	0/0	
transverse	0/0	---/---	1/1	0/0	
SIGN	Degree 1		Degree 2		Degree 3
close position	-----		-----		+/-0
retention	-----		-----		-----
root resorption	-----		-----		-----
adentia	-----		-----		-----

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UNDIFFERENTIATED CONNECTIVE TISSUE DYSPLASIA AS A KEY FACTOR IN PATHOGENESIS OF MAXILLOFACIAL DISORDERS IN CHILDREN AND ADOLESCENTS

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ABSTRACT — In order to detect pathomorphological changes and identify the severity of maxillofacial disorders, 137 children with different degrees of connective tissue dysplasia (CTD) and 46 healthy children were examined by means of cone beam computed tomography to check their X-ray morphometric index as well as lower jaw optical density index. At the same time, the quantitative ultrasonic densitometry method was employed to evaluate the status of the peripheral skeleton bone tissue. The quantitative X-ray morphometric index in healthy children and children with CTD were found to have strong positive correlation with the osteodensitometry Z-criterion, reflecting reliably the bone tissue status in the peripheral skeleton. The progression of connective tissue dysplastic disorders in children, which correlates with the intensity of maxillofacial bone structures destruction and the severity of collagen degradation mechanisms, was accompanied by an increase in chronic productive inflammation; reduced in x-ray density; fibrous transformation of bone tissue; a decrease in the thickness of the lower jaw cortical plate and its dissociation; predominance of medium- and fine-meshed bone pattern; impaired space orientation and thinning of the bone trabeculas as well as pathological processes in the periodontium.

KEYWORDS — connective tissue dysplasia, child population, X-ray morphometric index, cone beam computed tomography, ultrasound osteodensitometry, maxillofacial area.

INTRODUCTION

The growing interest in connective tissue dysplastic disorders in childhood is due to the following factors: high prevalence (9.8–35.7%) with stable growth dynamics; multiple affected areas; predisposition to chronic nature of acute processes; significant polymorphism of clinical and morphological manifestations;

difficulties in diagnosing certain clinical types; longer course of concomitant diseases; low effectiveness of treatment plans; longer convalescence; need to make additions to the treatment and diagnostic protocols as well as to include corrective therapy. In children with CTD, the frequency of referrals for medical assistance is six times as high compared to other groups of patients [1–3].

CTD is a nutritionally and genetically predetermined disorder affecting the development of connective tissue at the embryonic and postnatal stages, which manifests itself through defects in the main substance and fibrous structures, leads to homeostatic disorders at the levels of the body, inner organs and tissues, and features morphological and functional disorders of the locomotor and visceral organs with a progressive course, which determines the specifics of associated pathologies (Kadurina T. I., 2008).

The data accumulated by respective experts confirm that the connective tissue origin is to be found mainly in all maxillofacial components, while the structural and functional components of the connective tissue are actively involved in inflammatory, destructive and protective processes in various acute and chronic pathological conditions. There is special note to be made regarding the high prevalence of carious tooth lesions, periodontal pathologies, temporomandibular joint (TMJ) issues, dentofacial deformities and abnormalities, as well as occlusal disorders [4–12].

The authors have offered convincing proof showing an increase in the role played in clinical dentistry by morphological, anthropometric, and functional research methods [13–34]. The use of high-precision methods of X-ray examination allows not only minimizing the radiation harm to patients of all age categories, yet also analyzing the anatomical and topographic craniofacial features, as well as early and differential diagnostics of various diseases affecting jaw bones, periodontium, teeth, skull sinuses, and TMJ [35–47].

The need for a detailed study of the maxillofacial area of children belonging to the “critical” age groups is due to morphological and functional features, as well as to the intensive development and growth of their

organs and systems along with instability (lability) of dentofacial structures [48–60].

Until now, the available research data on the role of CTD in the development of child maxillofacial pathology has been fragmented. Also, there is no information available on peripheral skeleton bone strength in relation to the reference base of ultrasound osteodensitometry in children with CTD. Given that, studying the pathogenesis of the maxillofacial pathology in children with CTD through critical life periods appears relevant, while this is not only of diagnostic yet also has clinical value when explaining the tactics and monitoring the effectiveness of treatment and rehabilitation measures.

Aim of study

identification of pathomorphological maxillofacial changes in children with CTD based on X-ray morphometry of the lower jaw and the peripheral skeleton ultrasound osteodensitometry.

MATERIALS AND METHODS

As part of the work, 2013 through 2020 comprehensive clinical, paraclinical, and laboratory-instrumental studies were carried out involving 137 adolescents (76 girls, 61 boys; aged 12–16) with general somatic pathology and severe set of CTD symptoms, who were treated in the Pediatric Department of Filippsky Child Clinical Hospital (Stavropol, Russia). The diagnostics of undifferentiated CTD included the following symptoms: a minimum of six clinical and instrumental signs of connective tissue dysplasia; spread of the pathological process onto two or more organs (multi-organ nature) and systems (polysystem nature); signs of familial accumulation of collagenopathy (family history); biochemical and immunohistochemical evidence of impaired connective tissue metabolism (recommendation by T.I. Kadurina, 2009).

The evaluation of the adolescents' body structure, level of their individual physical development, harmoniousness in physical development, was done employing the Stuart scale, the WHO mass & height tables (WHO Standard, 2006), as well as anthropometric indices. Arachnodactyly and dolichostenomelia were diagnosed using the respective coefficients (Nechaeva G.I., 1994). Joint hypermobility was detected base on the P. Beighton criteria (1999). The muscular system status, the severity and the nature of the deformities affecting the thorax (Fokin A.A., 1984), the spine (Abalmasova E.A., 1973), and the lower extremities (Kadurina T.I., 2000) were evaluated.

Depending on the severity of external phenotypic manifestations and laboratory, clinical and instrumental signs, assessment of the CTD severity was done following the recommendations by L.N. Abbakumova,

T.I. Kadurina (2008). In view of only external phenotypic characters, a mild degree of CTD corresponds to the total score below 24, a moderate degree to 24–34 points, while a severe degree of CTD scores a total of 35 or above. When doing laboratory and clinical-instrumental examination, a mild degree of CTD corresponds to a total score of less than 30, a moderate CTD degree means a score ranging between 30 and 44, while a severe degree would score 45 or more. The final diagnosis of CTD was set taking into account the diagnostic tables for the child category where the diagnostic level was +70 (E.P. Timofeeva, 1996).

Children with CTD (main group) were divided into three subgroups: Subgroup 1 — mild degree ($n = 39$); Subgroup 2 — moderate degree ($n = 47$); Subgroup 3 — severe degree ($n = 51$). The control group included 46 *healthy* and *basically healthy* (Health Groups I & II) adolescents (Yu. E. Veltishchev, 1994), comparable in age and gender.

Bone mineral density indices were diagnosed on an Omnisense 7000 ultrasound densitometer equipped with a special computer software for children; the SOS ultrasound wave velocity (m/s) in two points of the skeleton — in the middle of the tibia and at the radius' distal third. We identified the Z-score, which is the standard deviation of the actual bone strength in relation to the child's average age norm, and is expressed in SD — mean square deviations units from the average peak values. The obtained bone tissue evaluation data was compared to the Russian age standards (L. Shcheplyagina, 2006) and percentile table data of the respective ages for the ultrasonic densitometer. Subject to the recommendations of ISCD, the criteria for bone strength in children were used employing the Z-score: $SD \geq 0$ (normal bone strength); SD ranging from -1 to 0 (a decrease tendency in the bone strength); SD from -2 to -1 (mild decrease in the bone strength); $SD \leq -2$ (significant decrease in the bone strength) (Fig. 1).

Dental volumetric tomograms and orthopantomograms were performed in the child imaging software on a KaVo OP300 Maxio cone beam computed tomograph with cephalostat using the LowDoseTechnology™. The data was processed using the OnDemand3D™ Dental and OnDemand™ Project Viewer software products. The orthopantomograms were used to evaluated the quantitative indices (FI — Fuchs index, GI — Gonion index, AI — Antigonion index, MI — Mental index, X-ray index — X-ray examination index, PMI — panoramic mandibular index) and one qualitative (MCI — Mandibular Cortical index). The x-ray density of bone tissue (Hounsfield units; HU) was identified on 3D mode computed tomograms.

The interalveolar septa resorption degree relative to the tooth root length was determined through the



Fig. 1. Quantitative ultrasound examination of the distal radius and tibia using an Omnisense 7000 densitometer

Fuchs index. The evaluation codes for the FI were: 0 — tooth outside the bone tissue or the tooth is missing due to a periodontal pathology; 1 — bone resorption of more than $\frac{2}{3}$ of the root length; 2 — bone resorption ranging from $\frac{1}{3}$ to $\frac{2}{3}$ of the root length; 3 — bone resorption up to $\frac{1}{3}$ of the root length; 4 — lack of the alveolar bone resorption. The formula for calculating follows below:

$$\text{Fuchs Index} = \frac{(n \cdot 0) + (n \cdot 1) + (n \cdot 2) + (n \cdot 3) + (n \cdot 4)}{\text{number of teeth}}$$

Evaluation scale: bone resorption at the apex level — 0 points; bone resorption exceeding $\frac{2}{3}$ of the root length — 0.25 points; bone resorption ranging from $\frac{1}{3}$ to $\frac{2}{3}$ of the root length — 0.5 points; bone resorption up to $\frac{1}{3}$ of the root length — 0.75 points; no loss of bone tissue — 1 point (Fig. 2).



Fig. 2. Fuchs Index

The cortical plate thickness was determined based on the J. Bras et al. method (1982) — GI, and the D. Ledgerton et al. method (1999) — AI.

The GI determination method: a tangent is made at the lower jaw angle; further, a perpendicular is restored from the point of intersection with the mandibular angle.

The AI determination method: a straight line is drawn along the front border of the lower jaw ascending branch. Next, a tangent is made to the intersection with the lower border of the lower jaw, followed by restoration from this point of the perpendicular. In both methods, the cortical plate thickness is calculated along the perpendicular (Fig. 3).

The alveolar bone resorption degree was determined through the A. Taguchi et al. method (1993) — MI, and with the X-ray examination index — X-ray index.

The MI determination method: in the foramen mentale projection a tangent was made to the lower border of the lower jaw, after which a perpendicular



Fig. 3. GI — Gonion Index, AI — Antigonion Index

passing through the foramen mentale center was restored. The distance ratio from the alveolar process edge to the mandible lower border, to the distance from the foramen mentale center to the mandible lower border, was calculated.

The X-ray index determination method: in the foramen mentale projection, a tangent was drawn to the lower border of the mandible alveolar part, to which the perpendicular passing through the center of the foramen mentale was drawn. Through the Autodesk AutoCAD Architecture 2018 software (2D format), the ratio of the lower jaw alveolar part to the tooth root total length was calculated (Fig. 4).

To improve the reliability of the data concerning the intensity of destructive processes in the mandibular bone, three variations of the PMI index were calculated — upper, middle and lower (D. Ledgerton et al., 1997).

The PMI determination method: below the foramen mentale, parallel to the mandibular bone lower border, a tangent was drawn. Further — a perpendicular passing through the center of the foramen mentale is made. The following values were calculated along the perpendicular: A — the cortical layer thickness; B — the distance between the foramen mentale lower edge and the mandibular bone lower border; C — the distance between the foramen mentale upper edge and the mandibular bone lower border. The distance between the foramen mentale center and the mandibular bone lower border was calculated as the half-sum between B and C. The PMI value was calculated as follows: the upper PMI is the ratio of the cortical plate thickness at the foramen mentale level to the distance between the mandibular bone lower border and the foramen mentale upper point; the lower PMI is the ratio of the cortical plate thickness at the foramen mentale level to the distance between the mandibular bone lower border and the foramen mentale lower point; the medium PMI is the ratio of the cortical plate thickness at the foramen mentale level to the distance between the mandibular bone lower border and the foramen mentale center. In case there was lack of a clear visualization of the upper part of the mandibular bone lower cortical plate, we used the lowest thickness value of the compact plate located below the foramen mentale (Fig. 5).

Qualitative description of the cortical plate, located below the foramen mentale, was carried out by the E. Klemetti method (1994) — MCI. The evaluation criteria for morphological types were: C1 — smooth and clear inner border of the cortical plate; C2 — the cortical layer border features single crescent defects with bilateral or unilateral stratification of the plate; C3 — the cortical plate is porous, featuring

a multilayer structure, with many defects, while the border is unclear and uneven (Fig. 6).

The mandible bone tissue optical density was identified based on the results of a mathematical reconstruction of the attenuation coefficients following the classifications by U. Lekholm and G. Zarb (1985), C. Mish (1992). Densitometric parameters (HU) offered reliable description of the x-radiation loss degree by the bone tissue. Subject to C. Ulm's recommendations (2009), the mandibular angle and the lower jaw body at the second premolar were used as *interest zones* (Fig. 7).

The mandible cortex thickness was identified at the foramen mentale level to clarify the sizes detected when calculating the MCI index through orthopantomograms (Fig. 8).

The statistical data processing was performed with the SPSS-14.0 software for Windows using parametric and nonparametric methods.

RESULTS AND DISCUSSION

An analysis of the osteodensitometry results in children with CTD, in view of the age standards and the percentile densitometer data, revealed that a decrease in strength, which depends on the microstructure, mineral density, elasticity, and thickness of the bone tissue cortical layer, is associated with a decrease in the broadband attenuation of ultrasonic vibrations. A downfall in this indicator, which determines the spatial orientation of bone trabeculae, is combined with an increase in the ultrasonic waves propagation velocity. As we see it, it is the degree of decrease in the ultrasound broadband attenuation — which develops against abnormal structure of elastin, collagen, proteoglycans and glycoproteins with existing defects in the main substance and the connective tissue fibrous structures — that can offer a proper reflection of the dysplastic disorders intensity. An analysis of bone tissue strength in children of Health Groups I and II showed that a decrease in the bone resistance to fractures below the respective reference values is due to lack of its mineral component caused by deficient calcium supply in the child's body, as well as a decrease in the calcium metabolic activity, proof to that being the positive dynamics of the ultrasonic vibrations propagation rate with no change in the broadband attenuation (Fig. 9).

Tables 1–4 offer the data on the index radiomorphometric assessment of the mandible bone tissue status in the studied groups.

An analysis of the mandible bone tissue status in the studied groups indicated that an increase in the CTD severity was associated with a tendency toward a decrease in radiomorphometric index values, the



Fig. 4. MI - Mental index, RI - X-ray index

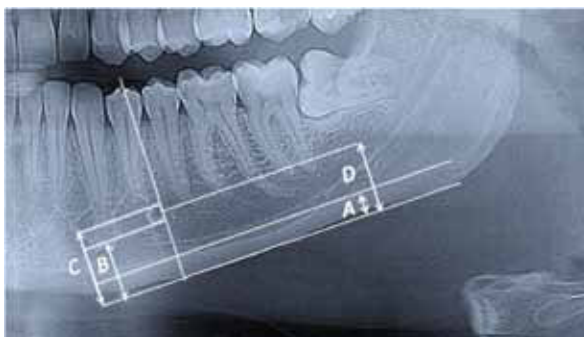


Fig. 5. Anthropometric benchmarks for measuring and calculating the PMI index: $PMIs = A/C$; $PMli = A/B$; $PMIm = A/D$

exception being the X-ray index. According to the GI value in children of Health Groups 1 and 2, the cortical plate thickness at the mandibular angle is significantly above similar indicators for the children of Subgroup 1 (1.04–1.24 times as thick), the children of Subgroup 2 (1.05–1.44 times as thick), and children of Subgroup 3 (1.10–1.41 times as thick). As for AI, the cortex thickness at the lower jaw branch in the control group also prevails (by 1.02–1.05 times) over the values registered in the main group, yet the differences are not statistically significant. The MI indicator (the alveolar process (bone) resorption degree of the lower jaw), is also statistically significantly less (1.01–1.21 times) in children with CTD, if compared to patients of Health Groups I and II. The index values in patients with different levels of bone strength indicate that children with a mild decrease ($SD \leq -1$) and a significant decrease ($SD \leq -2$) in the bone strength, feature a decrease in the cortical bone thickness over the entire mandible surface not only in the control group, yet also in the main group, too. This lack of difference, as we see it, can be accounted for by the physiological adjustment and compensation mechanisms that are to be observed in children with CTD.

The radiological indices of GI, AI and MI proved to have strong positive correlation (r_p) with the oste-



Fig. 6. MCI — Mandibular cortical index: C1 — the cortical layer is normal; C2 — the cortical layer is slightly damaged; C3 — the cortical layer is significantly damaged



Fig. 7. «Zones of interest» on a 3D panorama in sagittal projection VR mode with FOV 8×15 in the option "Shaded" "Bone"

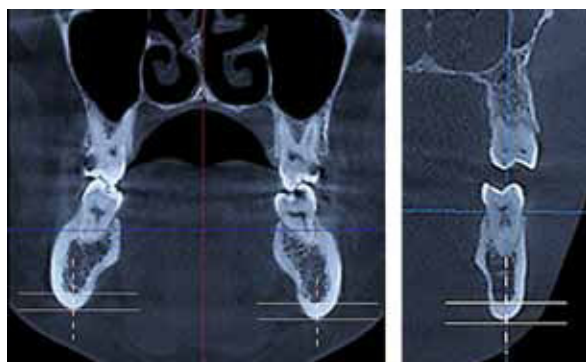


Fig. 8. The thickness of the cortical layer in the coronal, sagittal projections

odensitometry Z-criterion: 0.947 ($p = 0.000059$) for GI; 0.819 ($p = 0.00031$) for AI; 0.784 ($p = 0.00083$) for MI. The results of evaluating the values of PMIi, PMIIm, and PMIs revealed a similar trend, which manifested itself through strong positive correlation dependences (r_p) with the Z-criterion: 0.816 ($p = 0.000043$) for PMI; 0.782 ($p = 0.00027$) for PMIIm; 0.749 ($p = 0.00069$) for PMIs. Obviously, the peripheral skeleton bone tissue status offers a reliable reflection of the x-ray situation on the orthopantomograms, while an increased mandible porosity in children with CTD is diagnosed as a decrease in the cortical layer thickness both in the branch area and in the angle of the lower jaw, as well as changed topogra-

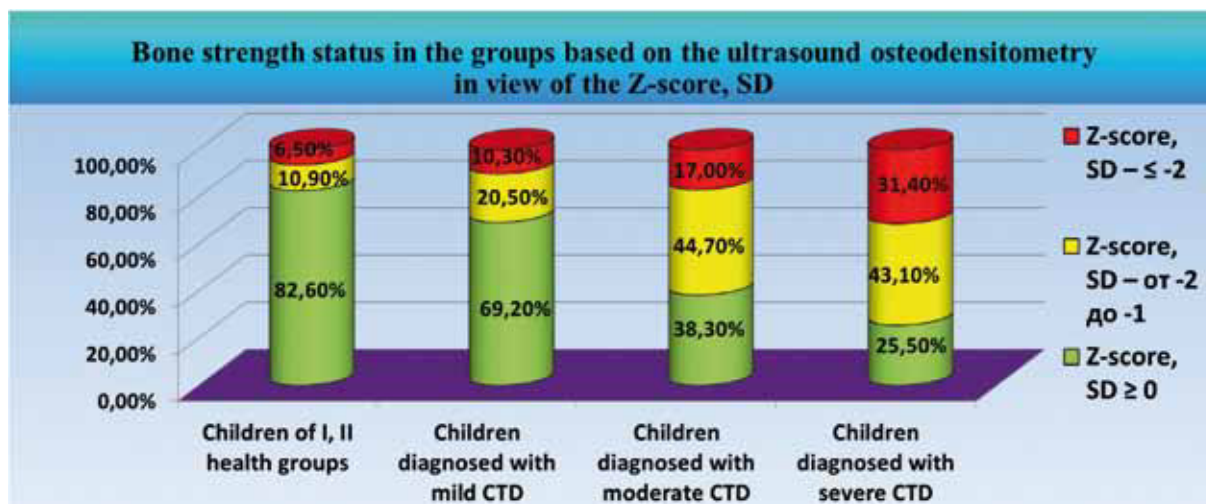


Fig. 9. Bone strength status in the groups based on the ultrasound osteodensitometry in view of the Z-score, SD

Table 1. Radiomorphometric indices, mandible, depending on bone strength status; Health Groups I & II, ($n = 46$), ($M \pm m$)

Learning Indexes, Units	Bone strength status		
	Z-score ≥ 0 SD, $n=38$	Z-score ≤ -1 SD, $n=5$	Z-score ≤ -2 SD, $n=3$
FI, points	1,0	$0,99 \pm 0,01$	$0,97 \pm 0,02$
GI, mm	$1,97 \pm 0,58$	$1,59 \pm 0,37$	$1,33 \pm 0,24$
AI, mm	$4,39 \pm 0,61$	$4,04 \pm 0,92$	$3,63 \pm 0,91$
MI, mm	$4,68 \pm 0,52$	$4,76 \pm 0,83$	$3,95 \pm 0,89$
X-ray index, points	1,0	$1,01 \pm 0,01$	$1,03 \pm 0,02$
PMIi, points	$0,43 \pm 0,09$	$0,39 \pm 0,06$	$0,34 \pm 0,08$
PMIIm, points	$0,39 \pm 0,08$	$0,35 \pm 0,05$	$0,28 \pm 0,07$
PMIs, points	$0,32 \pm 0,07$	$0,31 \pm 0,04$	$0,26 \pm 0,06$
MCI, mm	$3,9 \pm 0,1$	$3,9 \pm 0,2$	$3,8 \pm 0,3$

Table 2. Radiomorphometric indices, mandible, depending on bone strength status; children diagnosed with mild CTD, ($n = 39$), ($M \pm m$)

Learning Indexes, Units	Bone strength status		
	Z-score ≥ 0 SD, $n=27$	Z-score ≤ -1 SD, $n=8$	Z-score ≤ -2 SD, $n=4$
FI, points	$0,96 \pm 0,03$	$0,94 \pm 0,05$	$0,88 \pm 0,02$
GI, mm	$1,89 \pm 0,52$	$1,36 \pm 0,34$	$1,07 \pm 0,23$
AI, mm	$4,27 \pm 0,56$	$3,93 \pm 0,79$	$3,54 \pm 0,86$
MI, mm	$4,62 \pm 0,47$	$4,72 \pm 0,77$	$3,36 \pm 0,81$
X-ray index, points	$1,03 \pm 0,02$	$1,05 \pm 0,04$	$1,09 \pm 0,03$
PMIi, points	$0,41 \pm 0,07$	$0,37 \pm 0,03$	$0,31 \pm 0,02$
PMIIm, points	$0,38 \pm 0,06$	$0,33 \pm 0,04$	$0,26 \pm 0,03$
PMIs, points	$0,31 \pm 0,04$	$0,29 \pm 0,02$	$0,24 \pm 0,05$
MCI, mm	$3,8 \pm 0,2$	$3,8 \pm 0,3$	$3,7 \pm 0,1$

Table 3. Radiomorphometric indices, mandible, depending on bone strength status; children diagnosed with moderate CTD, (n = 47), (M ± m)

Learning Indexes, Units	Bone strength status		
	Z-score ≥ 0 SD, n=18	Z-score ≤ -1 SD, n=21	Z-score ≤ -2 SD, n=8
FI, points	0,89 ± 0,04*	0,85 ± 0,03*	0,79 ± 0,01*
GI, mm	1,87 ± 0,43*	1,28 ± 0,29*	0,99 ± 0,18*
AI, mm	4,24 ± 0,45*	3,88 ± 0,71*	3,50 ± 0,76*
MI, mm	4,59 ± 0,38*	4,69 ± 0,72*	3,32 ± 0,74*
X-ray index, points	1,08 ± 0,02*	1,09 ± 0,01*	1,12 ± 0,03*
PMIi, points	0,39 ± 0,04*	0,33 ± 0,01*	0,26 ± 0,02*
PMIm, points	0,31 ± 0,03*	0,30 ± 0,04*	0,24 ± 0,01*
PMIs, points	0,27 ± 0,03*	0,25 ± 0,01*	0,22 ± 0,04*
MCI, mm	3,7 ± 0,3*	3,6 ± 0,2*	3,5 ± 0,1*

Note: * $p < 0.05$ — the reliability of statistical differences compared with indicators of children of I, II health groups

phy of the foramen mentale in relation to the mandible lower border.

A qualitative evaluation of the mandible cortical plate status through the MCI value determined an identical orientation with respect to the Z-criterion, just like in the previously analyzed X-ray indices, while the differences were statistically significant ($p < 0.05$). In Health Groups I and II, as well as in Subgroup 1, the C3 type of cortical plate was not registered, while the occurrence of C1 and C2 types was 73.9% and 26.1%, and 61.5% and 38.5%, respectively, whereas the differences between the groups were considered unreliable ($p < 0.01$). In Subgroups 2 and 3, a slightly damaged cortical layer prevailed (53.2% and 43.1%, respectively), and the differences between the studied groups, too, did not reveal statistically significant difference ($p < 0.01$). The major difference between the children in Subgroups 2 and 3 was the occurrence of the C1 and C3 types: in children with mild CTD, this ratio was 31.9% and 14.9%, while in children with severe CTD — 23.5% and 33.4%, respectively, subject to the statistically significant differences ($p < 0.05$). The qualitative evaluation of the mandible bone tissue in Subgroup 3 and the C3 type revealed erosion, lack of uniformity, and severe damage to the cortex through its entire length with significant attenuation, as well as a large-cellular pattern of the spongy bone. It is to be noted that the MCI index is highly reliable and diagnostically significant, while the orthopantomograms obtained via CBCT, in contrast to the X-ray method, allow getting reliable results, as well as conducting objective differential diagnostics in a qualitative evaluation of the mandible cortical plate status.

Table 4. Radiomorphometric indices, mandible, depending on bone strength status; children diagnosed with severe CTD, (n = 51), (M ± m)

Learning Indexes, Units	Bone strength status		
	Z-score ≥ 0 SD, n=13	Z-score ≤ -1 SD, n=22	Z-score ≤ -2 SD, n=16
FI, points	0,82 ± 0,03**	0,76 ± 0,01**	0,72 ± 0,02**
GI, mm	1,79 ± 0,36**	1,23 ± 0,26**	0,94 ± 0,19**
AI, mm	4,19 ± 0,41**	3,84 ± 0,64**	3,44 ± 0,71**
MI, mm	4,55 ± 0,36**	4,67 ± 0,61**	3,26 ± 0,66**
X-ray index, points	1,09 ± 0,03	1,12 ± 0,02**	1,14 ± 0,01**
PMIi, points	0,37 ± 0,02**	0,28 ± 0,03**	0,23 ± 0,01**
PMIm, points	0,29 ± 0,02**	0,27 ± 0,03**	0,21 ± 0,01**
PMIs, points	0,25 ± 0,01**	0,22 ± 0,02**	0,19 ± 0,03**
MCI, mm	3,7 ± 0,2**	3,6 ± 0,3**	3,5 ± 0,1**

Note: * $p < 0.01$ - the reliability of statistical differences compared with indicators of children of I, II health groups

A study of X-ray morphometric indices shows that in case of an increase in the dysplastic disorders severity in children, a decrease in the bone density comes combined with a decrease in cortex thickness and destructed interalveolar septa, while the share of patients with severely damaged lower jaw cortical plate is increasing (Fig. 10).

Unlike children of Health Groups I and II (Fuchs index in the group — 0.99 ± 0.01 ; X-ray index — 1.01 ± 0.01 ; MCI — 3.9 ± 0.1 ; cortex thickness — 2.8 ± 0.4 ; mandible body X-ray density — 1727.6 ± 302.1 HU; mandible X-ray density angle — 2181.4 ± 297.3 HU), the patients with mild CTD (Fuchs index in the group — 0.93 ± 0.03 ; X-ray index — 1.06 ± 0.03 ; MCI — 3.8 ± 0.2 ; cortex thickness — 2.6 ± 0.1 ; mandible body X-ray density — 1538.9 ± 274.4 HU; mandible X-ray density angle — 1936.7 ± 281.2 HU) as well as the patients with moderate CTD (Fuchs index for the group — 0.84 ± 0.02 ; X-ray index — 1.10 ± 0.02 ; MCI — 3.6 ± 0.2 ; cortex thickness — 2.1 ± 0.3 ; X mandible body X-ray density — 1316.8 ± 251.7 ; mandible X-ray density angle — 1783.8 ± 264.5 HU) featured a slight and unevenly decreased height of the interalveolar septa (no more than $\frac{1}{3}$ of the root length), which came combined with a slight resorption (6–10%) of the mandible alveolar part. The children with severe CTD (Fuchs index in the group — 0.77 ± 0.02 ; X-ray index — 1.12 ± 0.02 ; MCI — 3.6 ± 0.2 ; cortex thickness — 1.9 ± 0.2 ; mandible body X-ray density — 1198.3 ± 236.2 HU; mandible X-ray density angle — 1652.9 ± 249.6 HU) were diagnosed with generalized, moderate, horizontal resorption of the mandible alveolar part, uniform de-

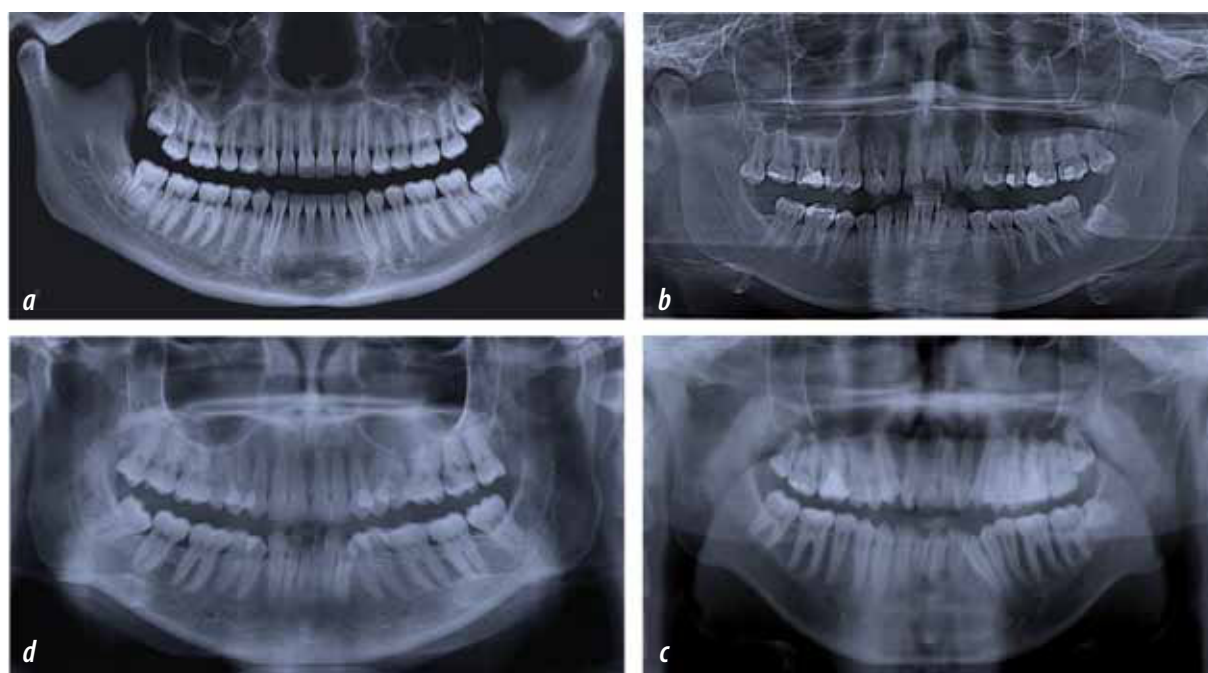


Fig. 10. X-ray specifics of the mandible bone tissue status in the groups: a — patient A., 16 y.o., Health Group I; b — patient M., 15 y.o., mild CTD; c — patient K., 16 y.o., moderate CTD; d — patient S., 16 y.o., severe CTD

crease in the interalveolar septa height (about $\frac{1}{3}$ of the root length), and an early stage of destructive change (12%) of the bone tissue.

Visualization of CBC tomograms of transverse sections of the mandibular bones alveolar part in Health Groups I and II determines the following features — a thickened cortical layer; bone trabeculae represented by a large-mesh pattern with crossed bone beams; the functional trabecular package features a horizontal orientation; interalveolar ridges are of pointed triangular shape with a pronounced closing cortical plate. CBCT evaluation of the mandible alveolar part cross sections suggests that an increase in the CTD severity comes along with the following focus in the pathomorphological changes — decreasing thickness of the cortical plates; predominance of medium- and fine-meshed patterns; destroying structure of the trabecular package with disturbed spatial orientation and thinning bone trabeculae; dissociation of the inner cortical plate; interalveolar ridge shape getting more of something semi-oval or flattened. The X-ray examination data makes it obvious that the bone resorption intensity is most prominent in children with severe CTD.

This suggestion gets confirmed through generalized chronic productive inflammation, which leads to a uniform decrease in the interalveolar septa height within a range of $\frac{1}{3}$ of the root length; a slight

expansion of the periodontal gap; a decrease in the optical density and a disturbed microarchitectonics in the mandible body (thinned bone beams; increased transparency of the bone pattern; fibrous transformation of the bone tissue structure; medium and fine-mesh pattern of the spongy bone; porosity; lack of contours; eroded thinned closing cortical plate along its with surface). The systematization of the available research data as well as the outcomes of our own studies indicates that patients with CTD feature the following pathomorphological changes — catabolism prevalence over synthesis and recovery; connective tissue edema; fibrous structures and major substance decomposition; violation of fibrillogenesis; reduced blood vessels in the microvasculature; development of perivascular dense productive infiltrates; fiber homogenization and changed ratio between certain types of collagen; connective tissue hyalinosis and sclerosis. The TMJ capsule-ligamentous complex responds to chronic productive inflammation with irreversible deformities in the articular disc, disturbed integrity of the intraarticular ligaments, joint bone elements hypoplasia, and periodontal disease — impaired function (plastic, protective, barrier, trophic, shock-absorbing functions), bone resorption, tooth mobility, and the development of secondary traumatic occlusion.

CONCLUSIONS

1. Comprehensive evaluation of the mandible bone tissue status using X-ray morphometric indices and X-ray density indices in children with CTD, allows identifying the nature and the degree of dysplastic disorders, detecting the manifestations of irreversible periodontal bone resorption, and can serve the basis for the developing a set of dental measures, as well as for designing proper approaches implying medication, non-medication, and symptom-based treatments.
2. Strong positive correlation relationship between quantitative X-ray morphometric indices and the osteodensitometry Z-criterion, which were detected in children with CTD, reveal that the peripheral skeleton bone tissue status offers a reliable reflection of the radiological picture observed on orthopantomograms. Quantitative calculation of X-ray morphometric indices in the dentist's clinical practice is not only a highly reliable method for screen-diagnosing the quality of skeleton bones in childhood, yet is also an effective way of early detection of decreasing bone strength.
3. The data obtained through identifying the mandible mineral density, its cortical layer morphological structure, the cortex thickness at the level of the foramen mentale, demonstrate a statistically significant decrease in the cortical plate thickness, as well as a decrease in the bone optical density in children affected with CTD. The data can be well used when examining patients in dental offices as indicators of the osteopenia syndrome progress with an increased risk of osteoporosis.
4. The progression of the child dysplastic disorders involving connective tissue, which correlates with the intensity of bone structures destruction at the maxillofacial area and with the collagen degradation progress, is associated with an increase in chronic productive inflammation, reduced X-ray density; fibrous transformation of bone tissue; a decrease in the thickness and the dissociation of the mandible cortical plates; prevalence of medium- and fine-meshed bone pattern; disturbed space orientation and bone trabeculae thinning; development of pathologies in the periodontium, which leads to the development of secondary traumatic occlusion.
5. A qualitative evaluation of the mandible cortical layer status should be performed through cone beam computed tomography in a panoramic mode, which can be explained with higher specific sensitivity, sensitivity, accuracy, and

prognostic value in terms of negative and positive outcomes, in contrast to similar data obtained through orthopantomography of maxilla bones.

6. When examining groups of children thus aiming at developing risk groups involving impaired musculoskeletal system development, we would recommended employing quantitative ultrasound osteodensitometry based on average age standards and percentile scales, whereas children with bone deficiency would need further comprehensive examination, correction with medication, preventive care, outpatient monitoring and densitometric control.

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METHODOLOGICAL APPROACHES TO STUDYING DENTAL ARCH MORPHOLOGY

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ABSTRACT — In order to develop a method for accelerated diagnostics of the dental arch gnathic type, we measured jaw cast models obtained from 213 people with an orthognathic bite, without congenital and/or acquired maxillofacial pathology. The difference between the actual and the calculated values of the inter-canine distance, which serves as a basis for the diagnostic method, was employed as a reference standard for mesognathic dental arches, where the triple selecting bias for the analysis of dental arches with physiological occlusion did not exceed 3 mm. The estimates for the inter-canine distance at various dental arch types (mesognathia, 39.62 ± 1.24 mm; brachygnathia, 41.50 ± 1.15 mm; dolichognathia, 34.54 ± 1.64 mm) were obtained in view of the circle geometry, where the radius was identified by the ratio of the triple width sum of the three front teeth crowns (medial and lateral incisors and canines), to π value (3.14). The dental arch anterior section height was half the circle radius. Inter-canine distance was calculated subject to the Pythagorean theorem. A width change (increase) exceeding 3 mm in the anterior section allowed attributing the dental arches to the brachygnathic type, while a decrease in the said index was considered typical of dolichognathia.

KEYWORDS — morphometry; upper jaw; gnathic types of dental arches; mesognathia; dolichognathia; brachygnathia.

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 [2, 13, 16, 21, 24, 27, 31, 37, 40].

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 [3, 10, 12, 15, 18, 23, 25, 29, 34, 39].

The anatomic features of teeth and dental arches have been the focus of numerous studies, and are of both applied and clinical value [4, 9]. There have been shown dentoalveolar segments' features with a description of the major anatomic structures, with a focus on the clinical use [8]. Knowing the maxillofacial features from the age view serves as a guideline for selecting the right method of prosthetic and orthodontic treatment, where the issues are often complicated by dental arches defects [5, 36]. Here we present some advanced methods for studying the main morphological maxillofacial elements [1, 11].

Many experts have already presented lots of convincing proof to the variety of shapes and sizes of dental arches with an orthognathic bite [7, 28]. There is data available on the major dimensions of dental arches for dolicho-, brachy- and mesognathia, in view of the odontometric values, namely for macro-, micro- and normodontia [6, 35].

The methods for identifying dental types are based on odontometric indicators and include determining the mean molars modulus whose value is indicative of normodontia if varies within 10.6–11.0 mm [14]. The said method is based only on the measurement of molars (large molars) in the vestibular-lingual and mesial-distal planes.

Other methods are based on measuring four incisors and there are values offered that point at normo-, macro- and microdontia [17]. The relationship of the tooth size and the craniofacial parameters can be seen from studies focusing on detecting individual normodontia [26, 39].

The said methods allow evaluating the size of certain teeth groups. It is worth saying that experts speak of the dental arch length that can be calculated through the summed width of 14 teeth crowns. The length of the dental arch varying within the range of 112–118 mm has been identified as speaking of the normodontia type of dental arches [19, 32].

Another parameter to identify the dental arch type is its gnathic element. The gnathic index, which is defined as the percentage of the diagonal and the transverse dimensions, is to be observed in people with a physiological bite [30]. It is to be noted that its digital values have been derived empirically and proven through a large number of observations. At the same time, in case of abnormal dental arch shape caused by the incisors protrusion or retrusion, it is almost impossible to identify the diagonal dimensions.

Given that, the gnathic indices for the dental arches have been proposed, which are based on the ratio of the 14 teeth crowns width sum to the dental arch transversal distal part [33]. However, the values presented by the authors are also based on measurements obtained from people with physiological occlusion. These methods are excessively complex, require numerous measurements and calculations for the dental and interdental types, as well as craniofacial measurements and a comparative-and-contrastive analysis.

Noteworthy is the opinion that experts express regarding the geometric and graphic reproduction of dental arches [22]. Of greatest importance is the Hauley-Herber-Herbst method, which is based on measuring the width of the three front teeth crowns on one of the sides (the medial and lateral incisors and the canine). The downside of this method is that the chord and length of the segment, following Hauley's calculations, correspond to the three front teeth sizes. In view of that, the correction factors were introduced where the arch lengths of the segment and the chord had different values [20]. However, this technique is acceptable only for arches of average size with the standard values of the front teeth.

Aim of study:

to develop a method for accelerated diagnostics of the dental arch gnathic type.

MATERIALS AND METHODS

The study involved 213 people aged 20–30 with a complete set of teeth, an orthognathic bite, featuring no congenital and/or acquired maxillofacial pathology. Cast models (die stone) were obtained from all the patients' jaws. In view of the expert recommendations, the jaw models were evaluated based on the gnathic index as the ratio of the 14 teeth crowns width half-sum to the width of the distal area between the second permanent molars [30]. Subject to the index, the patients were divided into 3 groups. Group 1 included 102 patients with mesognathic dental arches; Group 2 were those with brachygnathia (59 patients), while Group 3 included another 52 patients featuring dolichognathic dental arches.

Odontometry was done using an electronic caliper (accuracy — 0.01 mm). In this case, the mesial-distal diameters of the crowns of the 14 upper teeth were measured (excluding the wisdom teeth). The transverse dimensions of the dental arch anterior section were measured between the tearing tubercles of the permanent upper canines.

The dental arch construction following the Hauley method (Hauley-Herber-Herbst) was based on

the half-sum of the width of the 6 front teeth crowns (canines and incisors). Given the construction errors associated with the fact that the radius of the circle is shorter than the chord of the segment bounded by the radius, we employed a correction taking into account the circle geometry [15]. In this case, the radius was calculated as the ratio of the triple sum of the three anterior teeth crowns width to π (3.14). The obtained value corresponded to the front-canine diagonal.

After making the circle, the value equal to the front-canine diagonal, was used to build the segments on both sides starting from the circle upper point. The location of these points allowed identifying the inter-canine width of the dental arch anterior part (Fig. 1).

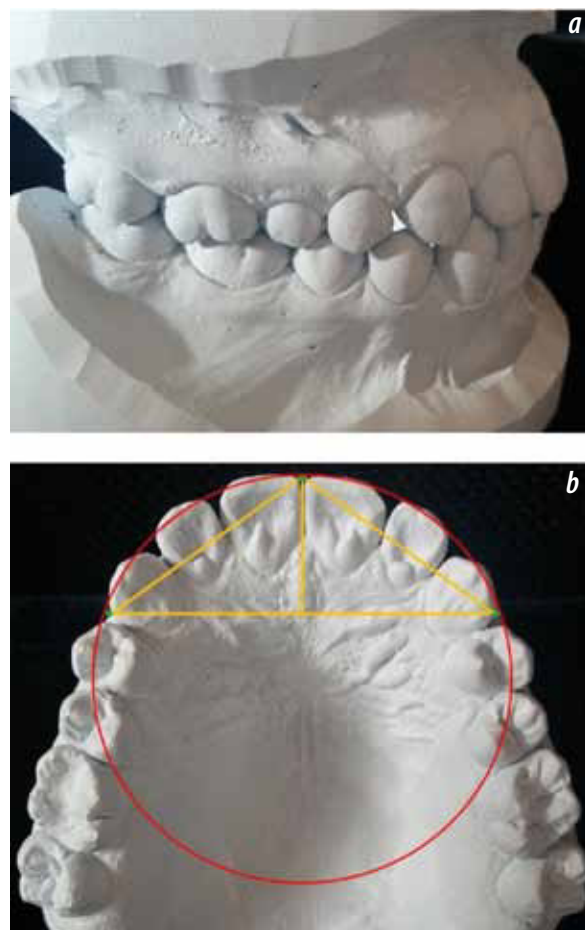


Fig. 1. Physiological occlusion (a) and the analysis method for the upper jaw model (b)

In order to avoid the graphic construction of the Hauley arch, we employed the Microsoft Excel software for the estimated inter-canine distance. In this case, the Hauley data with correction coefficients

were used [15]. The anterior dental arch depth corresponded to the chord half of the anterior segment, like a right triangle leg opposite an angle of 30 degrees. Besides, the chord corresponded to the calculated radius of the circle and the front-canine diagonal. Knowing the depth of the arch and the chord value, the value of the second leg — which was half the width of the dental arch anterior section between the canines — was calculated following the Pythagorean theorem.

The difference between the actual and calculated indicators of the width of the anterior section of the dental arch was regarded as the value of inter-canine correspondence or inconsistency.

RESULTS AND DISCUSSION

A comparative analysis of the major indicators for the dental arches of various gnathic types revealed that the average size of the teeth in the groups did not differ, which pointed at the similarity within the groups in terms of their odontometric features. Besides, we observed no significant differences in the front teeth size.

At the same time, there is a difference in the dental arches transverse dimensions that is to be noted, both in the anterior and in the distal section.

Table 1 offers a view on the cast model details in the groups in question.

A similar situation was to be observed when analyzing the transversal dimensions of the dental arch anterior section. The inter-canine distance in mesognathia was 39.62 ± 1.24 mm; in those with brachygnathia the similar value was 41.50 ± 1.15 mm, which was significantly above ($p \leq 0.05$) that same index in people with dolichognathic dental arches (34.54 ± 1.64 mm).

The greatest diagnostic value belongs to the mismatch between the actual inter-canine distance and the calculated indicators. In Group 1 — mesognathic dental arches — we observed no significant difference between the indicators of the anterior dental arch transversal size and the calculated values.

We employed this parameter as a reference for mesognathic dental arches. The triple error of the preliminary analysis representativeness for dental arches with the physiological occlusion did not exceed 3 mm.

Given that, an increase in the anterior section width by more than 3 mm allowed us to attribute the dental arches to the brachygnathic type, whereas a decrease by the said value was indicative of dolichognathia.

Therefore, the value of the inter-canine mismatch can be used as the major criterion for accelerated diagnostics of the dental arch gnathic type.

Table 1. The major indicators of teeth and dental arches in the studied groups, ($M \pm m$, $p < 0.05$)

Major indicators	Teeth and dental arch parameters		
	Group 1	Group 2	Group 3
Width sum for 14 teeth crowns (mm)	115.57 ± 3.29	112.92 ± 2.84	113.16 ± 3.12
Width between second molars (mm)	62.85 ± 2.14	67.12 ± 2.17	59.02 ± 2.24
Dental arch gnathic index	0.92 ± 0.02	0.84 ± 0.03	0.95 ± 0.01
Width sum for 3 front teeth (mm)	24.01 ± 1.16	23.05 ± 1.24	23.44 ± 1.37
Actual inter-canine width (mm)	39.62 ± 1.24	41.50 ± 1.15	34.54 ± 1.64
Estimated inter-canine width (mm)	39.73 ± 0.96	38.14 ± 1.03	38.78 ± 1.59
Inter-canine mismatch (mm)	-0.11 ± 0.83	4.24 ± 0.92	-3.36 ± 0.29

The largest transversal sizes of the upper dental arches' distal part were observed in people with brachygnathic dental arches (Group 2) where their size was 67.12 ± 2.17 mm. In this case, the gnathic index of the upper jaw dental arch was the lowest (0.84 ± 0.03) and indicative of brachygnathia.

In case of dolichognathia (Group 3), the dental arches were significantly narrower at the second molars (59.02 ± 2.24 mm, $p \leq 0.05$), whereas the arch index was much higher (0.95 ± 0.01 , $p \leq 0.05$).

CONCLUSIONS

1. A method for accelerated diagnostics of dental arches odontometric parameters and linear dimensions has been proposed and tested, which can be employed to evaluate the dental arch type. The method relies on the difference between the actual and the estimated inter-canine distance. The parameter was used as a reference for mesognathic dental arches, where the triple error in the dental arches analysis representativeness for

- physiological occlusion did not exceed 3 mm.
2. The inter-canine distance for mesognathic dental arches was 39.62 ± 1.24 mm; in people with brachygnathia, the value was 41.50 ± 1.15 mm, which was significantly above ($p \leq 0.05$) that in people with dolichognathic dental arches (34.54 ± 1.64 mm).
 3. The estimated inter-canine distance values were obtained in view of the circle geometry, where the radius was calculated through the ratio of the triple sum of the three front teeth crowns widths (the medial and lateral incisors and the canine) to the π value (3.14). The height of the anterior dental arch was half the circle radius. The inter-canine distance was identified following the Pythagorean theorem. An increase in anterior section width by more than 3 mm proved to be a reliable criterion allowing attributing the dental arches to the brachygnathic type, while a decrease in the indicated value — to the dolichognathic type.
 4. The introduction of an additional criterion (the inter-canine mismatch), as the major indicator for accelerated diagnostics of the dental arches gnathic type, will allow identifying individual features in the structure of dental arches; preventing potential relapse of a dentoalveolar pathology, as well as achieving optimal predictable functional and aesthetic outcomes through orthodontic treatment.

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MICROHEMODYNAMIC CHANGES AS INDICATOR OF PSYCHOEMOTIONAL STRESS AT DENTAL TREATMENT

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ABSTRACT — The article deals with studies on microcirculatory changes as indicators of psychoemotional stress development. Diagnosis of the capillary blood flow was made by studying LDF-grams obtained by carrying out laser Doppler flowmetry. The study was carried out in the area of the inflamed periimplant oral mucosa in the patients with psychoemotional stress (30 people). To obtain normalized characteristics, the control group comprised patients with postprosthetic complications after dental implants without any psychoemotional disorders. It was revealed that under stress capillary blood flow changes both at the oscillatory and non-oscillatory levels. Increased blood inflow and disordered venous outflow were noted against the blood vessels vasodilatation. When analyzing high and low frequency oscillations with the method of wavelet transformations, it was noted that endothelium activity increased, but sympathetic adrenergic vasomotors and precapillaries tone decreased.

Laser Doppler Flowmetry (LDF) can be applied as a diagnostic method for stress situations at dental treatment.

KEYWORDS — microcirculation, stress, periimplant area, inflammation, diagnostics.

INTRODUCTION

The relevance of modern diagnostic methods in applied dentistry is determined by the high prevalence and intensity of dental diseases. The knowledge of diagnostic approaches, the principles of constructing and making a diagnosis is of great importance for medical practice, since the formulated diagnosis is the rationale for the tactics of therapeutic and preventive measures [1–10].

Diagnosis of psychoemotional stress is a vitally important indicator, as it is a non-specific basis of numerous diseases including dental ones. Psychoe-

motional disorders resulting from stress cause chronic long lasting inflammatory diseases including diseases of the oral cavity [11]. Complications following dental implantation that manifests in inflammation of the periimplant tissue is not an exception. Patients are not able either eat normally or speak and all this affects their life. In this case psycho-physiological condition of these patients also changes. Early discovery of the stress factor and later the development of psychoemotional disorders is one of the important purposes of a dentist as it prevents development of complications during dental treatment.

At present, numerous methods exist to determine a person's psychoemotional condition. These are mainly various questionnaires that patients fill. In the era of modern technologies a software on Android platform examines microhemodynamics and determines the degree of stress: low, medium or high one within a few seconds. Though, more objectively, stress diagnostics can be carried out with laser doppler flowmetry by studying a few parameters. The method makes it possible to promptly and noninvasively reveal specific numerical indices by calculating the oscillation spectrum of different origin, essentially by increasing or decreasing the amplitudes of endothelial, myogenous and neurogenous oscillation [12].

Aim

To investigate changes in the microdynamics of the oral mucosa under psychoemotional stress using the data acquired with laser Doppler flowmetry.

MATERIAL AND METHODS

30 volunteers with inflammation of the peri-implant tissue of the oral mucosa participated in the study. The study was approved by the Regional Committee of Ethics, Protocol No 2115/1-2019 of April 19, 2019. Prior to LDF-metry, all patients with mucositis were given questionnaires that were analyzed using the method of psychological stress measure PSM-25. The results were interpreted and the data processed by calculating the total amount of points after answering all the questions. 125 points and higher showed a high level of stress, 100–125 points — a medium level and less than 99 points — a low level of stress.

Laser doppler flowmetry was performed while the

patient was sitting on the dental chair. The sensor was placed on the inflamed periimplant area to study hemodynamics of the oral mucosa. Capillary blood flow was monitored for 10 minutes. At the first stage the indicator of microcirculation, the root-mean-square deviation and coefficient of variation were estimated and at the second stage the contribution and oscillation of high and low frequency flux motions were studied.

RESULTS

Based on the data obtained from the questionnaires, it can be said that all the patients were in a stress situation. So, 12 patients (40%) showed 130 points, 10 patients had 160 points (33,3%), 5 patients — 180 points (16,7%) and 3 patients showed 195 points (10%). The average amount of points were $154,8 \pm 4,2$ that was the evidence of a high level of stress.

To obtain normalized indices of LDF-gram, while carrying out LDF-metry, there was a control group of normal people who did not suffer from stress. The absence of a psychoemotional factor was also confirmed by questioning. The patients under stress conditions showed blood vessels dilatation against lower activity of the sympathetic vasomotors and decreased tone of precapillaries, increased amplitude of endothelial, neurogenous and myogenous oscillations. So, increased amplitude of endothelial oscillations (VLF by 57%, $p < 0,05$) characterizes a higher activity of endothelial secretory function, development of endothelium-dependent dilatation of the vessels. Increased number of flux motions of the myogenous origin (LF_M by 64%, $p < 0,05$) characterizes a lower tone of precapillaries, Increased amplitude of neurogenous oscillations (LF_H by 54%, $p < 0,05$) is the evidence of a lower activity of sympathetic adrenergic vasomotors and development of sympathetic vasodilatation. Increased oscillations of the pulse and respiratory waves occur against pulse acceleration and respiratory impact on the vegetative heart nerves alongside with the inflow of arterial blood and difficulty in venous outflow. The study of the non-oscillatory indices showed the increase of the microcirculation index M by 37%, but the root-mean-square deviation and variation index are 35% lower and makes $5,32 \pm 0,3\%$. Lowered speed of the local blood flow is associated both with weakened active factors of blood flow regulation and decreased flux motions energy.

DISCUSSION

Thus, the analysis of the data obtained is the evidence of expressed microcirculatory changes in a stress situation. Laser doppler flowmetry is a noninvasive method of examination that shows objectively

the state of microhemodynamics and can be used as a diagnostic method of psychoemotional condition at dental treatment.

CONCLUSION

Investigation of microcirculation parameters in patients with dental implant complications has revealed disturbances of microhemodynamics. Therefore, further studies may help find the cause/effect relationships that justifies the need for such studies in the future.

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GINGIVAL FLUID AS A POTENTIAL OBJECT FOR DIAGNOSTICS PROCESS

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ABSTRACT — Gingival sulcus is a place where inflammation occurs due to microbial penetration into the periodontal tissue. Gingival fluid can be employed as the fastest and most accurate reflection of pathological changes taking place in the cellular composition, the protein spectrum, and the pH status so this is of interest as a research object. The difference in the outcomes obtained through studying the cytokines level has been attributed to the use of different methods for sampling and storage of fluid samples.

KEYWORDS — chronic generalized periodontitis, gingival fluid, cytokines.

INTRODUCTION

Periodontal diseases belong to multifactorial infections, resulting from disturbed interaction between various bacteria and the periodontal immune system cells. These processes lead to the release of an uncontrolled amount of pro-inflammatory cytokines and chemokines, which ultimately results in destroyed periodontal structures [1–7]. Gingival crevicular fluid (GCF) in persons with periodontal issues contains inflammatory cells, bacteria, tissue disintegration products, antibodies, the complement system proteins and enzymes, as well as many inflammatory mediators [8]. Its preparation and quantitative determination of its immunoregulatory biomarkers can be considered one of the most non-traumatic research methods to obtain details on the status and degree of periodontal tissues destruction, to identify the features of its damage in various periodontal diseases, and to predict their course [9–11].

The microbial biofilm — a generally recognized etiological factor behind the inflammatory periodontal diseases development — involves immune defense mechanisms in the pathogenetic circle. The imbalance between bacterial invasion and the oral cavity immune

defense systems is considered the major cause leading to the development of periodontal tissue destruction [12, 13]. The cell walls components in anaerobic periodontal pathogens, while interacting with Toll receptors (TLRs) lead to a change in their structure and function, which, in turn, leads to activation of signaling pathways, an increase in the cytokines/chemokines production by the periodontal tissue local immune system cells, which attract polymorphonuclear cells to the focus of inflammation for effective clearance of bacteria. Activated neutrophils, in turn, cause destruction of the gum tissue, periodontal and alveolar bones, the result of that being an increase in the periodontal pockets depth. GCF is considered to be one of the reliable sources in studying inflammatory processes in case of periodontal diseases [14, 15]. GCF is one of the main objects in which the cytokines content is associated with the development of the immune response of both cellular and humoral type. However, the feasibility of its use for the quantitative determination of immune regulatory mediators as biomarkers for the periodontal disease progression has not been identified finally. Despite the large number of research works published so far, there is no generally approved method for GCF sampling and subsequent processing to do quantitative analysis of cytokines, first of all — based on the enzyme-linked immunosorbent assay, which is the most available currently.

Aim of study

to develop a method for identifying cytokines in GCF in order to evaluate the inflammation degree in patients with chronic generalized periodontitis (CGP).

MATERIALS AND METHODS

40 patients aged 40–55 years were examined, including 20 of them suffering from mild chronic generalized periodontitis (CGP), and 20 basically healthy patients. The inclusion criteria: persons over 40, who signed the awareness consent and protocol regarding the purpose and nature of the study. The exclusion criteria were: age under 40; coagulation and hemostasis disorders; immune system issues; chronic infectious, mental, oncological diseases; HIV-positive; women through pregnancy and lactation, as well as the patient's refusal to undergo examination.

To assess the effect of the preanalytic stage, involving GCF sampling, on the cytokines concentra-

tion in the 20 healthy individuals and 20 patients with CP, the GCF was collected twice, simultaneously.

GCF sampling method. After cleaning the teeth and adjacent gums from plaque, they were isolated from saliva with cotton rolls and dried. The material was taken from the gingival sulcus and/or periodontal pocket using special targets as sterile endodontic absorbent paper points (Absorbent Paper Points, No. 25, Taper 02), which are used in therapeutic dentistry to dry the root canal before filling. The points are sterile, made of paper with high absorbent capacity and free from impurities of binders, of perfect density to be inserted into the gingival sulcus or periodontal pocket. Analytical weighing of 30 paper points inserted into the periodontal pockets and kept until completely saturated revealed that the average amount of the absorbed GCF was 5.0 ± 0.05 mg. Using dental tweezer and a carver, 2 points were placed in the gingival sulcus, each of them getting completely saturated with GCF for 100–120 sec and transferred into two Eppendorff tubes. One of the points contained 1000 μ l of 0.155M sodium chloride solution, while the other contained 0.2% of the biocide ProClin 300 series [16]. As a result, GCF samples were obtained with a 1:200 dilution, which were further frozen at -40° C and stored until analysis.

The concentration of IL-1 β , IL-8, MCP-1, VEGF, IL-1RA cytokines in the GCF samples was identified with enzyme-linked immunosorbent assay using the respective reagent kits (Vector-Best CJSC, Novosibirsk, Russia).

The statistical processing of the research results was done with the Statistica v6.0 software. When comparing the results, the nonparametric Wilcoxon-Mann-Whitney test was used in the Multi Experiment Viewer software ($P < 0.05$).

RESULTS AND DISCUSSION

Table 1 offers a view on the obtained results.

The study results showed significant differences in the composition of GCF in individuals without periodontal disease and with CP, the basis of that being the high content of such pro-inflammatory cytokines as IL-1 β (5.0 times as high, $P < 0.05$), IL-6 (23.8 times, $P < 0.05$), IL-8 (4.2 times, $P < 0.05$), MCP-1 (1.9 times, $P < 0.05$), TNF α (1.5 times as high). Their concentration increase is due to the simultaneous involvement into the inflammation of all the immune defense cells of the gingival sulcus (neutrophils, lymphocytes and monocytes, epithelial cells).

The presented differences in the increase degree of the content in the main group of pro-inflammatory cytokines in the GCF from patients with CP were obtained through GCF extraction medium with ProClin

300. The cytokines content was significantly higher in the GCF extracted with 0.155 M sodium chloride solution along with 0.2% ProClin 300. To a smaller extent, this medium had its effect on the level of the main pro-inflammatory GCF cytokines of individuals who were basically healthy. Significant concentration preservation in it was observed for IL-8 (1.49 times as high; $P < 0.05$); MCP-1 (1.67 times; $P < 0.05$); TNF α (2.3 times; $P < 0.05$). As for the patients with CP, in a medium containing ProClin 300, an increase of the entire major pool of pro-inflammatory mediators was registered. The increase in the mediators level in GCF was as follows: IL-1 β (1.95 times as high; $P < 0.05$); IL-6 (2.13 times; $P < 0.05$); IL-8 (2.23 times; $P < 0.05$); MCP-1 (2.35 times; $P < 0.05$); TNF α (2.98 times; $P < 0.05$). It means that the use of a medium with antimicrobial activity for GCF extraction straight after its collection with a paper point allows ensuring stability in identifying the true concentration of the major cytokines group. An advantage of a biocide such as ProClin is the blockage of various types of microorganisms contained in the discharge coming from the gingival sulcus/periodontal pocket. Their presence in the GCF obtained for the study, both in case of intact periodontium and, especially, with CP, leads to rapid destruction of nearly the entire cytokine group, which is currently identified through enzyme immunoassay.

CONCLUSION

Given all of the above, when identifying the cytokines concentration in GCF, the preanalytical stage is of crucial importance in terms of obtaining reliable and reproducible results of the analyses. The introduction of ProClin 300 gingival fluid into the solution for extraction and subsequent storage of gingival fluid can be used to increase the sensitivity and specificity of the entire group of cytokines in the diagnostics of inflammatory periodontal diseases. The introduction of GCF biomarkers examination for assessing inflammatory periodontal diseases is a promising area for the introduction of advanced decision-making systems in practical dentistry.

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Table 1. Effect of diluent solution at GCF sampling on major pro- and anti-inflammatory cytokines

Indicators (pg / ml dilution medium)	GCF in individuals without abnormal periodontal changes		GCF in patients with mild chronic generalized periodontitis	
	0.155M sodium chloride solution and 0.2% ProClin 300 solution	0.155M sodium chloride solution	0.155M sodium chloride solution and 0.2% ProClin 300 solution	0.155M sodium chloride solution
IL-1 β	4,2 (1,9;7,2)	3,1 (1,2;5,4)	21,1** (12,5;27,8)	10,8* ** (6,3;15,2)
IL- 6	4,9 (2,3;5,7)	3,7 (1,8;4,3)	116,6** (64,4;166,2)	54,5* ** (32,4;83,4)
IL-8	73,3 (65,6;79,7)	48,9* (43,5;52,5)	295,25** (167,9;322,9)*	132,3* ** (65,7;160,8)
MCP-1	28,9 (26,6;32,1)	17,3* (17,9;21,4)	110,4** (78,6; 120,5)	46,9* ** (39,3;59,8)
TNF α	7,6 (6,4;9,6)	3,3* (3,1;5,2)	11,3 (5,2;14,3)	3,8* (1,1;4,7)
IL-1RA	4279,5 (3794,25;4885,5)	2139,5* (1897,2;2442,8)	3885 (1894;4808)*	1928* (946;2403)

* — $P < 0.05$, when comparing the results of the GCF study placed in test tubes with 0.155 M sodium chloride solution and 0.2% ProClin 300 solution, and without it;

** — $P < 0.05$, when comparing the results of the GCF study in individuals without pathological changes in periodontal disease and in patients with mild CGP

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INVESTIGATION OF MAXILLARY BONE DENSITY IN DIABETIC PATIENTS WITH CONE BEAM COMPUTED TOMOGRAPHY

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ABSTRACT — The study comprises an analysis of maxillary alveolar process bone density. Dental computed tomography allows quantitative and qualitative evaluation of the bone tissue density in the jaw and serves an effective tool for assessing the bone tissue status in case of diabetes mellitus. The study showed that the structure and density of bone tissue depends on the severity of diabetes mellitus and respective complications. The study outcomes revealed a significant decrease in the bone density at the neck of the teeth in people with diabetes mellitus, whereas less pronounced changes were observed in the middle third of the teeth roots. Besides, slight changes or even an increase in density were identified around the teeth apices. Diagnostics of jawbone destruction caused by diabetes is more reliable when carried out with cone beam computed tomography.

KEYWORDS — bone tissue optical density, cone beam computed tomography, diabetes mellitus.

INTRODUCTION

According to the literature, the number of patients with diabetes in Russia has increased by more than 1 million people over the past few decades; however, the prevalence of the disease is 2–3 times as high [1].

Diabetes is a metabolic issue with a high risk of developing complications. Literature sources, for instance, point that it involves disturbed bonds of protein and mineral components, deteriorated tissue

trophism leading to a slowdown in bone remodeling, which, in turn, is responsible for its density [2, 3]. Diabetic arthropathies present a fairly frequent diabetes complication and are to be found, as certain authors claim, in 58% of patients with Type 1 diabetes and in 24% of patients with Type 2 diabetes [4]. The neurohumoral regulation system has an impact on the structure and function of musculoskeletal tissues. Therefore, excessive or insufficient production of a certain hormone, will lead, sooner or later, to the development of pathological changes in the connective tissue structure, namely in bones, joints and muscles [5, 6, 7].

At the same time, there is importance in studying the bone tissue quality parameters, including patients with Type 1 and Type 2 diabetes. The outcomes of histomorphometric analysis held through experiments involving laboratory animals with insulin deficiency, for instance, showed a decrease in the bone structure formation intensity [8, 9, 10]. In addition, a decrease in the bone trabeculae length, periosteal and endocortical surfaces of the cortical plate covered with osteoid, was revealed; another issues observed was a decrease in the number of osteoblasts, a disturbance in their function, and an increase in the apoptosis rate [11, 12, 13].

Diabetes mellitus was found to be a factor predisposing to the occurrence and development of destructive periodontal diseases, leading to the loss of gingival joint [17, 21–27]. The current theory states that in patients with Type 2 diabetes mellitus, the decisive role in the pathogenesis of inflammatory diseases of the alveolar ridge belongs to microangiopathies and acidosis due to high levels of blood glucose [16]. Lack of insulin in blood leads, on the one hand, to decreased synthesis of collagen and alkaline phosphatase by osteoblasts involved in intercellular matrix formation and mineralization, and on the other hand, to disturbed calcium absorption by small intestine microvilli and its increased excretion from the body with urine. Hypocalcemia, in turn, stimulates the parathyroid gland to release hormone, which leads to resorption and thinning of the bone tissue compact layer.

Therefore, in case of diabetes, metabolic processes in the bone structure are disrupted, the cellular elements function and organic structure change, which leads to disturbed biomechanical properties and increased risk of fracture. The mechanisms that are

presumed to partially explain the bone quality deterioration in case of diabetes mellitus, include hyperglycemia and microangiopathy [15]. The authors note that bone fragility is a consequence of insufficient exposure to insulin, and not a complication of diabetes. This means that the mechanisms underlying the developing fragility of bone tissue are similar for Type 1 and Type 2 diabetes. During that, it is not related directly to the disease and may occur long before its clinical manifestations develop.

Bone tissue of the maxilla and mandible, if viewed from the point of chemical composition and structure, reveals little difference from other human musculoskeletal system bones. However, internal rearrangement takes a much faster course in the alveolar process connective tissue if compared with other skeleton bones. Normally, the alveolar ridge height is maintained via a physiological balance between the bone formation and resorption, which are regulated not only by systemic, yet also by local factors [18, 19, 20].

Nowadays, X-ray diagnostics methods in dentistry have become an inevitable part of a comprehensive medical examination. Cone beam computed tomography (CBCT) is a relatively new method for examining the dentofacial system, which allows obtaining a high-resolution 3D model of teeth and jaws. The informational reliability of this method is much higher than the traditional 2D teeth radiography, which includes targeted intraoral X-rays and orthopantomogram. Compared to 2D X-ray images, 3D digital CBCT imaging can increase significantly the efficiency and accuracy of diagnostics, including differential diagnostics. All this is achievable since this research method enables improved differentiation of tissues and organs through cross-sectional images with high resolution without overlapping [6, 14, 28–37].

Aim of study:

to identify maxillary alveolar process bone density in patients with diabetes mellitus, employing CBCT.

MATERIALS AND METHODS

The comprehensive study involved 94 patients divided into 2 groups. Group 1 included patients with diabetes mellitus, 44 people, while Group 2 comprised 50 patients without an endocrine pathology.

The inclusion criteria for the study were: the age of 25 years and older, the presence of Type 1 or 2 diabetes in the history, no dentition defects or small (1 to 3 teeth missing) and medium (4 to 6 teeth missing) number of defects.

The criteria for not exclusion were: concomitant endocrine pathology in addition to diabetes mellitus, general diseases in the decompensation stage, cancer,

and the following dental issues: increased tooth abrasion, large dentition defects, periodontitis.

One of an exclusion criterion was refusal of a patient to join the proposed studies.

The participants' median age was 62.7 ± 1.8 , without a focus on gender differences.

The examination was carried out on a Gendex-GXCB-500 dental tomograph using the icat vision software. The optical density on the dental tomograph was evaluated with a density window (side = 3 mm). The measurements in the groups were performed in the interdental partitions of the upper jaw teeth at the levels of the middle and apex of their roots, as well as the alveoli' upper edges. The average density value was calculated automatically by the software. The density was measured in Hounsfield standard units. Measures of central tendency and data scatter were calculated employing descriptive statistics methods; quantitative parameters, depending on the distribution type, were presented as the mean value (M) and standard deviation (SD), or when estimated through nonparametric statistics — as the median (Xmed) and interquartile range QR within (LQ 25% ÷ UQ 75%). The analysis of the distribution type correspondence to the normal distribution law was done using the Shapiro-Wilk criterion; the critical level of significance for differences in testing statistical hypotheses was set at $p < 0.05$. To analyze the differences of the subgroups, identified through qualitative clinical diagnostic features, the non-parametric Mann-Whitney method was used. When assessing the Student criterion values, the Bonferroni correction factor was employed. The statistical processing of the obtained data was carried out using the Statistica 10, StatSoft software (identification number AGAR207F394525FA-6).

RESULTS AND DISCUSSION

As Figures 1–3 show, the most significant changes in bone density could be observed in the upper jaw teeth neck area. The bone density changes around the central part of the teeth roots were less significant. In patients with this pathology, the apex region of a number of tooth roots revealed an increase in the bone density.

A comparative analysis of the values revealed significant differences in the Gaussian density in the group of patients with diabetes, which was due to a decrease in bone density.

A nonparametric analysis revealed a range of differences in view of the median and interquartile range (QR). So, when assessing the values of the data describing the significance of differences in the upper jaw:

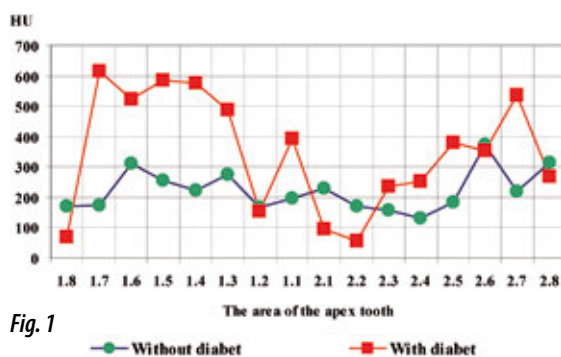


Fig. 1

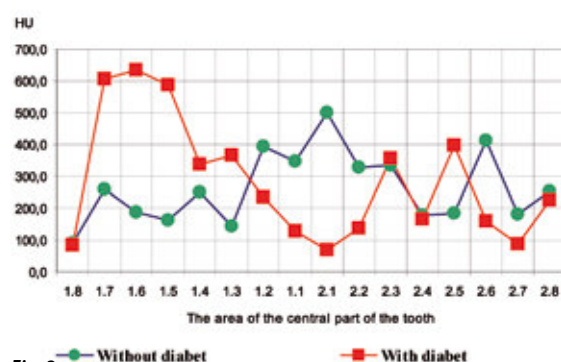


Fig. 2

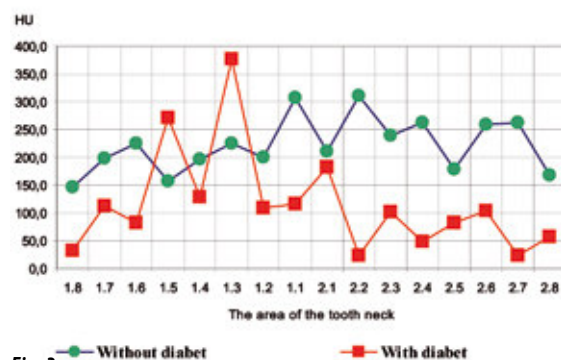


Fig. 3

Figure 1–3. Comparative characteristics of the bone tissue density (upper and lower jaws) in Hounsfield units based on Gaussian density

Upper jaw without NTG:

Tooth apex — 1.8 — Xmed = 268.0 by QR (130.5÷302.0); 1.7 — Xmed = 143.0 by QR (90.0÷263.0); 1.6 — Xmed = 266.0 by QR (124.0÷436.0); 1.5 — Xmed = 291.0 by QR (167.0÷421.0); 1.4 — Xmed = 224.0 by QR (145.0÷366.0); 1.3 — Xmed = 222.5 by QR (118.5÷392.0); 1.2 — Xmed = 155.0 by QR (100.0÷267.0); 1.1 — Xmed = 243.5 by QR (86.5÷283.0); 2.2 — Xmed = 165.5 by QR (115.0÷285.5); 2.4 — Xmed = 167.5 by QR (127.0÷257.5); 2.5 — Xmed = 257.0 by QR (173.0÷356.5); 2.7 — Xmed = 209.0 by QR (109.0÷329.0);

Central part of upper jaw tooth root — 1.8

— Xmed = 229.0 by QR (177.0÷266.5); 1.7 — Xmed = 260.5 by QR (152.0÷412.0); 1.5 — Xmed = 316.0 by QR (222.0÷385.0); 1.3 — Xmed = 301.0 by QR (264.0÷407.5); 2.2 — Xmed = 365.5 by QR (213.0÷541.0);

Tooth neck Area — 1.8

— Xmed = 299.0 by QR (234.0÷380.0); 1.7 — Xmed = 308.5 by QR (245.0÷444.0); 1.4 — Xmed = 421.0 by QR (329.0÷526.0); 2.2 — Xmed = 504.0 by QR (321.0÷631.0); 2.3 — Xmed = 293.0 by QR (221.0÷461.0); 2.4 — Xmed = 461.0 by QR (326.0÷589.0); 2.7 — Xmed = 229.0 by QR (98.0÷361.0); 2.8 — Xmed = 309.0 by QR (278.0÷445.0);

Upper jaw with NTG:

Tooth apex — 1.8

— Xmed = 168.0 by QR (141.0÷211.0); 1.7 — Xmed = 432.4 by QR (187.0÷802.0); 1.6 — Xmed = 419.0 by QR (117.3÷641.0); 1.5 — Xmed = 595.0 by QR (314.0÷901.0); 1.4 — Xmed = 402.5 by QR (123.5÷698.0); 1.3 — Xmed = 208.5 by QR (152.0÷640.0); 1.2 — Xmed = 166.0 by QR (98.0÷253.0); 1.1 — Xmed = 169.5 by QR (83.0÷475.0); 2.2 — Xmed = 148.0 by QR (115.0÷172.0); 2.4 — Xmed = 324.0 by QR (155.0÷407.0); 2.5 — Xmed = 245.0 by QR (128.5÷507.5); 2.7 — Xmed = 184.0 by QR (81.0÷617.0);

Central part of upper jaw tooth root — 1.8

— Xmed = 142.0 by QR (88.0÷172.0); 1.7 — Xmed = 190.0 by QR (47.0÷654.0); 1.5 — Xmed = 498.0 by QR (238.0÷824.0); 1.3 — Xmed = 206.0 by QR (77.0÷444.0); 2.2 — Xmed = 198.0 by QR (86.0÷223.0);

Tooth neck Area — 1.8

— Xmed = 64.0 by QR (45.0÷77.0); 1.7 — Xmed = 147.0 by QR (66.0÷179.0); 1.4 — Xmed = 157.5 by QR (76.0÷205.0); 2.2 — Xmed = 72.0 by QR (56.0÷79.0); 2.3 — Xmed = 83.0 by QR (50.0÷151.0); 2.4 — Xmed = 95.0 by QR (71.0÷120.0); 2.7 — Xmed = 92.5 by QR (84.0÷108.0); 2.8 — Xmed = 93.0 by QR (63.0÷120.0);

Similar outcomes are to be observed on dendrograms obtained through cluster analysis.

The presented data reveal significant changes in bone density according to the results of parametric and nonparametric analysis in patients with diabetes mellitus, if compared with the control group and the tooth features.

DISCUSSION

The comparative analysis carried out in the main and control groups, allowed showing that a decrease

Table 1. Bone tissue density parametric data, tooth top, upper jaw

Tooth number	M±SD	m	M±SD	m	t	P
Patients without diabetes			Patients with diabetes			
1.8	235,2±107,3	87,4	166,7±47,7	32,9	1,626*	0,0492*
1.7	193,1±124,6	103,2	479,3±362,1	286,1	-3,807*	0,0000*
1.6	284,0±163,8	140,7	418,7±320,1	250,8	-1,517*	0,0223*
1.5	302,0±158,6	134,3	566,7±294,9	232,1	-3,426*	0,0184*
1.4	252,1±138,5	116,1	449,4±348,9	299,9	-2,427*	0,0007*
1.3	255,3±143,1	124,2	395,6±345,3	288,1	-2,067*	0,0001*
1.2	187,3±127,3	102,1	238,3±249,0	152,0	-0,932*	0,0027*
1.1	218,5±133,0	108,5	291,3±283,5	221,8	-1,230*	0,0006*
2.1	227,1±146,2	124,7	196,6±195,9	137,1	0,540	0,2075
2.2	239,9±191,5	145,7	151,2±75,8	51,4	1,357*	0,0095*
2.3	270,9±120,8	98,9	306,3±161,8	129,1	-0,850	0,1638
2.4	194,1±104,2	85,1	305,7±170,6	131,0	-2,517*	0,0397*
2.5	260,6±111,1	87,1	378,1±290,6	208,7	-1,926*	0,0001*
2.6	358,2±229,9	196,2	411,8±269,1	200,3	-0,580	0,4961
2.7	223,7±127,2	101,3	307,9±258,0	210,7	-1,320*	0,0066*
2.8	238,9±181,0	148,7	292,5±144,5	129,8	-0,653	0,6504

Note: * — the reliability of statistical differences at $p < 0.05$

Table 2. Bone tissue density parametric data, central part of the tooth root, upper jaw

Tooth number	M±SD	m	M±SD	m	t	P
Patients without diabetes			Patients with diabetes			
1.8	237,0±95,1	68,8	133,6±40,4	30,8	2,781*	0,0411*
1.7	308,6±171,5	134,2	333,7±361,1	289,2	-0,281*	0,0058*
1.6	434,1±247,0	156,5	329,3±339,4	295,0	0,851	0,2688
1.5	302,8±106,9	87,2	506,6±282,3	228,4	-3,315*	0,0002*
1.4	447,4±184,1	148,3	364,8±211,3	163,5	0,987	0,5651
1.3	327,7±124,0	95,2	309,3±291,9	229,0	0,317*	0,0001*
1.2	434,0±222,2	189,0	189,5±193,5	145,8	3,203	0,6912
1.1	363,0±244,2	200,1	210,7±298,3	217,1	1,709	0,3630
2.1	473,6±256,1	227,1	181,1±329,1	193,5	2,982	0,2760
2.2	385,5±210,5	172,9	174,4±106,8	89,1	2,912*	0,0480*
2.3	475,4±265,8	188,7	314,0±242,2	209,5	2,029	0,4072
2.4	354,5±133,7	103,1	237,9±179,5	137,3	2,228	0,2124
2.5	470,4±224,4	193,8	304,0±244,2	195,8	0,649	0,1660
2.6	254,8±115,9	96,4	227,4±195,3	135,2	2,834	0,7479
2.7	304,5±170,4	143,9	132,4±54,8	44,8	2,712	0,0669
2.8	237,0±95,1	68,8	264,0±223,7	172,4	0,437	0,3879

Note: * — the reliability of statistical differences at $p < 0.05$.

in bone density can be observed in the area of the teeth neck in patients with diabetes mellitus. The least significant changes were in the area of the middle third of the teeth roots. Minor changes or even an increase

in the density were observed in the apex region. The revealed data are comparable with the outcomes presented in the national literature (Bondarenko N.N., Balakhontseva E.V., 2012, Nikolayuk V.I., Kabanova

Table 3. Bone tissue density parametric data, tooth neck, upper jaw

Tooth number	M±SD	m	M±SD	m	t	P
Patients without diabetes			Patients with diabetes			
1.8	318,5±132,9	89,5	66,9±33,5	23,8	5,244*	0,0010*
1.7	349,7±177,2	140,8	129,7±72,0	56,8	2,978*	0,0490*
1.6	400,2±281,6	200,3	176,2±144,1	101,8	1,733	0,1989
1.5	315,3±106,7	85,2	250,3±149,2	125,1	1,370	0,2010
1.4	433,5±184,1	143,3	145,2±67,6	53,4	3,753*	0,0339*
1.3	350,5±144,2	121,5	174,9±179,4	154,3	3,323	0,3250
1.2	391,5±163,7	131,7	156,0±166,3	98,2	4,077	0,8640
1.1	435,8±220,7	174,9	148,5±152,3	92,2	3,896	0,2350
2.1	430,6±235,4	134,7	130,9±107,1	93,0	5,472	0,4783
2.2	486,7±197,9	172,0	98,3±79,5	53,6	5,748*	0,0105*
2.3	426,4±463,7	245,7	129,4±118,5	85,5	3,655*	0,0260*
2.4	488,7±333,3	192,7	115,5±76,0	49,6	5,228*	0,0077*
2.5	389,5±236,8	146,7	173,8±174,9	111,9	3,018	0,5800
2.6	423,3±165,3	134,1	144,7±109,2	80,1	4,780	0,2184
2.7	281,2±195,6	153,8	101,0±59,6	37,3	2,217*	0,0144*
2.8	345,1±126,9	96,9	93,3±41,6	29,2	5,081*	0,0113*

Note: * — the reliability of statistical differences at $p < 0.05$

A.A., Karpenko E.A., 2015, Chuev V.P. et al., 2017; Khaibullina R.R. et al., 2018).

It is also notable that in the group of people with diabetes, the upper jaw bone density ranges from 151.2 to 566.7 standard units in the apical region of the teeth; from 132.4 to 506.6 standard units at the roots central part, and from 29.2 to 154.3 at the teeth neck. There was a direct dependence identified in terms of the density changes between the neck area of all teeth, especially in the area of molars, and incisors, which is accounted for by deteriorated trophic properties of periodont, inflammatory issues, and slowing bone remodeling. Changes in the area of the teeth apex were less obvious, while in the area of the teeth lateral group an inverse dependence was observed — here the bone density in people with diabetes was above that in the first group, which can be explained by reparative processes and the nature of blood supply to this area.

CONCLUSIONS

1. Cone beam computed tomography of the dentofacial segment allows a quantitative and qualitative evaluation of the optical density, as well as it also offers an effective method for evaluating the bone tissue status in case of diabetes mellitus.

2. The evaluation of the bone tissue of the upper jaw alveolar ridge, according to densitometry, showed

that changes in the bone density in case of diabetes mellitus, are symmetrical.

3. Patients with Type 1 and 2 diabetes mellitus has demonstrated a significant decrease in the upper jaw bone tissue density in the cervical region of all groups of teeth, which is due to the anatomical and physiological features of the periodontal tissue structure and the functional loads it is exposed to.

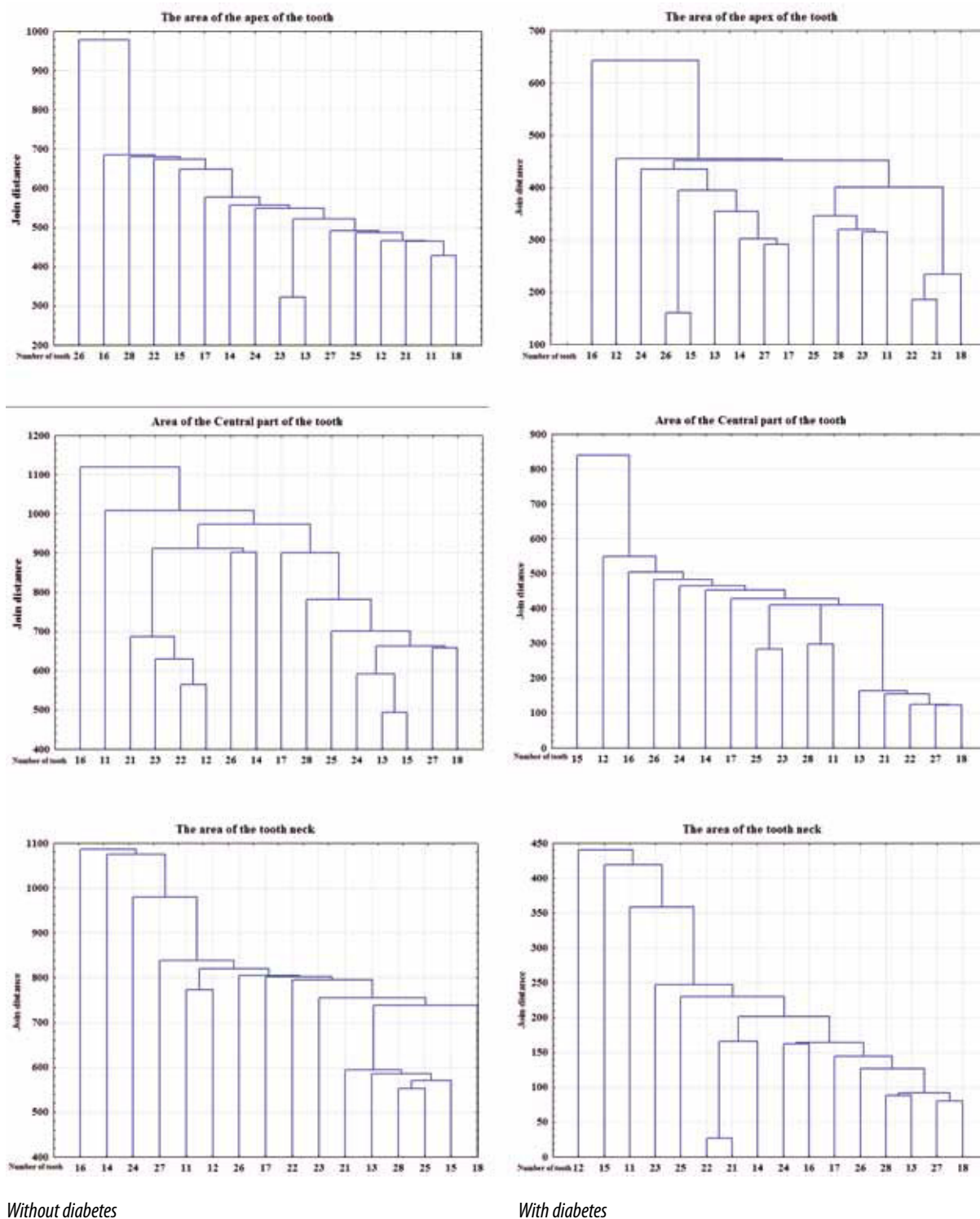
4. Changes in bone density in the apical and central parts of tooth roots are less significant. A decrease in the bone density in patients with diabetes is observed in the anterior group of teeth.

5. The central area of the molars and premolars roots, as well as the tops of the upper jaw teeth in patients with diabetes mellitus reveal an increase in the bone density.

6. The study outcomes suggest that the density change is a criterion for evaluating the jaw bone tissue, as well as the most important sign that allows diagnosing and forecasting periodontal disease in people with diabetes at an early stage.

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Without diabetes

With diabetes

Figure 4. Dendrogram. Single link method. Euclidean distance. Of the optical density of the bone tissue of the upper jaw

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BIOMECHANICAL EVALUATION OF STRESS-STRAIN CONDITION OF RESTORATIVE CERAMIC PIN STRUCTURES AND DENTAL ROOTS

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ABSTRACT — The authors have proposed a ceramic stump pin inlay featuring a ceramic coating of the over-the-root part, which acts as a covering aesthetic design, as well as strengthens the stump retention, distributes rationally the functional load and strengthens the resulting system. This work offers a view at the outcomes of studying the stress and strain status of the proposed design for a ceramic stump pin inlay through the method of finite elements on a three-dimensional mathematical model. The designed 3D mathematical model included, as initial data, the specific features of the cortical bone, the cobalt-chrome alloy, the facing field-spathic ceramics, and tooth dentin. We studied the distribution of stresses occurring while employing the specially designed pin structure under the effect of multidirectional loads of 150 N, directed strictly down relative to the tooth longitudinal axis (vertically), and the load at a 45° angle. The proposed newly designed inlay allows reducing the maximum stress within the ceramic coating by 51.8% at a vertical load, and by 43.2% at a side load of 45°, compared to traditional metal-ceramic structures.

KEYWORDS — stump pin inlay, tooth root, metal & ceramics cap, stress and strain status.

INTRODUCTION

There is a wide range of ways to restore severely damaged tooth crowns [5, 8] available nowadays. The leading position among the prosthetics methods used for this pathology belongs to pin structures, namely stump pin inlays covered with artificial crowns, as well as pin teeth. The successful outcome of orthopedic treatment will ultimately depend on the manufacturing technology and the pin structure design [2, 6, 7].

In order to detect the stress-and-strain status of complex geometric objects, only the finite element method will make the best choice [1, 3, 4]. Mathematical modeling allows displaying and forecasting

an enormous number of geometry behaviors as well as predict the future of the object of study, with no real experiment (<https://www.ansys.com/solutions/solutions-by-industry/healthcare>).

Through our work, we used the ANSYS Academic Research Release 2020K1 software package (academic license for scientific research), which includes modules for geometric modeling ANSYS Space Claim, ANSYS mechanical strength problems solutions, whereas professional advice was offered by Kondratyev D. V., an expert of the CADFEM-CIS company (Samara, Russia).

The Aim of this study

is to evaluate biomechanical effectiveness of the proposed ceramic pin structure using the finite element method on the designed 3D mathematical model with multidirectional loads.

MATERIALS AND METHODS

Two detailed mathematical models were developed to solve the tasks (Fig. 1). These two objects were used to model the same dimensions (root length and canal diameter, size of the pin part, etc.). The models were divided into 2 groups depending on the studied pin structure.

Group 1 studied the stress-and-strain status of the traditional method for restoring a missing clinical tooth crown.

The method implied the following: a stump pin was made of a cobalt-chrome alloy (CCA) for the tooth root, which was fixed in the root canal with cement (GC Fuji I). Further, a metal & ceramic crown was made, which, too, was fixed on the stump pin inlay with cement (GC Fuji I) (Figure 1a).

Group 2 included a model that studied the stress-and-strain status of the proposed pin structure (Federal Institute for Industrial Property, Decision to grant a patent of the Russian Federation under application 2019143931 dated 23/12/2019).

The point of this design was as follows. A pin tooth was made for the tooth root (a stump pin inlay with ceramics applied to it by firing), which was fixed in the tooth root canal by cement (GC Fuji I). The crown part attachment angle to the tooth root was 90 degrees. During that, the pin tooth specific design

feature is that the ceramics contacts the tooth supracardiac surface (Fig. 1b).

The geometric models were broken up by a finite element grid consisting of tetrahedral elements. The area of our interest — the crown and the pin were broken by elements with face sizes up to 0.1–0.2 mm, the rest of the model size — up to 0.4 mm (Fig. 2).

To calculate the stress-strain status, we used the data on the components of mathematical models (dentin, CCA, ceramics, etc.), as is shown in Table 1.

The strength analysis of the above models was performed with two loading options. Next, we will call these Step 1 and Step 2. At Step 1, a compressive load of 150 N with a constant intensity was applied to the crown part of the device, directed strictly downward relative to the tooth longitudinal axis (vertically) — Fig. 3a. At Step 2, a 150 N load of constant intensity was again applied at an angle of 45° relative to the tooth longitudinal axis — Fig. 3b. The model was fixed on the end-side surfaces, where the stresses were not taken into account. The study area was located at a distance of more than 5 typical dimensions (the tooth crown height) from the fixing point.

The models were analyzed regarding the stress distribution in ceramics, in the metal part of the pin structure, and in the tooth root. Given that the analyzed materials have different properties, several stress options were employed to evaluate the stress status. The first is the equivalent Mises stress (recommended for viscous bodies, such as metals — the greatest energy theory) and the maximum principal stress (recommended for brittle solids, such as ceramics or bone — the greatest stress theory).

For a more detailed understanding, the data for the resulting stresses was obtained separately in the ceramics, in the pin-stump part and in the tooth root.

RESEARCH OUTCOMES

Results of the stress & strain status in Group 1.

Figure 4 below shows the results of equivalent stresses in the metal & ceramics crown (Group 1) with a vertical load and a load applied at an angle of

45°. Fig. 5 shows the maximum main stresses in the ceramic coating.

The results of studying the stress & strain status of the experimental mathematical model in Group 1 showed that the maximum stress area under vertical load is the contact spot between the crown and the tooth root (Fig. 4a). When the angle of application of the functional load relative to the occlusal surface of the tooth crown changes within 45°, the stresses change towards increase (Fig. 4b). The most dangerous for the ceramic coating are the tensile stresses that occurred at a side load of 174 MPa (Fig. 5b). The tensile strength value is exceeded at Step 2 (the tensile strength of ceramics is 48 MPa). In case of a vertical load (Step 1), the maximum stresses were recorded within 14 MPa, which confirms a sufficient strength margin of the ceramic coating under this loading option (Fig. 5a).

Fig. 6 shows the equivalent stresses that occur in a cast stump pin inlay. The same goes about Steps 1 and 2.

Fig. 6 shows that the stress distribution pattern corresponds to the stress distribution pattern typical of cast metal pin structures. The major changes manifested as high stresses (MPa) were observed at a side load of 150N (Fig. 6b). In this case, the strength limit for the cast pin inlay was not exceeded (the compressive strength of the CCA is 450 MPa, the tensile strength is 655 MPa), which means there is still a safety margin remaining.

Fig. 7 shows the results of equivalent stresses in the tooth root (Group 1) with a vertical load and a load applied at an angle of 45°.

Fig. 7 shows that the maximum stress area is located in the root neck part (the contact spot between the crown and the root). The most dangerous are tensile stresses at a lateral load of 89 MPa (Fig. 7b) with a dentin tensile strength of 105 MPa. The dentin under the inlay and the crown was under a strong tensile stress and thus may be subject to future destruction.

Results of the stress & strain status in Group 2.

Figure 8 below shows the results of equivalent stresses in the crown part of the pin tooth (Group 2)

Table 1. Materials properties

Material	Young's Module (Pa)	Poisson's Rating	Strength	
			Compressibility (MPa)	Tensile (MPa)
Cortical Bone	13.7e9	0.30	156	85
Cobalt-Chrome Alloy	225e9	0,35	450	655
Ceramics	69e9	0,28	450	48
Tooth dentin	18e9	0,31	310	105

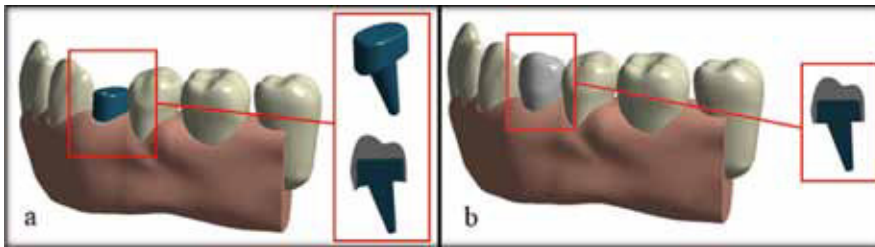


Fig. 1. Solid-state model of the lower jaw sector with a stump pin inlay installed in the tooth root: a — Group 1; b — Group 2

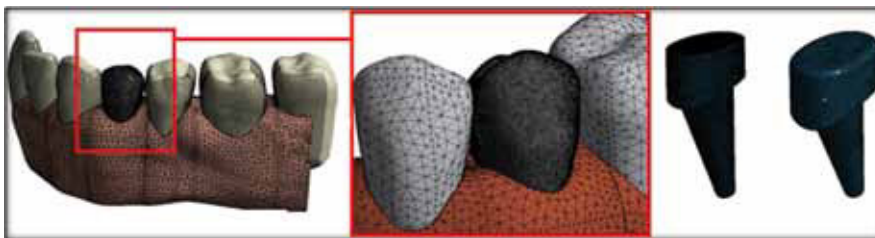


Fig. 2. Finite element model of the system

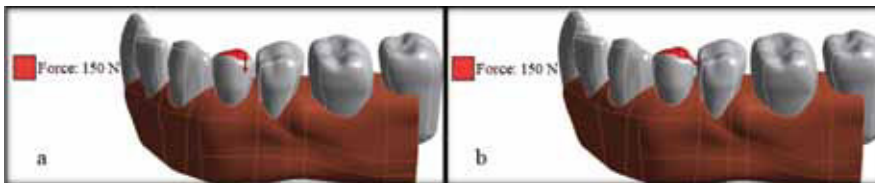


Fig. 3. Boundary conditions of the design model: a — Step 1, vertical load; b — Step 2, load at an angle of 45°

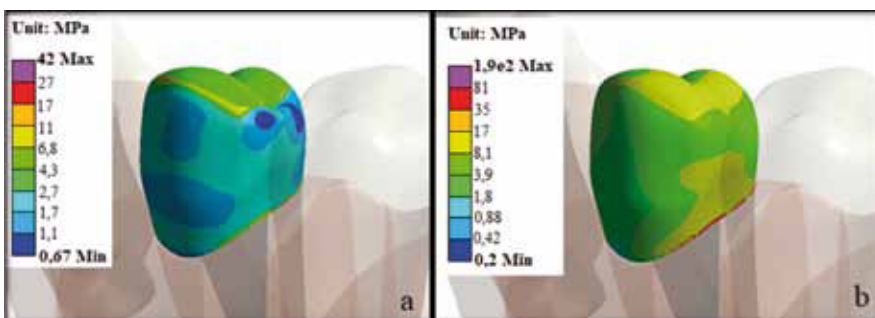


Fig. 4. Equivalent stresses in the metal & ceramics crown. Group 1: a — Step 1 (vertical load); b — Step 2 (load at an angle of 45°)

with a vertical load and a load at an angle of 45°. Fig. 9 shows the maximum major stresses in the ceramic coating of the pin tooth.

The results of studying the stress & strain status of the experimental mathematical model in Group 2 revealed that the maximum stress area under vertical load was the area of contact between the crown and the tooth root (Fig. 8a). When the functional load application angle relative to the occlusal surface of the tooth crown changes within 45°, the stresses change upwards (Fig. 8b). The most dangerous, yet not critical for the ceramic coating were the tensile stresses that occurred at a lateral load equal to 30 MPa (Fig. 9b). The tensile strength value at Step 2 was not exceeded (the tensile strength of ceramics is 48 MPa). Under a vertical load (Step 1), the maximum stresses were recorded within 6.2 MPa (Fig. 9a), which points at a significant strength margin that the ceramic coating has under this loading option.

Fig. 10 shows the equivalent stresses that occur in the cast base of the pin tooth. The same with Steps 1 and 2.

Fig. 10 shows that the stress distribution corresponds to the stress distribution pattern typical of cast metal pin structures. The main changes revealed as high stresses were identified at a side load of 77 MPa (Fig. 10b). In this case, the strength limit for

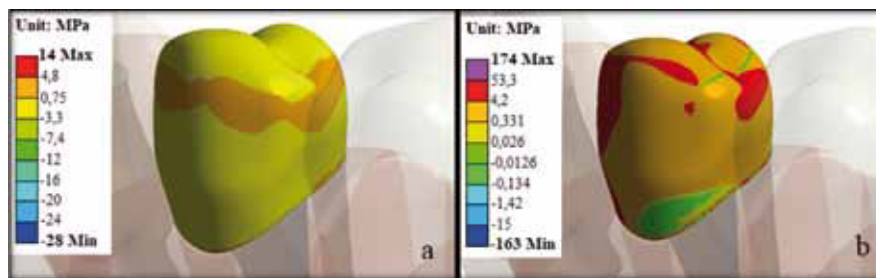


Fig. 5. The maximum principal stresses occurring in the ceramics. Group 1: a — Step 1 (vertical load); b — Step 2 (load at an angle of 45°)

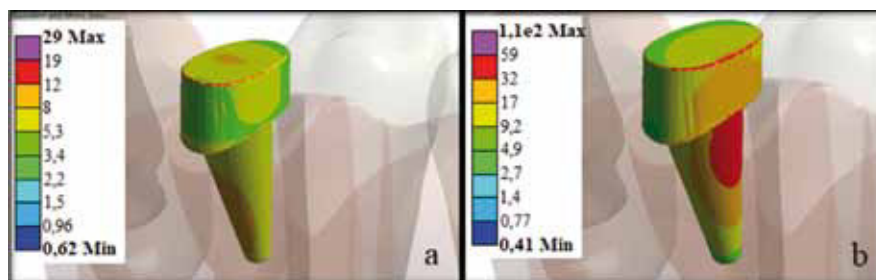


Fig. 6. Equivalent stresses in the stump pin inlay. Group 1: a — Step 1 (vertical load); b — Step 2 (load at an angle of 45°)

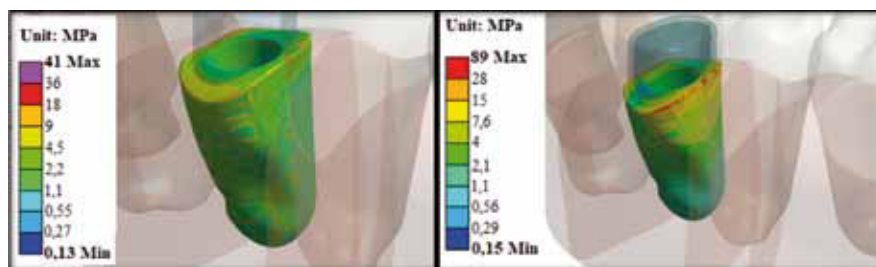


Fig. 7. Equivalent stresses in the tooth root. Group 1: a — Step 1 (vertical load); b — Step 2 (load at an angle of 45°)

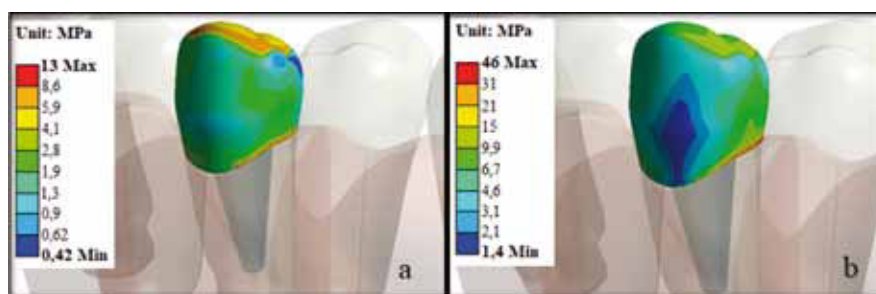


Fig. 8. Equivalent stresses in the crown part of the pin tooth. Group 2: a — Step 1 (vertical load); b — Step 2 (load at 45° angle)

the cast pin inlay was not exceeded (the compressive strength of the CCA is 450 MPa, the tensile strength being equal to 655 MPa), which points at a safety margin available.

Fig. 11 shows the outcomes for equivalent stresses in the tooth root (Group 2) with a vertical load and a load at an angle of 45°.

Figure 11 offers a clear picture showing that the area of maximum stress is the neck part of the root (the contact spot between the crown part of the device and the tooth root). The most dangerous are tensile stresses at a lateral load of 29 MPa (Figure 11b) with a tensile strength of 105 MPa for dentin. The dentin of the tooth under the inlay and the crown was subjected to a slight tensile stress, which is expressed through a sufficient safety margin available.

Tables 2–4 offer a look at a comparative analysis of the obtained quantitative data for the maximum and average stresses depending on the study group as well as the part of the system.

Table 2 shows that the resulting maximum stresses registered in the pin structure's crown part were the highest in Group 1, where the traditional method was employed to manufacture the stump pin inlay followed with its further coating with a metal & ceramics crown. These indicators were the highest for both the vertical (27 MPa) and the lateral load (81 MPa). Given the

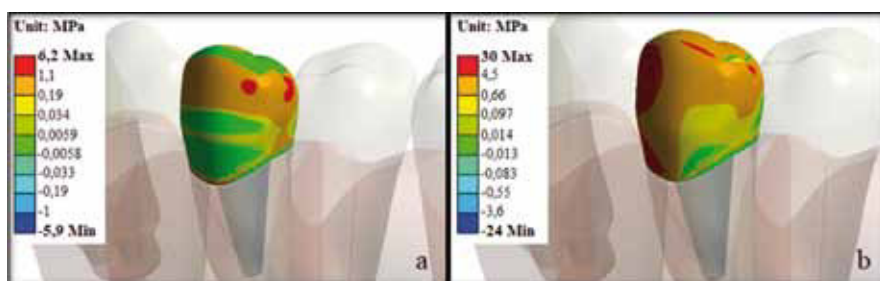


Fig. 9. The maximum major stresses occurring in the ceramics. Group 2: a — Step 1 (vertical load); b — Step 2 (load at 45° angle)

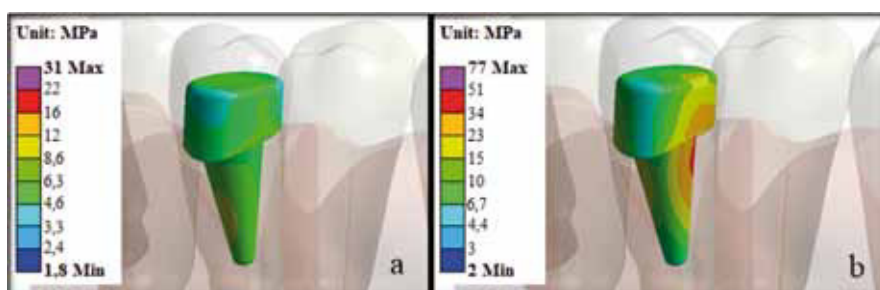


Fig. 10. Equivalent stresses in the metal base of the pin tooth in group 2: a — Step 1 (vertical load); b — Step 2 (load at an angle of 45°)

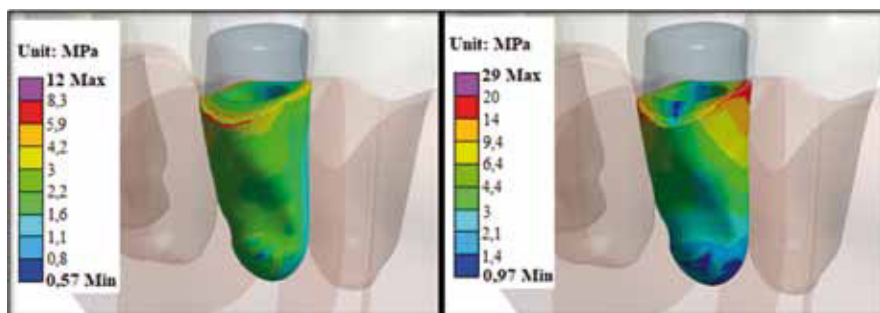


Fig. 11. Equivalent stresses in the tooth root. Group 2: a — Step 1 (vertical load); b — Step 2 (load at 45° angle)

fact that the critical stresses leading to the ceramics chipping were those at 48 MPa, we are safe saying that the ceramic coating of this type of the orthopedic structure will prove more susceptible to destruction in the future. Using the newly proposed version of the pin tooth allowed reducing the occurrence of maximum stresses in the ceramic coating. A mathematical analysis in Group 2, for instance, showed that under a vertical load this indicator decreased by 51.8% (13 MPa), while in case of a side load of 45° it went down by 43.2% (46 MPa), compared to Group 1.

The obtained results of maximum equivalent stresses in the pin structure metal base (Table 3) offered a slightly different picture rather than the ceramic coating. Under a vertical load, we found the lowest values of the maximum stresses

in Group 1 (19 MPa). In Group 2, this indicator was higher by 15.7% (22 MPa). Under a side load, the maximum stresses in the cast base of the pin structure in Group 1 reached 59 MPa, whereas in Group 2 they were 51 MPa. However, given that the critical stresses leading to the CCA destruction imply 665 MPa, both groups have a huge margin of safety, this, in turn, meaning that the destruction would likely affect the fragile items (tooth root or crown part) and this element had no critical role within our system, *the crown part of the device – the pin – the tooth root.*

The results of maximum stresses occurring in the tooth root (Table 4) under a vertical load and at an angle of 45° were highest in Group 1 reaching 36 and 99 MPa, respectively. So in Group 2, the vertical and the lateral load led to the maximum stresses of 9 and 20 MPa, respectively, which is 75 and 65% below similar indices in Group 1, which indicates rather a significant load on the root, whereas when in case of bending loads, destruction of the root edge areas cannot be excluded.

CONCLUSION

In view of the above, based on the data obtained from the stress & strain status analysis for three-dimensional mathematical models of destroyed teeth restored through various types of stump pin structures, the following conclusions can be made:

Table 2. Results of maximum stresses in the crown part of the pin structure

Group	Maximum equivalent stresses, MPa		Critical stresses leading to ceramics chipping (MPa)
	90°	45°	
1	27	81	48
2	13	46	

Table 3. Results of maximum stresses in the metal base of the pin structure

Group	Maximum equivalent stresses, MPa		Critical stresses leading to CCA destruction (MPa)
	90°	45°	
1	19	59	665
2	22	51	

Table 4. Results of maximum stresses in the tooth root

Group	Maximum equivalent stresses, MPa		Critical stresses leading to tooth root destruction (MPa)
	90°	45°	
1	36	99	22
2	9	20	

1. The proposed ceramic stump pin inlay will not only minimize the stresses in the tooth hard tissues yet also will reduce significantly the stress & strain status on the border of the pin structure and the locking cement under various-direction loads, thus reducing the risk of decementation and broken orthopedic structure.
2. The stress distribution pattern for all the examined types of stump pin structures is in line with the nature of stress distribution typical of rigid solids with a load concentrating predominantly at the pin top. A significant stress reduction in the proposed ceramic stump pin inlay, if compared to the conventional design, is due to a significant stress reduction at the *fixing material — pin structure* border under lateral and oblique loading.
3. As the area of the greatest stress concentration in Group 1 is located in the tooth dentin at the border with the artificial crown edge and embraces a small area of maximum stress, maintaining the inlay precision in the tooth neck could be a good option.
4. The newly designed ceramic stump pin inlay allows significant reduction in the equivalent stresses not only at the area where the different materials come in contact — in the root dentin

— yet also at the pin structure top with no risk of dangerous loads concentration, thus minimizing the probability of root fractures.

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COMPARATIVE ANALYSIS OF IMMUNOLOGICAL PARAMETERS AGAINST THE BACKGROUND OF VARIOUS TREATMENTS FOR ORAL LICHEN PLANUS

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ABSTRACT — The study of immunological parameters was conducted to investigate the state of pro- and anti-inflammatory cytokines in saliva of patients with lichen planus. The patients were divided into two groups by simple randomization: the first group was treated with Celestoderm applications: Solcoseryl 1:1, the second group was injected with platelet autoplasm. In the near terms of observation (1–7 days), the level of pro- and anti-inflammatory cytokines was evaluated. It was revealed that all patients with lichen planus showed a significant increase in the level of pro-inflammatory cytokines and immunoglobulins; that indicates a pronounced inflammatory reaction in the oral cavity. At the same time, all patients showed a decrease in inflammatory potential due to the local therapy. However, in the group treated with injections of platelet autoplasm, a significant improvement in immunological parameters and more rapid relief of inflammation compared to the other group was noted.

KEYWORDS — oral lichen planus, immunoglobulins, cytokines, saliva, treatment.

INTRODUCTION

The oral cavity possesses not only general immunity, which equally protects all organs and tissues of the body, but also its own local immunity, which plays the main role in protecting against infection [1]. The effectiveness of protection depends on many factors, such as the integrity of the mucous membrane, the state of the lymphoid system, changes in the constitution of lymphoid tissue, which form transition states and a predisposition to a number of diseases and pathological conditions, and the content of protective factors (secretory immunoglobulins, lysozyme, lactoferrin, etc.). The inflammatory process is a very finely regulated balance between pro- and anti-inflammatory mediators that neutralize the harmful effects of irritation and minimize damage to their own tissues

[2, 3]. The secretion of cytokines is a short, self-limited process that is initiated by certain gene-determined receptors [4].

The diagnostic value of determining cytokines significantly increases when they are studied directly in the focus of the inflammatory process [5,6]. For this purpose, the determination of cytokines directly through liquids in cavities is used, i.e. in mixed saliva of the oral cavity [7]. The content of cytokines in the oral fluid does not correlate with their level in the blood, which once again proves the autonomy of local oral immunity [8].

MATERIALS AND METHODS

As a result of a comprehensive clinical examination and treatment of 60 patients with an erosive and ulcerative form of lichen planus at the age of 45–59 years, divided into 2 equal groups: group I — they carried out the traditional treatment regimen, the applications of Celestoderm and Solcoseryl 1: 1, were used in group II platelet autoplasm injections. The level of pro- and anti-inflammatory cytokines and immunoglobulins after 3 and 7 days was evaluated.

The results of an immunological study of patients with erosive and ulcerative form of lichen planus demonstrated the high effectiveness of drug therapy in the treatment of the above pathology, in particular the use of platelet autoplasm injections. Prior to the initiation of drug therapy, patients of all both clinical groups had a high level of pro — and anti-inflammatory cytokines and immunoglobulins. Directly in the focus of inflammation, the level of cytokines increases significantly during their study, which is consistent with data from other authors [8]. The content of cytokines in the oral fluid does not correlate with their level in the blood, which once again proves the autonomy of local oral immunity. Increased pro-inflammatory cytokine profile (IL-1 β — 41.24 ± 1.87 pg/ml; IL-8 — 51.3 ± 1.21 pg/ml; IFN γ — 6.33 ± 0.54 pg/ml; TNFa — 3.95 ± 0.37 pg/ml) characterizes a violation of the immunity regulation, a pronounced inflammatory process and damage to the tissues of the oral mucosa. A high level of the anti-inflammatory cytokine interleukin-4 (10.1 ± 2.3 pg/ml) indicated the develop-

ment of compensatory reactions aimed at suppressing the inflammatory process. The increased content of immunoglobulins (sIgA — 0.43 ± 0.01 IU/ml, IgG — 0.022 ± 0.001 IU/ml, IgM — 0.15 ± 0.01 IU/ml) indicates an imbalance between their synthesis and decay in the background of a damaging factor in acute and chronic inflammatory and destructive diseases of the oral cavity.

After 3 days from the start of treatment, the concentration of pro-inflammatory cytokines began to decrease, however, the difference compared with the data obtained at the beginning of the treatment and between the comparison groups was statistically unreliable ($p > 0.05$, $p > 0.01$). The concentration of anti-inflammatory IL-4 and immunoglobulins continued to increase in all treatment groups, although this difference was not statistically significant relative to the start of the treatment and between the observation groups ($p > 0.05$).

Seven days after the start of the treatment, there was a tendency to a decrease in the level of pro-inflammatory cytokines in patients of all clinical groups. For example, the concentration of IL-1 β in the group of patients who received traditional drug treatment (group I) was 33.8 ± 1.23 pg/ml, while using PRP therapy it was 34.1 ± 0.91 pg/ml. The concentration of interleukin-8 was 42.5 ± 1.23 pg/ml, which is 10.8% more compared with the comparison group II ($p < 0.01$). It should be noted that in the group of patients, the treatment regimen of which included injections of platelet autoplasm, a significant difference was also obtained relative to the first observation group ($p < 0.01$). When studying the concentration of TNF α , there was also a significant decrease in this indicator relative to the start of treatment in all observation groups. Between comparison groups the following was noted in group II relative to group of observation I: (2.61 ± 0.16 pg/ml and 3.48 ± 0.23 pg/ml, respectively, at $p < 0.01$). The interferon-gamma concentration continued to decrease in all cohorts, however, no significant difference was obtained between the comparison groups ($p > 0.05$). So, IFN γ in group I was 5.27 ± 0.33 pg/ml, in group II — 4.83 ± 0.21 pg/ml. The value of the anti-inflammatory cytokine indicator continued to increase in all comparison groups: in the first group, 13.3 ± 2.2 pg/ml; in II — 12.8 ± 2.1 pg/ml. The concentration of secretory immunoglobulin A practically did not change its value and amounted to 0.39 ± 0.06 IU/ml in group I, and 0.37 ± 0.08 IU/ml in group II. A similar situation was observed when determining the IgG index.

CONCLUSIONS

Thus, a week after the start of the treatment, the initiation of the restoration of immunological param-

eters was noticed. More pronounced dynamics was reported in patients of the second observation group. A decrease in the concentration of cytokines on the 7th day of observation is a reflection of a decrease in the activity and severity of the inflammatory process in the oral cavity. In addition, since there was no increase of immunoglobulin concentration, a decrease in the activity of the inflammatory process was observed. The study confirmed the effectiveness of this dental treatment for elderly patients. The analysis of the obtained data justifies the need to include the above pharmacotherapy method in the treatment regimen.

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GINGIVECTOMY AS A METHOD OF PREPARATION FOR ORTHOPEDIC TREATMENT IN PATIENTS WITH BOTTOM DENTAL CROWN OF ABUTMENT TEETH

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ABSTRACT — The problem of prosthetics for patients with a bottom dental crown of abutment teeth is relevant for orthopedic dentists. In this case, it is advisable to make a special preparation of the oral cavity before prosthetics. One of these methods is gingivectomy. **GOAL.** In this paper, a comparative analysis of the clinical parameters of the dentogingival complex before and after gingivectomy was performed. **MATERIALS AND METHODS.** The oral hygiene index, PSR, PCR, Schiller–Pisarev test, and PMA were determined. The study involved 26 patients at a young age, according to the WHO (World Health Organization) classification. Clinical indicators were evaluated before gingivectomy and 21 days later. **RESULTS.** At all stages of observation, the positive dynamics of the healing of the dentogingival complex was marked. There was a positive prognostic value of gingivectomy before prosthetics. However, no complications or side effects were detected. **CONCLUSION.** The necessity of gingivectomy for patients with a bottom dental crown of abutment teeth has been proved and justified.

KEYWORDS — gingivectomy, prosthetics, bottom dental crown, dentogingival complex.

INTRODUCTION

Dentofacial system is one of the top human body systems in terms of the arrangement complexity, anatomical structure and the variety of functions performed. At the same time, dentofacial system, taken as the main craniofacial element, is the initial segment of the digestive and respiratory systems, also being responsible for the interconnection of the speech-related, facial and aesthetic functions [1–10]. Bottom clinical crowns are a common phenomenon in the clinic of orthopedic dentistry. This fact causes a lot of inconvenience, and sometimes it is a relative contraindication to prosthetics, because for adequate

fixation of fixed orthopedic structures, a sufficient height of the stump of the tooth is necessary to ensure the longest possible path of the prosthesis [11]. The so-called contact area is necessary for the mechanical retention of the structure. For prosthetics of patients with this problem, it is necessary to resort to a number of methods aimed at improving the conditions that affect the fixation of the future prosthesis. There are many methods to improve the fixation conditions. They can be divided into orthopedic, orthodontic, and surgical. Among the most common are gingival retraction, gingivectomy and gingivoplasty.

The purpose of this work

is to conduct a comparative analysis of the clinical indicators of the dentogingival complex for patients with low height of the clinical crown of the tooth when using gingivectomy before orthopedic treatment.

MATERIALS AND METHODS

To achieve this goal, 26 patients with low clinical crown of abutment teeth who needed an orthopedic treatment were examined and treated. The study was conducted with patients in the age group of 25–44 years (young age according to WHO). The clinical study included anamnesis collection and clinical examination according to the *gold standard* principle.

Special attention was paid to measuring the dentogingival complex to the top of the alveolar ridge using a graduated probe to determine the position of the alveolar ridge and the biological width. The condition of periodontal tissues was assessed using periodontal indices, the risks of further progression of periodontitis (at the presence), and patients with risks were identified.

According to the *gold standard* principle, negative or positive prognostic value and sensitivity were evaluated based on the probability that an existing disease scores positive points. We took into account the patient's psycho emotional state, shifts in which were the criterion for exclusion from the study [12]. The results of treatment were taken into account for 21 days of treatment. Processing and analysis of the received information will be performed using the

Microsoft Windows 10 operating system. Statistical processing of the obtained results is performed in the program Statistica 13.0. Statistical analysis was performed by variation statistics with the definition of the average value (M), its average error ($m \pm m$) evaluation of reliability of differences between groups using the student's criterion (t) when $p < 0.01$, $t \geq 2$.

RESULTS

The first goal of the study was to detect the early symptoms of periodontal tissue inflammation. In addition to achieving this goal, we also tried to improve the gingival contour and bone architecture in order to facilitate the control of plaque, which is an additional factor that leads to gum inflammation. Functional therapy, selective polishing, improvement of function, morphology and aesthetics, replacement of missing teeth and restoration of anatomical shape were also performed.

Before the gingivectomy, the oral hygiene index was determined. The simplified plaque index PCR was $67.8 \pm 2.3\%$, which corresponds to poor oral hygiene. In this case, the Schiller–Pisarev sample is positive, the PMA is $32.2 \pm 2.4\%$ (light and medium severity). The average PSR was 2.1 ± 0.2 points (it is recommended to make professional oral hygiene, removal of supra- and subgingival tooth stone). After removing dental deposits, patients were warned to observe daily oral hygiene, which will prevent the development of complications and accelerate the regeneration of the wound surface. Gingivectomy of the gums consisted of standard stages. After 21 days, a clinical evaluation of the effectiveness of treatment was performed based on the determination of the hygienic and periodontal indices. Thus, the PSR was $24.3 \pm 1.2\%$, provided that the patients used a soft toothbrush. The Schiller–Pisarev test is negative, so the RMA was not determined. Periodontal screening was 0.7 ± 0.1 points.

DISCUSSION

Thus, when performing gingivectomy as a preparatory stage before orthopedic treatment, no complications or side effects were detected for patients with a bottom dental crown of abutment teeth. There were no symptoms of suppuration of the wound and septic phenomena, as well as the development of gingivitis, periodontitis. It's worth mentioning, that in the future, systematic and thorough oral care is required. This will not only avoid relapse, but also prevent the development of inflammatory and destructive complications, which justifies the need to study this issue in subsequent studies.

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STUDY OF ELASTIC ELEMENTS OF LOWER JAW EXOSKELETON

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ABSTRACT — THE AIM OF THIS STUDY is to prove compensatory abilities of anti-gravity elastic traction of lower jaw exoskeleton. **MATERIALS AND METHODS.** The test involved 97 volunteers who were divided into 3 groups depending on their level of physical activity. In each group, all participants were randomly divided into 2 subgroups: without load compensation and with load compensation on the lower jaw. The load test was carried out for each participant using a special device simulating a one-way load on the lower jaw. Load compensation was made by elastic elements. Registration of subjects' postures was carried out by the method of photometry of subjects' spines with pre-marked markers of Th-1 and L-1 vertebrae. Photos were analyzed in Photoshop CS. For this purpose, the line between the markers Th-1 and L-1 has been drawn. Analysis of the results was carried out on the angle of deviation of the vertebral column before and after the study. **RESULTS.** In the course of the study on volunteers it was found that the one-sided load on the lower jaw is reflected on the posture of the tested person, but elastic elements are able to compensate for the one-sided load and minimize the angle of inclination of the vertebral column. It has also been found that the angle of inclination is affected by the initial physical preparation to the test. **CONCLUSION.** During the study, the compensatory abilities of the anti-gravity elastic pull of the lower jaw exoskeleton have been proved.

KEYWORDS — posture, exoskeleton, photometry, load, lower jaw.

INTRODUCTION

Diagnostics in dentistry, on the one hand, has its own specifics; on the other hand, it is based on general medical research methods. All diagnostic methods and tests to varying degrees are objective and informative, have their sensitivity, specificity and reproducibility. [1–12]. One of the most common injuries to the bones of the facial part of the head is fractures of the lower jaw [13, 14]. In view of surgical and cosmetic features of carrying out operations in maxillofacial

area [15], for restoration of functional activity at a fracture of the lower jaw we developed the device an exoskeleton of the lower jaw (patent No. 2655086 of 17.07.2017) — the device consisting of the device of external fixing of otlomk of bones, which is fixed on them by means of osteoclamps, a submandibular arch and a head-mounted hat connected by anti-gravitational elastic elements (Fig. 1).

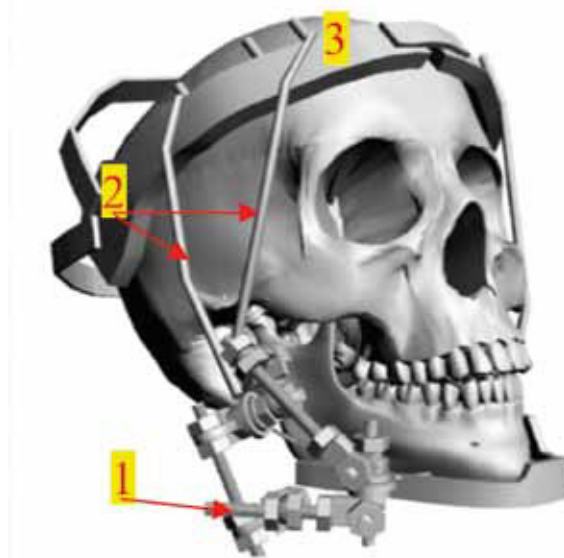


Fig. 1. Exoskeleton of the lower jaw. 1 — external fixation device, 2 — elastic elements, 3 — head cap

MATERIALS AND METHODS

In order to model the one-way load and analyze the possibility of its compensation, a special device was used consisting of parallel plates: 1 — a plastic individual impression spoon obtained by printing on a 3D printer (Fig. 2.1), placed in the oral cavity and 2 — an arc with slots for the attachment of a weight of 0.3 kg, located on the lower edge of the lower jaw (Fig. 2.2). Parts of the device are interconnected by rods (Fig. 2.3) [15].

The study was conducted with the participation of 97 volunteers of both sexes (54 female and 43 male) between the ages of 18 and 34 who had previously been acquainted with the trial, and the voluntary informed consent of the patient to participate in the study was obtained. The main criteria of exclusion

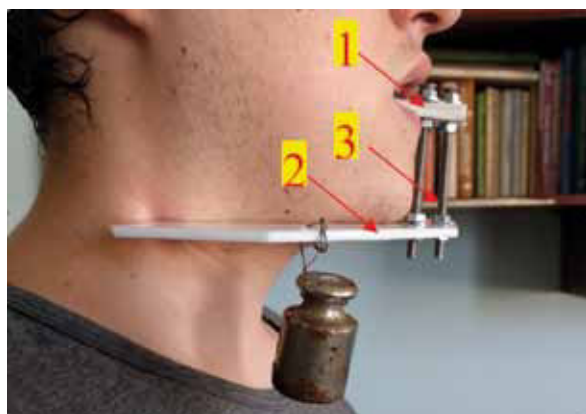


Fig. 2. Load simulation Device. 1 — Plastic individual impression spoon, 2 — Arc with slots for cargo fastening, 3 — Connecting rods

were: refusal to undergo the whole scope of research provided for in the protocol, presence of inflammatory processes in the maxillofacial region, disabled persons of 1–3 groups, and other socially vulnerable groups of the population. Before the trial, all participants underwent an anonymous questionnaire, the results of which were divided into 3 groups depending on the level of their physical activity.

In each of the groups, all subjects were divided into 2 subgroups randomly. Each participant was modeled a one-way load on the lower jaw (300 g) for 30 minutes. Participants of the first subgroups did not have load compensation devices, and participants of the second subgroups wore a special head cap, to which elastic elements compensating for one-way load were attached (Fig. 3).



Fig. 3. Elastic elements that compensate for one-way load

The effectiveness of the pathological load compensation was evaluated by anthropometry. For this purpose, markers were applied to the skin of the participants 'back in the area of acute processes of vertebrae Th-1 and L-1. With the help of a stationary camera and accurate positioning of the test person in front of the camera, the postura (pose taken by the person) was photographed before the beginning of the study and after 30 minutes of wearing the apparatus. Photos were analyzed in Photoshop CS. To do this, the program drew a line between the Th-1 markers and the L-1 for photos up to (Fig. 4.1) and after the test (Fig. 4.2), the lines were aligned and the inclination angle between the formed straight lines was calculated (Fig. 4.3).

RESULTS

The results of the study are shown in Table 1. The table shows that the angle of inclination in a group with a high level of physical training without load compensation is 2.3 times less relative to a group with a low level of training and 1.4 times less relative to an average level of physical training. At the same time, the statistical significance of the differences is noted between the groups. Patients with an average level of physical training also show statistical significance of differences relative to people with a low level (1.6 times less, at $p < 0.05$). In load compensation, there is also a statistically significant difference between high and medium training relative to subjects with low training, with a minimum angle of inclination in people with high physical training (at $p < 0.05$).

DISCUSSION

In the course of the study on volunteers it was found that the one-way load (300 g) for 30 minutes on the lower jaw is reflected on the post of the tested person, but elastic rods are able to compensate for the one-way load and minimize the angle of inclination. It has also been found that the angle of inclination is influenced by the initial physical training of the subject — volunteers with a high level of physical training much more easily carried the load both by subjective and objective criteria. All this shows that elastic rods used to compensate for the load are able to fully ensure the adequate functioning of the human bone-muscle system as a whole.

CONCLUSION

During the study, the compensatory abilities of the anti-gravity elastic pull of the *lower jaw exoskeleton* have been proved. The design of the apparatus enables not only to achieve a reponiating effect, but also allows the patient to maintain the usual lifestyle and social orientation in society.

Table 1. Angle of inclination, in degrees, °

Level of physical training of the respondent	High level of physical training	Average level of physical training	Low level of physical training
Without compensation of loading	1,02 ± 0,05*	1,47 ± 0,08*	2,35 ± 0,11*
With compensation of loading	0,03 ± 0,01*	0,15 ± 0,01*	0,23 ± 0,02*

Note: * statistical significance of differences between comparison groups relative to group with low level of physical training, at $p < 0.05$

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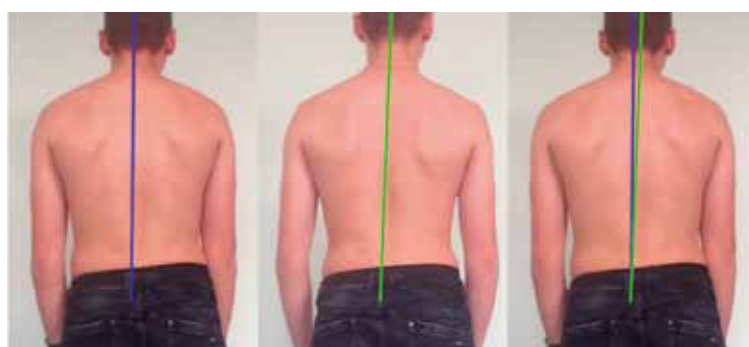


Fig. 4. 1 — Line between the Th-1 and L-1 markers before the study, 2 — Line between the Th-1 and L-1 markers after the study, 3 — Align the lines and calculate the angle between them