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DIE ZUKUNFT DER INFektionsdiagnostik-Kontrolle VON BAKTERIENKULTUREN DURCH MESSUNG VOLATILER MARKER AUS DEM HEADSPACE

WISSENSCHAFTLICHE KURZMITTEILUNG

**Gunther Becher, Roman Purkhart,
Rolf Graupner, Werner Schüler**

Graupner medical solutions, Geyer, BecherConsult GmbH, Bernau,
IFU, Oberlichtenau, STEP Sensortechnik, Pockau, Germany

ABSTRACT

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

Speziell bei langsam wachsenden Keimen wie Mycobacterium tuberculosis und atypischen Mycobakterien (Mycobacterium avium paratuberculosis (MAP)) dauert eine Kultur 6 bis 8 Wochen zum sicheren Befund. Mit der Ionenbeweglichkeitsspektrometrie ist es möglich, flüchtige Produkte des durch Bakterien im Wirtsorganismus oder auf der Kultur ausgelösten Stoffwechsels sehr frühzeitig und sicher nachzuweisen. Am Beispiel einer MAP-Kultur wurde mit der Methode ein signifikanter Befall schon nach 3 Tagen nachgewiesen.

Die Methode basiert auf der spektrometrischen Messung von volatilen Peaks und einer patentierten Auswertung zur Differenzierung der Stichproben nach dem Auftreten oder Fehlen von Peaks in den Messungen. Die tatsächliche chemische Identität der Peaks muss dazu nicht bekannt sein. Unbekannte Messungen konnten den vorher differenzierten Lernstichproben mit 100%iger Spezifität zugeordnet werden.

Die Methode ist auch geeignet, einen Keimnachweis aus Ausatemluft, Abstrichen aus Rachen und Nase, Sputum oder anderen biologischen Proben zu sichern (Becher; Buszewski). Andere schnellwachsende Keime wie E. Coli, Staphylococcus aureus u. a. sind auch detektierbar (Steppert 2014). Für noch nicht validierte Erkennung von einem Keim ist eine spezifische Methode mit der selbstlernenden Software jederzeit beim Anwender selbst erstellbar.

EINFÜHRUNG

Die traditionellen Methoden der Infektionsdiagnostik, Bakterienkultur oder PCR, sind langwierig oder teuer. Zum anderen ist gerade die PCR nicht beweisend für eine floride Infektion und bedarf vielfach der kulturellen Bestätigung. Deshalb wird nach neuen, preiswerten und schnellen Verfahren zur Infektionsdiagnostik gesucht.

Es ist allgemein bekannt, dass Bakterien volatile Marker freisetzen (Lieuwe; Crespo; McNerney). Das wird teilweise schon genutzt, um in biotechnologischen Anwendungen Wachstum und Reinheit von Kulturen zu prüfen. Die dazu nutzbaren diagnostischen Methoden wie Gaschromatographie oder MALDI-TOF MS sind allerdings ebenfalls sehr aufwändig und teuer. Die Ionenbeweglichkeitsspektrometrie (IMS), die kombiniert werden kann mit unterschiedlichen Detektoren oder Vorsäulen zur chromatographischen Trennung, ist eine im Vergleich dazu preiswerte und gleich empfindliche Methode. Es könnten sich hier also neue Möglichkeiten einer Infektionsdiagnostik ergeben.

Auch nur für die Ionenbeweglichkeitsspektrometrie (IMS) sind Geräte verfügbar, die den großen Vorteil haben, transportabel zu sein. Sie sind ggf. auch mit Akkubetrieb ausgestattet und ihr Hauptcharakteristikum besteht darin, auch unbehandelte Proben ohne jede Präanalytik vermessen können. Der Einsatz einer geschlossenen Strahlenquelle zur Ionisation der Probe ist sicher und bedarf keiner Zulassung gemäß Strahlenschutzverordnung. Das Gerät selbst ist wartungsarm und benötigt im Betrieb keine Zusatzstoffe oder Chemikalien. Das ergibt erstmals auch die Möglichkeit für eine Point-of-Care-Anwendung.

Die prinzipielle Erkennbarkeit von spezifischen VOC in Ausatemluft oder Headspace von Bakterienkulturen ist mittels GC-MS, oder auch PTR-MS (Protonen-Transfer-Reaction-MS) nachgewiesen worden. In verschiedenen Studien wurden Marker gefunden bei Tuberkulose (Phillips 2010) oder auch anderen Erkrankungen, wie Brustkrebs, M. Crohn, COPD u.a. (Crespo 2012, Filipiak 2012, Phillips 2010, Buszewski 2007, Lieuwe 2013).

Diese Befunde wurden in der vorliegenden Studie mittels GC-IMS überprüft.

METHODEN

Es wurden Kulturen von zwei verschiedenen Stämmen des Mycobacterium avium paratuberculosis (MAP: DSM 44133 [DSMZ, Braunschweig] und JII-1961 [Isolat vom Rind]) angelegt und gemäß den

Vorschriften über 6 Wochen verfolgt. Messpunkte für Volatile Marker (VOC) aus der Headspace der Kulturröhrchen waren 1, 2, 3, 4 und 6 Wochen nach Start der Kultur. Als Nährboden wurde Herrold's Egg Yolk Medium ausgewählt. Als Kontrollen dienten unbeimpfter Nährboden, Nährboden mit Aufgabe von Sterilfiltrat und Aufgabe von hitzeinaktivierter Kultur. Es wurden zum Überprüfen störender Effekte des Probenhandling Proben mitgeführt, die nur einmal geöffnet wurden und Proben mit Messung zu jedem Messpunkt.

Die Messungen erfolgten mit einer differenziellen IMS (SIONEX™) mit vorgeschalteter Multikapillarsäule (MCC) bzw. einem Muster einer GC-IMS der Autoren. Die Probe wurde über einen Teflonschlauch aus dem Probenröhrchen abgesaugt, während der Druckausgleich über einen Filter erfolgte. Bei der Methode erfolgt nach der Massentrennung in der MCC eine Ionisation der Probe und Detektion der gebildeten Ionen in einem gepulsten elektrischen Feld. Die Differenzierung der Peaks und Zusammenfassung zu Clustern erfolgte in einem eigenen Programm beruhend auf Support-Vector-Machine Errechnung der Sign. mit U-Test. Bei dieser Methode ist es nicht notwendig, die gefundenen Peaks chemisch zu identifizieren (Purkhart).

ERGEBNISSE:

Es zeigte sich, dass je nach Geräteeinstellung bezüglich Empfindlichkeit und Rauschverhalten bis zu 182 unterschiedliche Cluster in den Messungen erkannt wurden.

In der folgenden Abb. 1 ist ein Screenshot der Auswertegrafik dargestellt. Sie zeigt exemplarisch Cluster 46 (rot markiert) von 182 dargestellt, mit welchem in Woche 1 eine Differenzierung zwischen Keimwachstum und Nährboden erfolgen konnte. Nach einer Woche sind beim langsam wachsenden MAP signifikante Unterschiede zum unbewachsenen Nährboden ersichtlich.

Andere Cluster gestatten eine Trennung der beiden MAP-Stämme voneinander. Die Hinzunahme weiterer Cluster in die Auswertung kann die Trennschärfe weiter erhöhen.

Weiter konnte gezeigt werden, dass ebenfalls aus Proben der Ausatemluft und Geruchsproben vom Kot erkrankter eine sichere Trennung zwischen gesund und krank möglich war. Man muss also nicht warten, bis eine Bakterienkultur angewachsen ist und die mikrobiologische Diskriminierung ein eindeutiges Diagnoseergebnis erlaubt.

Die Methode und die patentierte Auswertesoftware beruht darauf, dass in den gasförmigen Proben

eine Vielzahl spezifischer Peaks identifiziert werden können. Die Software ist selbstlernend und die Sicherheit der Aussage steigt mit der Anzahl der gemessenen Proben. Auch wenn die chemische Identität dieser Marker nicht bekannt ist, können im Vergleich zwischen Kontrollen und den erkrankten signifikante Unterschiede gefunden werden, die dann bei weiteren Messungen an unbekannten Proben eine Zuordnung der Probe bzw. des Patienten zu den bekannten Kontrollgruppen (Lernstichprobe) gestatten. Die Trennschärfe krank-gesund wächst mit der Anzahl der positiven und negativen Befundungen. Mit Blick auf neue pathogene oder opportunistische Keime ist die Methode in der Konsequenz also geeignet, bakteriellen Befall auch in den Fällen zu detektieren, wenn das mikrobielle Taxon vorab nicht bekannt war.

Hervorzuheben ist, dass bei entsprechender Vorbereitung der Probennahme kein weiteres Handling der geschlossenen Kulturen oder von Nativproben notwendig ist. Das Ansaugen der Probenluft kann über geeignete Bakterienfilter erfolgen. Ein Infektionsgefährdung für das Personal kann somit ausgeschlossen werden.

Bei Vorliegen entsprechender Lernstichproben und Trainingsdatensätzen kann die Methode hochempfindlich und hochspezifisch sein. Weiterhin kann laborintern durch Mitführung eigener Kontrollproben die diagnostische Aussage überprüft werden und das Qualitätsmanagement sichergestellt.

In unseren Proben ergab sich eine Sensitivität zum Nachweis des MAP in der Kultur in der ersten Woche von 100%, obwohl die Kulturen üblicherweise erst nach 6 Wochen abgelesen werden sollen.

FAZIT

Die Methode ist geeignet, im bakteriologischen Labor einen Schnelltest für die Erkennung von Keimwachstum einzuführen, auch für andere Keime. Weiterhin besteht die Möglichkeit, auch in frischen Nativproben oder Ausatemluft eine Infektion zu erkennen.

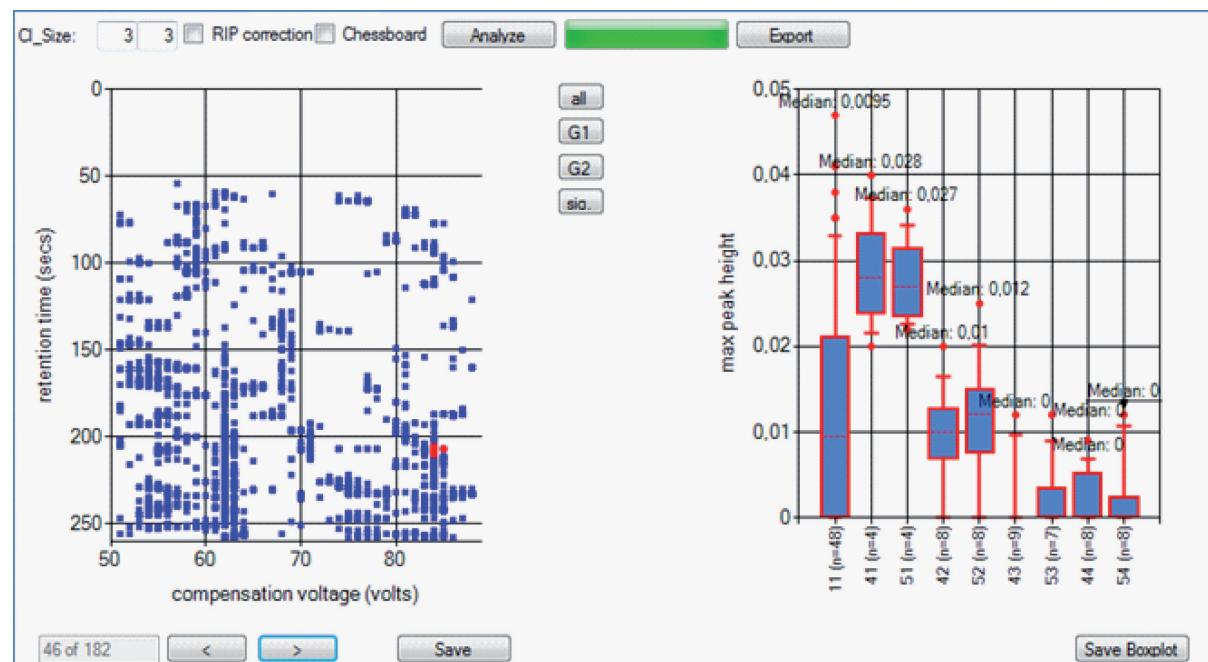
Das sind beste Voraussetzungen für den Einsatz in der Point-of-Care Diagnostik.

LITERATURVERZEICHNIS

BECHER, G.: Atemkondensat-Diagnostik (Exhalat-Diagnostik); In: „Spezielle Lungenfunktionsprüfung“, Hrsg.: Prof. K.-H. Rühle, München: Duxtri Verlag Dr. Karl Feistel, 2013, S. 105–124.

BUSZEWSKI, B.; KESY, M.; LIGOR, T. AND AMANN, A.: Human exhaled air analytics: biomarkers of diseases. Biomed. Chromatogr. 21: 553–566 (2007)

Abb. 1:

**Legende:**

11: Kontrollen; 4 DSM 44133; 5: JII-1961; 41 und
51 / 42 und 52 / 43 und 53 / 44 und 54 : jeweils
Woche 1, 2, 3 oder 4.

CRESPO, E., ET AL., Potential biomarkers for identification of mycobacterial cultures by proton transfer reaction mass spectrometry analysis. *Rapid Commun Mass Spectrom*, 2012. 26(6): p. 679–85.

FILIPIAK, W., SPONRING, A., BAUR, M.A., FILPIAK, A., AGER, C., WIESENHOFER, H., NAGL, M., TROPP-MAIR, J., AMANN, A.: Molecular analysis of volatile metabolites released specifically by staphylococcus aureus and pseudomonas aeruginosa. *BMC Microbiology* 2012, 12:113

LIEUWE D.J. BOS, PETER J. STERK, MARCUS J. SCHULTZ: Volatile Metabolites of Pathogens: A Systematic Review. *PLOS Pathogens*, 1 May 2013; Volume 9 ; Issue 5; e1003311: www.plospathogens.org

MCNERNEY, R., ET AL., Production of volatile organic compounds by mycobacteria. *FEMS Microbiol Lett*, 2012. 328(2): p. 150–6.

PHILLIPS, M., ET AL., Breath biomarkers of active pulmonary tuberculosis. *Tuberculosis (Edinb)*, 2010. 90(2): p. 145–51.

PURKHART, R., KÖHLER, H., LIEBLER-TENORIO, E., MEYER, M., BECHER, G., KIKOWATZ, A., REINHOLD, P., 2011. Chronic intestinal Mycobacteria infection: discrimination via VOC analysis in exhaled breath and headspace of feces using differential ion mobility spectrometry. *J. Breath Res.* 5, 027103 (10pp).

STEPPERT, ISABEL: Diskriminierung verschiedener Bakterienspezies mittels Ionenmobilitätspektrometrie. Bachelorarbeit Hochschule Coburg 2013.

SIGNIFICANCE OF HYPOPLASTIC LEFT HEART SYNDROME PRENATAL DIAGNOSIS FOR OUTCOMES

**E. Bespalova, O.Pitirimova,
M. Bartagova**

Bakoulev Center for Cardiovascular Surgery,
Moscow, Russia



*Elena D. Bespalova, MD
Professor, Director*



*Olga A. Pitirimova, MD
Obstetrician, Vice-Director*



*Maria N. Bartagova,
physician*

ABSTRACT

OBJECTIVE — Prenatal echocardiography is very important for diagnosis of hypoplastic left heart syndrome, the management of affected fetuses, including parental counseling for the therapeutic options, the planning of the delivery and the postnatal care.

METHODS — Multiple B-scan planes, Doppler color flow mapping and pulsed Doppler, 3–4 Dimensional Fetal Echocardiography. Methods of the echocardiographic identification of fetal CHD are: postnatal echocardiography, angiography, surgery, or autopsy.

RESULTS AND CONCLUSION — A total of 310 fetuses which HLHS were obtained during a period between 2011–2013 years from which 161 with a prenatal diagnosis of HLHS and 149 with postnatal diagnosis were enrolled. Hypoplastic left heart syndrome can be easily recognized on prenatal ultrasound and is one of the most common serious cardiac defects diagnosed prenatally. Hypoplastic left heart syndrome (HLHS) is frequently diagnosed prenatally, but Multiple-stage palliation surgery, postoperative complications determine low quality of life as the consequence.

KEYWORDS — Fetal echocardiography, congenital heart diseases, postnatal care.

OBJECTIVE

Hypoplastic Left heart syndrome is a congenital heart disease with a more dramatic change in diagnostic approach, management and outcome. During this time, survival to the age of 5 years (including Fontan) has ranged from 50% to 69% [1].

The stages of care of HLHS are:

- pre-Stage I: fetal and neonatal assessment and management;
- Stage I: perioperative care, interstage monitoring, management strategies;
- Stage II: surgeries;

- Stage III: Fontan surgery;
- Stage VI: long-term follow-up.

The reports have concluded that mortality is not reduced if a prenatal diagnosis is made [2, 3], though some have reported improved survival [4]. At present time significance of hypoplastic left heart syndrome prenatal diagnosis for outcomes also is permission potential fetal intervention. In select cases? Prenatal balloon dilatation of the aortic valve has been associated with decreased progression of the left ventricular hypoplasia [5].

METHODS

Definition of fetal CHD was attempted from multiple scan planes including four-chamber, long- and short-axis, aortic arch and ductal arch views [fig. 1, 2]. We use 3–4 Dimensional Fetal Echocardiograms dimensional echo.

Doppler color flow mapping and pulsed Doppler interrogation were used to facilitate identification of great vessel relationship, location and severity of ventricular outflow obstruction [fig. 3].

Initial fetal echocardiograms were obtained between 12 and 39 weeks of gestation (median 24.5 weeks).

HLHS usually are diagnosed during the first echo.

Age at first examination ranged between 17 and 41 years v (median 30 years). The median number of echocardiographic studies performed was one, ranging from one to four examinations.

We think, major cardiac malformations should be followed serially by fetal echocardiography as progressive alterations in flow may affect growth of cardiac



Fig. 1. 24 weeks of gestation. Hypoplastic left heart syndrome. RV — right ventricle, LV — left ventricle

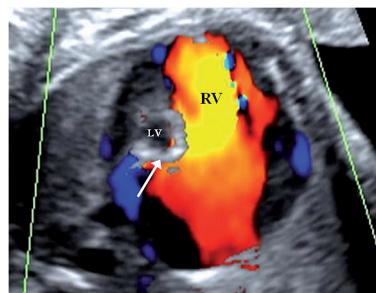


Fig. 2. 32 weeks of gestation. Hypoplastic left heart syndrome. RV — right ventricle, LV — left ventricle. Color Doppler Mapping

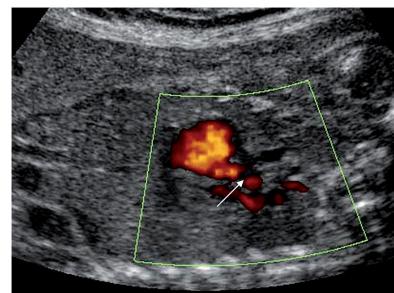


Fig. 3. 18 weeks of gestation. Hypoplastic left heart syndrome. Power Doppler Mapping. Arrow — hypoplastic aorta ascendens

structures over time: for example, very often, after prenatal diagnosis of hypoplastic left-heart syndrome couples have been offered termination of pregnancy. But termination of pregnancy should not be proposed when it is only a small left ventricle (on echo), because many of those patients end up with only coarctation of the aorta." A second echo should be carried out in these cases.

Maternal age was from 17 to 41 years old.

- 23% of fetal echocardiograms were obtained before 18 weeks of gestation.
- 69% of fetal echocardiograms were obtained between 18–28 weeks of gestation.
- 8% of fetal echocardiograms were obtained between 29–39 weeks of gestation.
- All infants with HLHS are borne by mothers with no known risk factors.

Methods of the echocardiographic identification of fetal CHD are: Postnatal echocardiography, angiography, surgery, or autopsy.

Fetal echocardiography has opportunity to study the most important parameters of fetal heart with HLHS for postnatal surgical repair, such as left/right ventricular diastolic dimensions in M-mode, B-mode (right-to-left ventricular disproportion, ultrasound indication of endocardial fibroelastosis). Mitral valve anomaly (congenital Parachute mitral valve, stenosis/ atresia), aortic valve or aortic root disease, left ventricular outflow obstruction, dimension of foramen ovale and ductus arteriosus

RESULTS AND DISCUSSION

A total of 310 fetuses which HLHS were obtained during an period between 2011–2013 years from which 161 with a prenatal diagnosis of **HLHS** and 149 with postnatal diagnosis were enrolled.

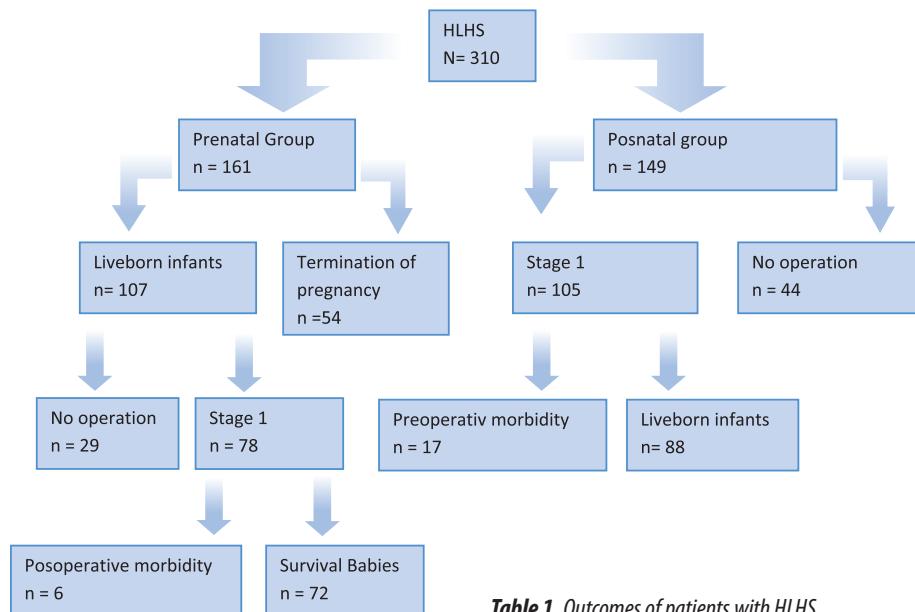
Nobody had major extracardiac malformations and/or chromosomal abnormalities.

In our group, there are patients with HLHS, in our group, who are diagnosed prenatally and postnatally have improved survival after first-stage palliative surgery compared with those who have survived after Norwood procedure. We were not included patients after Norwood procedure in further analysis. Outcome showed at the tables 1, 2.

We don't mean the comparison of features of clinical treatment in these two groups as a We would like to analyse parameters which improve the initial clinical status of patients with HLHS.

Our results showed The Key parameter defining influence of prenatal diagnostics to surgical treatment patients with HLHS is time of arrival of the newborn in a cardiovascularsurgery hospital. Age At admission was more uniform and significantly younger in the prenatal group, than in the postnatal group. The difference follows from this indicator in time of carrying out of surgical operation. About 1 day from the moment of the diagnosis statement. There are no preoperatively metabolic acidosis, dysfunction RV in the prenatal group of patients. Dysfunction of RV takes place only in the postnatal group of patients in low interest, children with late arrival to clinic, more than 6–7 days. Children from all regions of our country come to our center, that's why, unfortunately, there may be cases of late initial diagnosis. There is significantly lower incidence of preoperative inotropic medications in the prenatal group of patients. 15–20% versus 55–60%. And significantly lower incidence of hospital lethality after the first stage as the consequence (7,1% in the prenatal group versus 19,2% in postnatal group).

The reasons of lethality are various. First of all is the severity of disease. Our study demonstrates that prenatal diagnosis of HLHS was associated with improved preoperative clinical status and with improved

**Table 1.** Outcomes of patients with HLHS**Table 2.** Comparison of characteristics of patients with hlhs in the prenatal and postnatal groups

PARAMETERS	Prenatal Group (n = 78)	Postnatal Group (n = 105)	P
Age at admission (hours)	5,2 ± 1,6	15 ± 7,4	p < 0,001
Age between delivery and operation (hours)	22,4 ± 3,1	34 ± 3,9	p < 0,001
preoperative Metabolic acidosis	3,5%	45%	p < 0,001
Preoperative inotropic medications	16,8%	58,4%	p < 0,001
dysfunction of RV	0,9%	4,9%	NS
Postoperative mortality	7,1%	19,2%	p < 0,05

survival after first-stage palliation in comparison with patients diagnosed after birth.

Hypoplastic left heart syndrome can be easily recognized on prenatal ultrasound and is one of the most common serious cardiac defects diagnosed prenatally. The standard "4-chamber cardiac view" used by obstetricians for screening of congenital heart disease demonstrates either a small left side or an echogenic left ventricle from endocardial fibroelastosis.

Hypoplastic left heart syndrome (HLHS) is frequently diagnosed prenatally, but Multiple-stage palliation surgery, postoperative complications determine low quality of life as the consequence.

REFERENCES

1. J.A. FEINSTEIN, D.W. BENSON, A.M. DUBIN AT ALL. Hypoplastic left heart syndrome. Journal of the American College of Cardiology, 2012, Vol. 59, No.1 s1-s42.
2. W.T. MAHLE, R.R. CLANCY, S.P. MCGAURN, J.E. GOIN, J.B. CLARK. Impact of prenatal diagnosis on survival and early neurologic morbidity in neonates with the hypoplastic left heart syndrome. Pediatrics, 2001, 107:1277–82.
3. V. SYVARAJAN, D.J. PENNY, P. FILAN, C. BRIZARD, L.S. SHEKERDEMIAN. Impact of antenatal diagnosis of hypoplastic left heart syndrome on the clinical presentation and surgical outcomes: the Australian experience. J. Pediatr. Child Heart, 2009, 45: 112–7.
4. W. TWORETZKY, D.B. McELHINNEY, V.M. REDDY, M.M. BROOK, F.L. HANLEY, N.H. SILVERMAN. Improved surgical outcome after fetal diagnosis of hypoplastic left heart syndrome. Circulation, 2001, 103:1269–1273.
5. D.B. McELHINNEY, W. TWORETZKY, J.E. LOCK. Current status of fetal cardiac interversion. Circulation, 2010, 121: 1256–63.

AGE-RELATED METABOLIC DISORDERS BY CARDIOVASCULAR DISEASES IN WOMEN WITH CONSIDERATION OF THE GENETIC PREDISPOSITION

Maia Dgebuadze Prof. MD,
Levan Ratiani MD

*Tbilisi State Medical University,
Tbilisi, Georgia*



**Maia Dgebuadze, MD,
PHD, ScD, Professor of the
Department of Human Normal
Anatomy at Tbilisi State
Medical University**

**Levan Ratiani PhD,
researcher**

INTRODUCTION

Cardiovascular disease is a most frequent cause of early disability and high mortality. The influence of various risk factors is different between men and women; the effect of the menopause is important in women and age-dependent risk factors play additional role along with well-known atherosclerotic factors, as well as the genetic predisposition. Despite of this, many studies of cardiovascular disease have included mostly men [1, 2]. Postmenopausal women's life is characterized by loss of ovarian follicular activity and estrogen deficiency [1]. Metabolic rearrangement of the organism is an increased risk of atherosclerosis progression and atherosclerotic damage of blood vessels [3]. Numerous studies conducted on genetics of cardiovascular diseases [4].

AIM

The aim of our study was to establish age-related metabolic disorders of cardiovascular diseases in women with consideration of the genetic predisposition.

MATERIAL AND METHODS

58 reproductive-aged (less than 45 years) and 32 menopausal (more than 45 years) women with dislipidemia, arterial hypertension, obesity, metabolic syndrome and other symptoms, who had been admitted to the Central Clinic of Tbilisi State Medical University (Georgia) during 2009–2011, were investigated and compared with each other. Subjects with cystic disease, ovariectomy, or using hormone-replacement therapy was excluded from studying group.

In each group we investigated blood estradiole, Lipid spectrum (LDL, HDL, TG, VLDL, TC), Fibrinogen, C-reactive protein levels (CRP). Estrogens content in blood was measured by ELISA method. Lipid spectrum in peripheral blood from patients was investigated by enzyme-colorimetric method. Using Doppler investigation of arteries in color duplex scan mode carotid intima-media thickness was established.

Statistical analyses of the obtained results were performed by SPSS (version 10.0) program package. Result were obtained in form of standard deviation of average values. Difference between groups was assessed by Student *t*-criterion. In all cases statistical confidentiality was defined according to < 0.05 index.

Research complies with the norms of the bioarticle's Foundations. The local ethics committee approved the protocol, and informed consent was obtained from all participants.

RESULTS AND DISCUSSION

According to our data in menopausal women blood estradiol levels and HDL were statistically significantly

reduced. Fibrinogen, LDL, triglycerides and total cholesterol levels and catalase activity were increased, while C-reactive protein and VLDL levels were not significantly changed in these two age groups. It is noteworthy that the lipid metabolism disorders were more expressed especially in menopausal women with the genetic predisposition to atherosclerotic-induced cardiovascular diseases. At the same time, in menopausal, as well as in reproductive-aged, women with the genetic predisposition to atherosclerotic-induced cardiovascular diseases a positive correlation between VLDL, TC, TG levels and the severity of hypertension was revealed, but between HDL level and the severity of hypertension the negative correlation was established; estrogen-dependent factor does not play a major role in the pathogenesis of these diseases in women with the genetic predisposition to atherosclerotic-induced cardiovascular diseases.

Some correlations were detected between the parameters of lipid metabolism, atherogenesis intensity (carotid artery intima-media thickness) and inflammatory markers (C-reactive protein and fibrinogen levels). There is positive correlation between fibrinogen and CRP, between fibrinogen and TG, TC levels. CRP level increase was revealed in patients with the genetic predisposition to atherosclerotic-induced cardiovascular diseases, as well as in diabetic patients. Increasing of fibrinogen and CRP levels correlates with carotid intima-media thickness. In women with the genetic predisposition to atherosclerotic-induced cardiovascular diseases CRP level was increased in both reproductive and menopause ages, but in women, who had not genetic predisposition to atherosclerotic-induced cardiovascular diseases, statistically significant increase of CRP level was detected only in menopause age. In women with the genetic predisposition to atherosclerotic-induced cardiovascular diseases the level of blood pressure was increased.

REFERENCES

1. LOBO RA. Menopause and stroke and the effects of hormonal therapy. *Climacteric*. 2007; 10 (2, supplement): 27–31.
2. YAHAGI K., DAVIS H R., ARBUSTINI E. Sex differences in coronary artery disease: Pathological observations. *Atherosclerosis*. 2015; 239 (1) : 260–267.
3. HULLEY S., GRADY D., BUSH T., FURBERG C., HERRINGTON D., RIGGS B., VITTINGHOFF E. Randomized Trial of Estrogen Plus Progestin for Secondary Prevention of Coronary Heart Disease in Postmenopausal Women. *JAMA*. 1998; 280(7):605–613.
4. CAMBIEN F., TIRET L. Contemporary Reviews in Cardiovascular Medicine. Genetics of Cardiovascular Diseases: From Single Mutations to the Whole Genome. *Circulation*. 2007; 116: 1714–1724.

SHAPE INDIVIDUALIZATION IN LOWER DENTAL ARCHES DRAWN ON BASIC MORPHOMETRIC FEATURES

D.A. Domenyuk¹, Ernessa Vedeshina, S.V. Dmitrienko²,

¹ Department of General Practice Dentistry and Pediatric Dentistry, Stavropol State Medical University, Stavropol, Russia

² Department of Dentistry, Pyatigorsk Medical-Pharmaceutical Institute (Branch of Volgograd State Medical University, Pyatigorsk, Russia

ABSTRACT

The dentoalveolar arch was constructed by connecting the dots of the lingual alveolar arch in the anterior part (between the distal surfaces of the mandibular canines) and the middle point of the distal surface of premolars and molars' occlusal contour. The width of the dentoalveolar arches was measured between the second molars while its depth was determined as a distance from the frontal vestibular point to the line connecting the corresponding points of the second molars along the projection of the median palatal suture. The frontal distal diagonal of the dentoalveolar arches was found to be the key parameter which allows determining whether or not the teeth size matches the dentoalveolar arch measurements.

KEYWORDS — vestibular dental arch, alveolar lingual arch, alveolar palatal arch, dentoalveolar arch, physiological occlusion.

Nowadays the progress in clinical dentistry can be described with a high level of fundamental and applied research related to morphogenesis, as well as generic and individual variability in the morphological structures of the dento-facial region. Yet, despite the large scale of the research projects carried out both nationally and abroad, there are still numerous aspects pertaining to this complicated issue that remain unresolved [11].

The dento-facial region is part of the body which undergoes dynamic changes through its growth and development, which has been the focus of many works by Russian and foreign authors. The issues relating to the link between the sizes of the dental arches and the structural features of the jaws and the craniofacial complex on the whole, have acquired some particular relevance lately, which, above all, could be accounted for by an expanded range of the reasons behind the indications for orthodontic treatment [1,4].

The society nowadays is paying more and more attention to the human face and the balance in its structure. There is a certain dependency between the shape and size of the dental arches and the face, where-



Dmitry Domenyuk, Doctor of Medicine, Associate Professor



Ernessa Vedeshina, Candidate of Medical Science, Junior Lecturer



Sergey Dmitrienko Doctor of Medicine, Professor, Head of Department

as identification of misbalance may help identify the disorder. The shape of the face has been found to be subject to an impact from the dimensions of the facial and partially brain skull, their positional relationship, as well as the dimensions and the arrangement of the soft tissues in the dento-facial area [5,9].

An integrated analysis of the respective research has demonstrated both Russian and foreign scientists pay currently rather serious attention to various points connected with the match of the permanent teeth sizes and the craniofacial complex' parameters, and the dental arches in particular. The concept of the "ideal" match for the parameters in question may prove a useful tool for an Orthodontist when diagnosing anomalies and selecting the treatment options since there is a biological basis for that [7].

Both Russian and foreign literature nowadays offers overviews of numerous research projects specifically focusing on the anatomy of the dento-facial region taking into account the racial and gender features,

as well as on the variability of the dento-facial system for different somatotypes. There is also quite detailed description available on the shape of the teeth and the dental arches based on a particular somatotype [10].

Among the paramount tasks for Orthodontics we could mention stable functional and aesthetically acceptable shape of the dental arch, and the key point in reaching the aim here is a search for the ideal shape of the dental arch appropriate per each clinical case [2]. For over a century now researchers have been trying to decide on the ideal shape of the dental arch exploiting the idea of its symmetry and compliance with rules of Mathematics and representing it through algebraic or geometric formulae [3,8].

Today, one of the most popular ideas holds about an individual choice of the dental arch shape subject to the original arch of the mandibula. Given the progress in computer analysis, this approach to an individualized design for the arch form may contribute to

types of dental arches have been proposed for the evaluation: the dental vestibular arch, the alveolar lingual arch, and the dentoalveolar arch. The cast models of the lower jaw were dotted in order to construct and perform morphometric measurements in the dental arches. When studying the dental arch, the main points were set in the middle of the vestibular surface of the incisors, canines and premolars' occlusal contour (the most prominent part in the vestibular contour of the tooth crown' occlusal surface); the most protruding points on the vestibular contour' occlusal surface of the vestibular distal cusps were marked on the molars. The alveolar lingual arch was formed through connecting the dots located at the lingual surface of the dental arch in the interdental spaces. When constructing and measuring the dentoalveolar arch the dots were set in the middle of the teeth crowns' distal surface in proximity to the occlusal contour (Fig. 1).

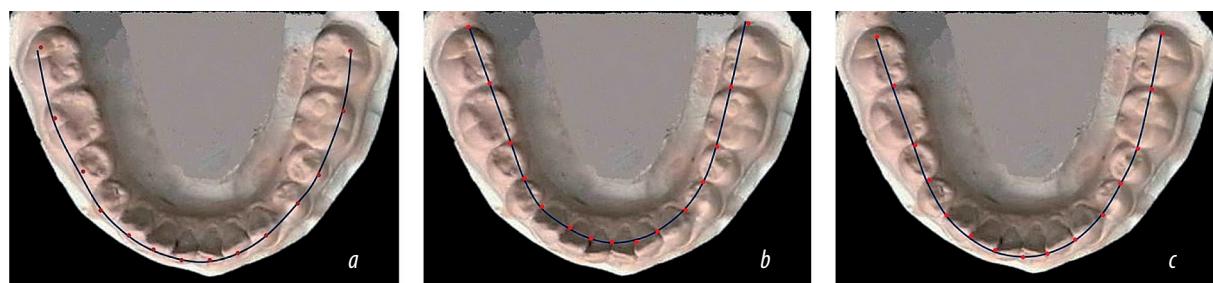


Fig. 1. Cast models with the contours of the dental arch (a), the alveolar arch (b), and the dentoalveolar arch (c)

developing an optimal solution regarding the proper choice of the arch through all the stages of orthodontic treatment [6].

While steel arches may solve the issue due to individual preformation of the standard (or the closest in size) arches manufactured industrially, altering the shape in the standard nitinol arches appears quite a concern. Therefore, identifying the major clinical forms of dental arches for developing industrial arcs that would stand similar to them yet remains an urgent question in Orthodontics.

Purpose — to investigate the clinical variants and the basic morphometric parameters of the lower dental arches in their shape variations.

A comprehensive analysis of the relationship between the sagittal and the transversal sizes of dental arches was held involving 309 patients (146 men and 163 women) in their early adulthood who revealed physiological occlusion of the permanent teeth. Three

The key parameters for measuring the dental arch included its length, width, and depth as well as the frontal distal diagonal (Fig. 2).

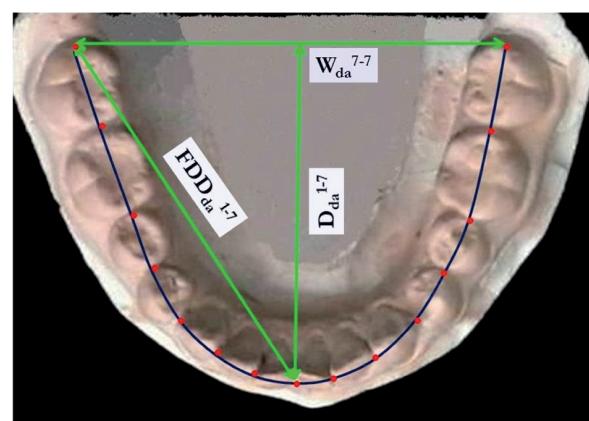


Fig. 2. Mandibular cast model bearing the contour of the dentoalveolar arch and the key parameters to be measured

The longitudinal length of the dentition was detected through the Nance method as a sum of the mesial distal diameters of the compounding teeth. The third molars were not included in the measurements due to their being the most variable ones. When measuring the dental arch and the dentoalveolar arch, the frontal vestibular point was arranged amidst the medial incisors. The width of the mandibular arches (dental arch, dentoalveolar arch, and alveolar arch) was measured between the second molars (W_d^{7-7} , W_{da}^{7-7} and W_a^{7-7}). The depth of the arch (D_d^{1-7} , D_{da}^{1-7} и D_a^{1-7}) was determined as a distance from the frontal vestibular point to the line connecting the corresponding points of the second molars along the projection of the median palatal suture.

The arch form was determined through the arch index (the ratio between its depth and width). The mandibular dental arch form was defined as mesognathic in the cases where the dental arch index was 0.73 ± 0.03 , that of the dentoalveolar -0.85 ± 0.05 , and of the alveolar arch 0.83 ± 0.05 , regardless of the teeth size (macrodontia, microdontia or normal teeth size). For the brachygnathic form of the dental arch the index was below 0.7, the indices for the dentoalveolar and the alveolar arches being less than 0.80 and less than 0.78, respectively. In the event the dental arch index went beyond 0.76, that in the dentoalveolar arch exceeding 0.9 and in the alveolar arch exceeding 0.88, such form was classified as dolichognathic.

To estimate the size of the teeth we used the mean module of the molar crowns (half-sum of the first and second molar crowns modules). The crown module was calculated employing the A.A. Zubov method, taken as half-sum of the vestibular lingual and the mesial distal diameters of the tooth crown. The mean module of the molar crowns residing in the range of 10.6–11 mm was viewed as normal teeth size. A reduced value was typical of microdontia, while the value's increase was indicative of macrodontia in the permanent molars.

The outcomes suggest that in case of physiological occlusion of permanent teeth there were nine major types of dental arches to be found. Individuals with the mesognathic, brachygnathic, and dolichognathic arch forms revealed variants of microdontia, normal teeth size, and macrodontia of the permanent molars. There has also been an investigation into the parameters of the dental, the alveolar, and the dentoalveolar arches in patients with the above-mentioned forms of the dental arches.

The study has shown that regardless of the form of the dental arches and the teeth size, the matching index for the teeth size in relation to the frontal distal diagonal (the ratio between the sum of the mesial

distal diameters of the seven teeth on one side to the length of the frontal distal diagonal) was stable, and for the dental arches it was 1.12 ± 0.011 , for the dentoalveolar arches – 1.08 ± 0.01 , while for the alveolar arches it was 1.14 ± 0.01 . This index is of high pragmatic value and allows determining whether or not the size of the teeth conforms to the size of the jaws, as well as it allows predicting a deficit or an excess of space for permanent teeth in the jaw bones. Mention to be made here that the dental arch length (which is the sum of the mesial distal diameters of 14 teeth) in case of normal teeth size in the permanent teeth averaged 107.0 ± 4.0 mm. In case of macrodontia the dental arch length was over 112 mm, while for microdontia it was typical to have the dental arch length less than 103 mm.

We have studied the key parameters in the dental, the alveolar and the dentoalveolar arches also evaluating the interrelation between the major features. Table 1 contains the outcomes obtained through a study of the lower dental arches.

The outcomes have shown that under macrodontia of permanent teeth virtually all the measurements in the dental arches were significantly higher than in case of microdontia. The major indicator for the teeth size was the frontal distal diagonal (FDD_d^{1-7}).

During that, the key parameter for the dental arch form was the dental arch index, and the ratio between the depth of the dental arch (D_d^{1-7}) and the width between the second permanent molars in those with mesognathic dental arch was 0.72 ± 0.03 for normal teeth size, 0.71 ± 0.02 for macrodontia, and 0.71 ± 0.02 under microdontia. The dental arch index for dolichognathic form was, on average, 0.81 ± 0.05 , while in case of brachygnathic form it averaged 0.67 ± 0.03 . Note to be made here of the ratio of the dental arch depth (D_d^{1-7}) to the depth of the anterior part of the arch (D_d^{1-3}), which in case of mesognathia was 5.75 ± 0.3 , for dolichognathia it was 4.61 ± 0.3 , while under brachygnathia it was 6.29 ± 0.4 , which indicates the variability of sagittal dimensions of the anterior part of the dental arch and is due to the teeth protrusion under dolichognathia and their retrusion in case of brachygnathia.

Table 2 contains the results of the lower alveolar arches measurements.

The results showed that the absolute values of the alveolar arches' parameters were significantly lower if compared to the dental ones. However, the comparative indicators revealed the same proportional relationships. The ratio of the depth of the alveolar arch (D_a^{1-7}) to the width between the second permanent molars (W_a^{7-7}) in those with the mesognathic alveolar arches was 0.82 ± 0.02 for the normal teeth size, 0.83 ± 0.03 for macrodontia, and 0.81 ± 0.01 in case of microdontia

Table 1. The key parameters of the lower dental arches in their shape variations

Forms of the dental arches	Main measurements in dental arches (mm)				
	W_d^{7-7}	D_d^{1-7}	W_d^{3-3}	D_d^{1-3}	FDD_d^{1-7}
Mesognathic, normal teeth size	53.49±1.52	38.49±1.04	28.51±0.99	6.98±0.62	46.52±1.64
Mesognathic macrodontia	62.31±1.94	44.02±1.16	29.02±1.12	7.51±0.58	51.01±1.81
Mesognathic microdontia	51.68±1.41	36.51±1.07	24.03±0.89	6.22±0.54	43.79±1.82
Dolichognathic, normal teeth size	56.47±1.62	43.02±1.22	27.97±0.91	8.82±0.81	49.51±1.82
Dolichognathic macrodontia	55.51±1.94	49.04±1.86	29.01±1.11	10.03±1.35	52.02±1.75
Dolichognathic microdontia	51.49±1.42	40.53±1.47	27.49±1.08	9.96±1.14	45.29±1.87
Brachygynathic, normal teeth size	59.02±2.03	38.51±1.47	27.49±1.18	6.02±0.52	47.02±1.33
Brachygynathic macrodontia	60.04±2.12	40.03±1.28	26.51±1.16	6.61±0.87	47.18±1.97
Brachygynathic microdontia	54.01±1.84	35.49±1.12	25.78±0.84	5.53±0.46	44.02±1.27

Table 2. The key parameters of the lower alveolar arches in their shape variations

Forms of the lower arches	Main measurements in alveolar arches (mm)				
	W_a^{7-7}	D_a^{1-7}	W_a^{3-3}	D_a^{1-3}	FDD_a^{1-7}
Mesognathic, normal teeth size	46.52±2.12	38.02±1.45	27.71±1.23	6.48±0.79	45.51±1.28
Mesognathic macrodontia	53.48±2.13	44.12±1.47	28.03±1.07	8.51±0.96	50.49±1.97
Mesognathic microdontia	46.53±1.92	37.01±1.28	24.98±1.04	6.79±0.72	43.18±1.55
Dolichognathic, normal teeth size	49.51±2.37	44.97±1.28	27.39±1.08	9.49±0.89	48.48±1.54
Dolichognathic macrodontia	46.03±2.29	47.02±1.71	29.51±1.38	10.18±0.92	51.02±2.21
Dolichognathic microdontia	44.28±1.18	39.01±1.16	25.78±0.84	8.02±0.74	43.97±1.94
Brachygynathic, normal teeth size	50.96±1.59	38.02±1.14	27.97±1.09	5.51±0.43	45.97±1.94
Brachygynathic macrodontia	50.02±2.03	39.03±1.28	27.52±1.11	6.02±0.54	47.03±1.59
Brachygynathic microdontia	47.51±1.26	36.49±1.12	26.98±0.67	5.48±0.87	43.01±1.28

Table 3. The key parameters of the lower dentoalveolar arches in their shape variations

Forms of the lower arches	Main measurements in dentoalveolar arches (mm)				
	W_{da}^{7-7}	D_{da}^{1-7}	W_{da}^{3-3}	D_{da}^{1-3}	FDD_{da}^{1-7}
Mesognathic, normal teeth size	49.02±1.59	39.82±1.35	30.03±1.12	9.51±0.72	47.72±1.66
Mesognathic macrodontia	55.01±1.86	46.01±1.59	30.52±1.63	11.03±0.92	53.01±1.74
Mesognathic microdontia	47.98±1.44	39.29±1.42	27.48±1.02	8.79±0.85	45.52±1.36
Dolichognathic, normal teeth size	52.03±1.84	47.01±1.49	30.02±1.23	12.49±1.03	51.18±2.03
Dolichognathic macrodontia	48.49±1.65	50.49±1.93	31.04±1.13	14.01±1.24	54.12±1.95
Dolichognathic microdontia	46.01±1.88	41.98±1.33	29.01±1.11	10.52±1.03	46.53±1.24
Brachygynathic, normal teeth size	53.01±2.05	40.48±1.17	30.03±1.25	8.03±0.99	48.31±1.38
Brachygynathic macrodontia	53.49±1.91	42.51±1.77	31.01±1.12	9.01±0.97	49.28±1.93
Brachygynathic microdontia	49.02±1.54	39.02±1.81	28.99±1.12	8.19±0.88	45.52±1.51

of the permanent teeth. The ratio of the depth of the alveolar arch (D_a^{1-7}) to the depth of the anterior part of the arch (D_a^{1-3}) under mesognathia was 5.5 ± 0.03 , while for dolichognathia it was 4.7 ± 0.4 , and for brachyg-

nathia — 6.7 ± 0.04 , coinciding with the similar dental arch indices.

Table 3 offers the study results regarding the dentoalveolar arches.

The dentoalveolar arch index under mesognathia averaged 0.82 ± 0.03 and depended on the ratio of the sagittal and the transversal dimensions, while being virtually irrespective of the actual sizes of the teeth. The dentoalveolar arch index in case of the dolichognathic form was, on average, 0.95 ± 0.04 , while for the brachygnathic form it was 0.78 ± 0.02 . The fact that stands out here is the ratio of the depth of the dentoalveolar arch (D_d^{1-7}) to the depth of the anterior part of the arch (D_d^{1-3}), which under mesognathia was 4.3 ± 0.2 , under dolichognathia – 3.8 ± 0.3 , being equal to 4.8 ± 0.03 for brachygnathia.

CONCLUSIONS

The major key parameter that determines the match between the teeth sizes and the dental arches' measurements is the frontal distal diagonal.

The proposed methods for the constructing and measuring of the dental arches based on the anatomical and topographical landmarks allow differentiating the three major types of dental arches: dental vestibular arch, alveolar lingual arch, and dentoalveolar arch.

The conventional dot placement will allow not only a comparative evaluation of the research outcomes at various stages of orthodontic treatment yet also will individualize the relationship between the parameters of the dental arches and the teeth size for each individual case.

Each of the dental arch forms proposed (dental vestibular arch, alveolar lingual arch, and dentoalveolar arch) reveal key parameters that may be used to determine the strategy for orthodontic treatment and to decide on the shape and size of metal dental arches when treating patients with the Edgewise technique.

REFERENCES

1. ALEXANDER R.G. A Practical Approach to Arch Form. // Clinical Impressions. – 1992. – № 3. Vol. 2 – P. 34–38.
2. BRADER A.C. Dental arch form related to intra-oral forces // American Journal of Orthodontics. – 1972. – № 61. – P. 541–561.
3. CHUCK G.C. Ideal arch form. Angle Orthodontist. – 1932. – 116. – P. 1–12.
4. DOMENYUK, D.A. Clinical anatomy of teeth and dentofacial segments / D.A. Domenyuk, E.G. Vedeshina, S.V. Dmitrienko. – Stavropol: Publishing House of Stavropol State Medical University, 2015. – 210 p.
5. DOMENYUK, D.A. Interrelation between sagittal and transversal sizes in form variations of maxillary dental arches / D.A. Domenyuk, S.V. Dmitrienko // Archiv euromedica, 2014. – Vol. 4. – № 2. – P. 10–13.
6. DOMENYUK, D.A. Modern classification of dental arches / D.A. Domenyuk, S.V. Dmitrienko // Archiv euromedica, 2014. – Vol. 4. – № 2. – P. 14–16.
7. FELTON J.M., SINCLAIR P.M., JONES D.L., ALEXANDER R.G. Computerized Analysis of the Shape and Stability of Mandibular Arch form.// American Journal of Orthodontics. – 1987. – № 92. – P. 478–483.
8. HAWLEY C.A. Determination of the normal arch and its application to orthodontia // Dental Cosmos. – 1905. – № 47. – P. 541–552.
9. McLAUGHLIN, R., BENNETT, J., TREVISI, H. Systemized Orthodontic Treatment Mechanics. Translated from Eng. – Lvov: GalDent, 2005. – 324 p. – 950 fig.
10. SCOTT J.H. The shape of dental arches // Journal of Dental Reseach. – 1957. – № 36. – P. 996–1003.
11. TUGARIN V.A., PERSIN L.S., POROKHIN A.YU. Modern fixed-type orthodontic appliances Edgewise. – M., 1996. – 220 p.

KOMMUNIKATION IM NOTFALL — WAS IST WICHTIG FÜR EINE EFFEKTIVE NOTFALLVERSORGUNG

Dr. med. Markus Flentje

*DESA Medizinische Hochschule Hannover – Simulationszentrum
Flentje.Markus@mh-hannover.de*



EINLEITUNG

In der Gesundheitsversorgung sind verschiedenste Situationen denkbar, in denen eine zeitkritische Behandlung von Patienten notwendig ist. In diesen Situationen kommen oft multidisziplinäre und interprofessionelle Teams zusammen, um medizinische Maßnahmen koordiniert und schnell durchzuführen. Beispielhaft kann hier die Situationen der Reanimation, die Versorgung Schwerverletzter und die Durchführung von Notfall-Kaiserschnitten genannt werden. Teams, die mit Ihrem Handeln und deren Konsequenzen eine hohe Verantwortung für das Leben und die Gesundheit tragen, werden auch High Responsibility Teams genannt (1). Die Kriterien dieser Teams werden im Einzelnen in Tabelle 1. gezeigt. Neben den technischen Fähigkeiten, wie z.B. die Durchführung einer Katheteranlage, wird für diese Teams das Training von „nicht technischen Fähigkeiten“, wie Teamführung und Kommunikation empfohlen. Diese Ansätze der Teamarbeit wurden seit 1979 unter dem Begriff „Crew Ressource Management (CRM)“ in der zivilen Fliegerei entwickelt und behandeln die effektive Nutzung aller menschlichen und materiellen Ressourcen für die zeitkritische Situation (2). Für die Anästhesie haben Rall & Gaba 15 Schlüsselkompetenzen definiert, die eine effektive Teamarbeit beschreiben (Tabelle 2). Eine dieser Kernkompetenzen ist die sichere effektive Kommunikation (3).

Medizinische Teams sind in der Regel mit einer Führungsperson versehen, die die Endverantwortung für den medizinischen Behandlungsprozess trägt. Sind mehrere Fachrichtungen beteiligt, gibt es in Deutschland Vereinbarungen zwischen den Fachrichtungen, welche Behandlungsabteilung für einen bestimmten Bereich die Verantwortung trägt. Kommunikation ist im Rahmen von Auftragsverteilung, Austausch zur Diagnosefindung und im Entscheidungsprozess zur Prioritätenfindung denkbar. Die Prinzipien des CRM fordern eine Aufmerksamkeit aller Teammitglieder und fordern die Rückmeldung der Teammitglieder an die Führungsperson, wenn sie mögliche Probleme

im Behandlungsablauf sehen. Wie dies der nächste Abschnitt zeigt, sind Behandlungshinweise vom Team zu der Führungskraft notwendig.

PHYSIOLOGISCHEN GRUNDLAGEN

Um die Kommunikationsprobleme zu verstehen, die bei der täglichen Bewältigung der Notfälle vorkommen, hilft es, wenn das ganze Team Grundlagen der menschlichen Psychologie beherrscht. Missverständnisse und Meinungsverschiedenheiten sollen als Teil der Situation und nicht als persönlichen Angriff verstanden werden.

WAHRNEHMUNG

Das menschliche Gehirn ist in der Lage im Mittel sieben Reize gleichzeitig aufzunehmen (4). Die Aufmerksamkeit zu bestimmten Prozessen findet nach Relevanz und Neuartigkeit der Reize statt (5), so dass hier schon eine Interpretationsebene vorhanden ist. Somit kann eine Führungsperson nicht alle am Patienten parallel laufenden Prozesse aufnehmen. Informationslücken werden mit bekannten Inhalten und Erwartungen gefüllt. Rawlinson stellte schon 1976 fest, dass die Lesbarkeit eines Textes unbeeinflusst bleibt (Abb 1.), wenn nur der Anfangs- und Endbuchstabe der Wörter an der korrekten Stelle steht (6). Die Wahrnehmung des Handlers kann also durchaus von der „Wahrheit“ am Patienten abweichen.

Die Wahrnehmung stellt die erste Ebene des Situationsbewusstseins dar. Nach Endsley (7) besteht das Situationsbewusstsein in den nächsten Ebenen aus „Verstehen der Situation“ und „Vorhersagen des zukünftigen Patientenstatus“. Das Situationsbewusst-

sein ist eines der wichtigen Eigenschaften, um kritische Situationen zu bewältigen.

Alle Teammitglieder unterliegen diesen psychologischen Voraussetzungen, die auch durch Training nicht veränderbar sind. Funktionsunabhängig sind also Situations- und Befundinterpretationen möglich, die von dem eigentlichen Patientenzustand differieren. Aus diesem Grund muss ein Informationsaustausch über Hierarchiegrenzen hinweg jeder Zeit möglich sein.

KRITERIEN EINER KLARER KOMMUNIKATION AUSTAUSCH VON INFORMATIONEN

Während einer Notfallsituation ist der Geräuschpegel oft erhöht und wird von den Team-Mitgliedern eher als Dauerrauschen wahrgenommen. Daher sollte vor einer Anweisung immer der Name des Informationsadressaten genannt werden. Die Teammitglieder hören im Geräuschpegel ihren Namen (vertraute Ansprache, sog. Cocktail-Effekt (8)) und können Ihr Aufmerksamkeit auf den Sprecher richten. Durch Blickkontakt kann die Aufmerksamkeit bestätigt werden.

Anordnungen sollen nach dem readback/hearback- Prinzip durchgeführt werden (9). Dieser Dreierschritt kann zwischen Arzt und Pflegekraft beispielhaft folgendermaßen aussehen:

- 1.Der Arzt gibt eine Medikamentenanweisung mit den oben genannten Informationen
- 2.Die Pflegekraft wiederholt die Anweisung (Readback – Zurücklesen) und der Arzt kann sich von der Richtigkeit des Verstandenen überzeugen.
- 3.Der Arzt wiederholt noch mal die Anordnung (hearback- Zurückhören), die sich mit der initialen Anordnung decken muss.

Insbesondere eine Medikamentenanweisung stellt durch mangelnde Informationsweitergabe einen Risikofaktor dar. Es muss immer der Medikamentenname, die Dosierung mit Einheit und der Applikationsart genannt werden. Schwierigkeiten können entstehen, wenn die gleichen Wirkstoffe von wechselnden Herstellern eingekauft werden und Ampullenetiketten in ihrem Design verändert werden.

Sollen Medikamente verdünnt werden, ist dies abteilungsintern durch Standardlösungen zu definieren. Ist dies nicht der Fall, muss explizit allen Teammitgliedern klar sein, welche Dosierung benötigt wird.

10-FÜR-10

Um in einer Notfallsituation das unkoordinierte Arbeiten einzelner Teammitglieder zu verhindern,

hat die Arbeitsgruppe Rall am Simulationszentrum Tüpass in Tübingen, Deutschland, das Prinzip 10-für-10 definiert (Abbildung 2). Dabei soll durch eine 10 Sekunden-Pause 10 Minuten Zeitgewinn in der Notfallversorgung gewonnen werden (10). Diese taktische Maßnahme soll immer durchgeführt werden, wenn eine neue Situation oder Arbeitsdiagnose eintritt. Da in 10 Sekunden in der Regel kein Patientenschaden auftritt, soll diese Zeit effektiv genutzt werden, um das Problem zu benennen (z.B. „Ich glaube der Patient hat einen Pneumothorax“) und anschließend eine Aufgabenverteilung vorgenommen werden.

TEAMKOMMUNIKATION

Im Simulationszentrum der Medizinischen Hochschule in Hannover haben wir die Erfahrung gemacht, dass auch nach der Simulation viele Teammitglieder nicht wussten, welche Verdachtsdiagnosen der verantwortliche Arzt im Notfall hatte. Zur Lösung kann empfohlen werden, dass die Führungsperson regelmäßig Zusammenfassungen laut kommuniziert. Inhaltlich sollen diese Zusammenfassungen die Verdachtsdiagnose und die bisher getroffenen Maßnahmen beinhalten. So kann das ganze Team auf fehlende Maßnahmen aufmerksam werden.

Sollte der Behandler aus gutem Grund abweichend von Standards oder ähnlichen Therapien handeln müssen, so sollte er dies kurz erklären. Damit wird verhindert, dass es eine stille Unruhe im Team gibt. Bei sehr komplexen Situationen, wie z.B. die Kombination aus thromboembolischen Ereignis und Trauma kann das Thema Antikoagulation sehr individueller Therapieschemata bedürfen.

ARBEITEN NACH STANDARD OPERATION PROCEDURES UND CHECKLISTEN

Als Qualitätskriterium für High Responsibility Teams wird die Verlässlichkeit und Zuverlässigkeit in ihrem Handeln beschrieben. Für einzelne Notfallsituationen gibt es Akronyme, die leicht zu merken sind. Diese Akronyme können in den oben beschriebenen Zusammenfassungen genutzt werden, um Diagnose und Therapielücken zu entdecken. Beispielsweise soll hier das DOPES-Schema (D=Dislokation des Tubus, O=Obstruction, P=Pneumothorax, E=Equipmentversagen, S=Stomach) bei Oxygenierungsproblemen (11) und das ABCDE-Schema (A=Airway, B=Breathing, C=Circulation, D=Neurologisches Defizit; E=Exposition) zur Trauma-Versorgung genannt werden (12). Wichtig ist für alle Akronyme, dass sie vor Anwendung im Team geschult werden und jedes Teammitglied ihre Bedeutung kennt. An zentralen Punkten können

Plakate oder Aushänge mit der Akronymbeschreibung ausgehängt werden.

NACHBESPRECHEN

Nach der Notfallsituation sind die Teammitglieder oft emotional von der Situation ergriffen. Eine Teamnachbesprechung sollte nach kritischen Situationen immer durchgeführt werden und hat die Aufgabe, die Teammitglieder in Ihrer Emotion aufzufangen, die durchgeführten Maßnahmen zu evaluieren und für die nächste kritische Situation das Vertrauen des Behandlungsteams zu gewinnen. Keinesfalls dürfen einzelne Teammitglieder vorgeführt werden. Unter Berücksichtigung der physiologischen Voraussetzungen gilt jede Wahrnehmung eines Teammitglieds als wahr und muss aufgenommen werden. In der Nachbesprechung sollen erst die positiven, anschließend die negativen Aspekte genannt. Die negativen Aspekte des Behandlungsablaufes sollen neutral beschrieben und anschließend nach medizinischen Guidelines beurteilt werden.

TRAINING

Auch wenn ein flächendeckendes Simulationstraining in der Medizin noch nicht vorhanden ist, gibt es mehrere Modelle nach denen Notfallsituationen trainiert werden können. Bei diesen Simulationstrainings stehen nicht die medizinischen Maßnahmen im Vordergrund. Vielmehr können die Mitarbeiter ihre Kollegen unter Stresssituationen kennenlernen und Notfallkonzepte in Ihrer Anwendung üben. Der Mehrwert in einem videogestützten Training liegt in der möglichen Selbstreflexion. Besonders eindrucksvoll ist die Wahrnehmung, welches Teammitglied zu einem bestimmten Zeitpunkt über welche Informationen verfügt.

ZUSAMMENFASSUNG

In der Gesundheitsversorgung gibt es verschiedenste Situation, in denen ein ruhiges Einholen von Informationen, Beratschlagen und Aufgabenmanagement nicht möglich ist, ohne einen potentiellen Patientenschaden zu riskieren. Zeitkritisch müssen sich Teams finden und eine Aufgabe bewältigen. Damit gehört die Gesundheitsbranche mit zu den High Responsibility Teams. Zur erfolgreichen Bewältigen der Situation tragen die „non technical skills“, insbesondere die Kommunikation bei. Die Gabe von Anweisungen muss zielgerichtet, eindeutig und nachvollziehbar sein. Um sicherzustellen, dass der entsprechende Teampartner die Anweisung verstanden hat empfiehlt es sich, das readback/hearback -Prinzip zu verwenden.

Werden Behandlungsstandards für Notfälle genutzt, müssen alle Teammitglieder den dazugehörigen

Sprachcode kennen und verwenden. Regelmäßige Zusammenfassung über den Zustand des Patienten und die bereits getroffenen Maßnahmen helfen, den Informationsfluss im Team zu verbessern. Hat ein Teammitglied bei den getroffenen Maßnahmen Bedenken und alternative Behandlungsideen, sollen diese respektvoll geäußert werden. Eine sachliche Nachbesprechung der Notfallsituation hilft, das Vertrauen in das Behandlungsteam zu stärken.

Die anspruchsvollen „non technical skills“ können in einem Simulationszentrum regelmäßig geübt werden. Das Beobachten der eigenen Person unterstützt dabei die Reflexionsmöglichkeit.

LITERATURVERZEICHNIS

1. HAGEMANN V, KLUGE A, RITZMANN S. High Responsibility Teams- Eine systematische Analyse von Teamarbeitskontexten für einen effektiven Kompetenzerwerb. Journal Psychologie des Alltagshandels. 2011; p. 1998–9970.
2. SALAS. Does crew resource management training work? An update, an extension, and some critical needs. Hum Factors. 2006 48(2): p. 392–412.
3. RALL M GD. Millers's Anesthesia. 7th ed. Miller, editor. Oxford: Elsevier; 2010.
4. MILLER GA. The Magical Number Seven, Plus or Minus Two: Some Limits on Our Capacity for Processing Information. The Psychological Review. 1956; 63(81–97).
5. ANDERSON JR. Kognitive Psychologie. 2nd ed.: Spektrum Akademischer Verlag; 1996.
6. RAWLINSON GE. The significance of letter position in word recognition. Nottingham: University of Nottingham, Psychologie Department; 1976.
7. ENDSLEY MR, GARLAND DJ, EDITORS. Situation Awareness Analysis CL; 1995.
8. CHERRY E. Some experiments on the recognition of speech, with one and with two ears. Journal of the Acoustical Society of America. 1953; 25.
9. BROWN J. Closing the communication loop; using readback/hearback to support patient safety. J Comm J Qual Saf. 2004; 30(460–464).
10. RALL M, LACKNER CK. Crisis Resource Management - Der Faktor Mensch in der Akutmedizin. Notfall Rettungsmed. 2010; 13(349–356).
11. TIMMERMANN A, BYHAHN C, WENZEL V, EICH C, PIEPHO T, BERNHARD M, ET AL. Handlungsempfehlung für das präklinische Atemwegsmanagement. Anästhesie Intensivmed. 2015; 53(294–308).
12. HELM M, KULLA M, LAMPL L. Advanced Trauma Life Support – Ein Ausbildungskonzept auch für Europa. Anaesthesist. 2007 November; 56(11)(1142–6).

Tabelle 1. Unterschiede von klassischen und High Responsibility Teams (1)

Konsequenzen	Klassische Teams	High Responsibility Teams
Reversibilität der Ereignisse	In der Regel ja	In der Regel nein
Körperliche & psychische Schäden	Dem Team & der Firma	Dem Team, der Firma und Dritten
Verantwortung für das Leben anderer	Nein	Ja
Abbruch der Situation möglich	Ja	Nein
Arbeitsunterbrechung möglich	Pausen sind möglich	Pausen etc. sind nicht möglich
Mediendruck / Öffentlichkeitsarbeit	In der Regel nicht	ja

Tabelle 2. CRM-Leitsätze als Qualitätskriterien zur Bewältigung einer Notfallsituation

CRM Leitsätze nach Rall und Gaba (3)

1. Kenne Deine Arbeitsumgebung
2. Antizipiere und plane voraus
3. Fordere Hilfe an – lieber früh als spät
4. Übernimm die Führungsrolle oder sei ein gutes Teammitglied mit Beaharrlichkeit
5. Verteile die Arbeitsbelastung (10-für-10-Prinzip)
6. Mobilisiere alle verfügbaren Ressourcen (Personen und Technik)
7. Kommuniziere sicher und effektiv – sag was Dich bewegt
8. Beachte und verwende alle vorhanden Informationen
9. Verhindere und erkenne Fixierungsfehler
10. Habe Zweifel und überprüfe genau (Double check)
11. Verwende Merkhilfen und schlage nach
12. Re-evaluiere die Situation immer wieder, wende das 10-für-10-Prinzip an
13. Achte auf gute Teamarbeit, andere unterstützen und sich koordinieren
14. Lenke Deine Aufmerksamkeit bewusst (Situation Awareness)
15. Setze Prioritäten dynamisch

Ncah enier nueen Sutide, die uetnr aerdnam von der Cmabirdge Uinertvisy dührurhgeft wrdoen sien slol, ist es eagl, in wlehcer Rehenifloge Bcuhbstaen in eneim Wrot sethen, Huaptschae, der esrte und Itzete Bcuhbstaen snid an der rhcigten Settle. Die rsetclhien Bshcuteban kenönn ttoal druchenianedr sien, und man knan es tortzedm onhe Poreblme lseen, wiel das mneschilhe Gherin nhcit jdeen Bcuhbstaen enizlen leist, snodren das Wrot als gnazes. Mti dme Pähonemn bchesfätgein shci mherere Hhcochluen, acuh die aerichmkianse Uivnäseritt in Ptstbigurh. Esrtmlas üebr das Tmeha ghseibren hat aebr breteis 1976 – und nun in der rgchitien Bruecihsetnafoelngbe – Graham Rawlinson in sieenr Dsiestraiton mit dem Tetil "The Significance of Letter Position in Word Recognition" an der egnlsicehn Uitneivrsy of Nititongahm

Abbildung 1. Dr. Graham Rawlinson zeigt, dass trotz falscher Buchstabenfolge der Text gelesen werden kann (6)**Abbildung 2.** Das 10-für-10 Prinzip nach Rall kann bei jeder Veränderung der Situation durchgeführt werden (10)

RESULTS OF SURGICAL TREATMENT OF HYDATID LIVER DISEASE IN CHILDREN

H.I.Ibodov, R.R.Rofiev, D.S.Mirzoev, T.Sh.Ikromov

Department of Pediatric Surgery, Anesthesiology and Intensive Care
Institute of postgraduate health education, Dushanbe, Tajikistan

RELEVANCE

Echinococcosis (hydatid disease) — a life-threatening parasitical disease for humans and domestic animals. The disease spreads rapidly in children, which leads to profound morphofunctional changes in the affected organ [1, 2, 6]. Despite various antrum removal techniques (ART), recrudescence of non-parasitical cysts is observed in 4-20% of the medicated areas. Long-term complications associated with the ART occur in 8–14% of the medicated areas. There are 15 ARTs but the conditions under which these can be employed, such as accessibility and size of the echinococcal cysts (EC), remain unspecified. Peculiar complications arise when medium, big or large-size EC are centrally located in the subdiaphragmatic area of the liver. Due to erroneously chosen ART the rate of recrudescence after a subdiaphragmatic hydatid liver infection (SHLI) of the treated areas amounts to 5–12%. In addition there is a 7–46% rate of ulcerous or biliary intestinal fistula formation. [1, 3, 4, 6].

PURPOSE OF THE STUDY

To evaluate antrum removal techniques concerning the echinococcal cysts's location.

MATERIAL AND RESEARCH METHODS

Analysed were the results of studies and treatment of 153 children operated on because of hydatid liver disease in the past 15 years. 159 surgeries were performed on 153 patients. There were 35 children in the age group of 2–7 year-olds (35%), 51 (33.3%) 8 to 10-year-olds and 64 (43.9%) 11–15 years old children. 94 (61.5%) children had unicystic echinococcosis while the other 59 (38.5%) children suffered from polycystic echinococcosis. In 18 cases (11.7%) both liver and lungs were infected. 85.5% of the cysts were found in the right lobe of the liver and were distributed as follows: I — 12–4.1%; II — 14–4.8%; III — 17–5.6%; IV — 72–24.6%; V — 531–17%; VI — 48–16.4%; VII — 41–14.5%; VIII — 35–13.5%. At first the safest



Habibullo Ibodov, Professor, Doctor of Medicine

insight providing diagnostic methods were applied, such as ultrasound scan, x-ray of the chest from two different perspectives, radioisotope scan if required, CT, angiography and laparoscopy. It is particularly difficult to differentiate EC containing a multitude of smaller (daughter) cysts holding a small amount of liquid from liver formations. The following six ART were employed: employment of the catgut purse-string suture by Delbet's method (10); reduction of the fibrous capsule's (FC) volume by placing its edges on top of each other (5); coiling up the antrum's edges inwardly employing N.F. Berezkin's method and subsequently sealing reduced antrum with a duplicated gland on the vascular pedicle with A.T. Pulatov's method (13); sealing a lobe of the diaphragm to the bottom of EC located on the liver (9); reduction of the antrum's volume through invagination of the cyst (6) — a continuous catgut suture is made into the antrum and the FC's side walls through a thin layer of the liver parenchyma (and FC). Subsequently, the filament re-emerges while capturing the dissected edge of the FC. The next step is capturing the antrum's bottom. The other side of the FC is sewn the same way using the same thread, which leaves both ends emerged on the side wall of the AFC. Finally the dissected edges of the FC and a thin layer of liver tissue are invaginated and attached at the bottom of the antrum which makes them subside into the AFC and eliminates the antrum. Depending on the size of the EC, two or three invaginating sutures are necessary; AR with a cut lobe of the FC combined with a thin layer (up to 1cm) of the liver parenchyma on top of each other attached to each other and the bottom of the antrum (31). It should be noted that the

great gland appeared to be insufficiently developed in most cases (86.5%) to seal the antrum. In nine cases (12.1%) a drainage of the subdiaphragmal area was performed by machines such as the "cigar", tamponade with the Mikulicz method, drainage by means of a duct and active aspiration of the antrum.

RESULTS AND DISCUSSION

Surgery performed on a patient infected with echinococcosis is built up of two parts. First — removal of EC, disinfection of the AFC and second — AR FC. To achieve these goals it is important to have sufficient supervision surface during the operation because both the FC and the serous antrum in which the affected organ is located need to be controlled frequently. Appropriate surgical approach considering size and location of EC on the liver allows to: decrease incidence of postoperative complications and, if possible, prevent from recrudescence because of undiscovered parasitic residues; reliably suture biliary fistulas and eliminate deep AFC. The surgical approach ought to be safe, provide an overview over the area the surgery is performed on and an appropriate access to the affected area of the liver. In case the EC is located in the subdiaphragmatic space (segment II, VI, VII, VIII) the most convenient ART is a continuous transverse laparotomy continued on VIII or IX intercostally in the pleura up to the mid-axillary line on the left or right by a cut from the rib arc to anterior axillary line. The next step is, depending on the chest type, the dissection of the cartilage VIII or the rib IX in the intercostal space up to the mid-axillary line which simultaneously dissects the intercostal muscles. At first, preserving the integrity of the pleural antrum, a piece of the peritoneum is cut open on the side of the abdominal cavity and the muscles of the diaphragm with the parietal layer of the pleura are pushed apart upwards which broadens the wound (Appropriate proposals no. 26 from 11.04. 'Virpi, TIPPMK). As a result the depth of the wound decreases from 10 to 5–6 cm and the vertical angle of vision increases from 40–45% to 100–110% while the horizontal angle of vision increases from 35–40% to 70–75%. Reasons to employ this ART were big or vast EC in segment VII–VIII that caused a raise or second relaxation of the diaphragm up to the II–III intercostal space. The patients receives additional lobes after the AR.

The reasons to operate horizontally from the upper part by dissecting straight or oblique abdominal muscles are if the EC is located in the bottom, front or side (segment I, III, IV, V, VI) surface of the liver. In doing so the EC, protruding from the liver tissue, is carefully fenced off by soaked in 96°–alcohol gauze tissue, leaving enough space for puncture. Now, the EC is

punctured and entirely emptied by means of a needle with rubber passage linked to a 20 ml syringe. Then the FC is dissected and its chitin shell removed. The AFC is disinfected with 96°–alcohol and loosely tamponated. The next immensely important step is the elimination of the AFC. The antrum is widely dissected, the biliary fistulas are sutured and the choice of the ART has to be made. In order to remove the antrums of centrally located medium, big and vast size EC located in the subdiaphragmal liver area we employed the ART of sewing lobes of the FC cyst (Appropriate proposal no. 41 from 8.04.2000 adopted Virpi TIPPMK). The FC and 1,5–2 cm of the liver parenchyma are dissected simultaneously parallel to the vessels which makes the top and bottom lobe of the FC form a semi concave surface. The goal is to easily suture the lobes of the FC to the antrum's bottom. The resulting top and bottom lobe are dissected into two or three parts, depending on size of EC or AFC, of 1,5–2 cm in the liver parenchyma. Usually four to six FC lobes are created. Therefore the AFC can be opened to 1/2 or 1/3 of its surface which gives the surgeon a good overview and sufficient space to suture the biliary fistula. An eight-shaped suture and a polyethylene filament is used. It should be noted that after the removal of a centrally located medium, big or vast-sized EC by decreasing the pressure in the antrum's wall the AFC's walls contract in the depths of 2–3 cm. To prevent pathological accumulation of fluid or the formation of antrum are sewn together, which decreases its depth by up to 3–4 cm. The remaining antrum is 5–10 cm deep. It is eliminated by systematically suturing the lobes of the FC; to its wall, to its bottom and subsequently on top of each other. Thus, the antrum is entirely eliminated by suturing the contracted surface to the bottom of the FC and systematically attaching the FC lobes to the remaining AFC. Complications did not occur in the immediate postoperative period after the employment of the previously described ART.

In the immediate postoperative period three patients who underwent a laparotomy (2) with an additional broadening along the VIII intercostal space through the pleura to the mid-axillary line (1) suffered from a festering wound. Two out of three patients who were having complications with the postoperative wound were also having festering EC on the liver.

Altogether in 30% of the cases complications after the antrum removal occurred. Each of these had festering antrums that required another drainage. Two children also developed an inflammatory infiltration of the liver tissue which was confirmed by an ultrasound and caused by the disruption of the blood circuit and the drainage during the surgery. The patients each received two antibacterial and anti-inflammatory therapies.

Complications after AR by rolling inwards the FC edges with a thin layer of liver tissue with N.F. Berezkin's method were observed in four cases where medium or big-sized EC were located centrally in the form of the formation of an antrum (1), a biliary fistula (1) and a subphrenic abscess (4). In the postoperative period all of these patients suffered from hepatitis and liver failure even though neither of these symptoms had been observed before the surgery. These changes seem to have been associated with the deformation of the FC and liver tissue as well as with the blood circuit disruption and the development of the inflammatory infiltration and a hypoxia of the liver cells. One patient died of severe liver failure.

Complications after the AR by suturing a lobe of the relaxed diaphragm to the bottom of the antrum occurred in one case, in which the child suffered from partial pneumonia. The appearance of pneumonia is associated the limited mobility of the diaphragm that was sutured to the antrum's bottom. This resulted in hypoventilation, disruption of the drainage process and the blood circuit in the lower part of the right lung.

Postoperative complications associated with the AR by invagination were observed in one case in form of an antrum in the subdiaphragmatic space which was caused by the remaining antrum between the liver and the relaxed diaphragm. Being aware of these problems, we subsequently started to apply diaphragmal duplication or removal of the relaxed diaphragm with individual corrugating seams. As a result of the diaphragmal duplication, 36 patients with a relaxed diaphragm did not require a drainage of the subdiaphragmal area and no antrum formed.

Long-term consequences of the surgery were observed in 97 (63.3%) of the cases in the period of two years. U10-year-olds (10.3%), 21 two to five-year-olds (21.6%), 22 five to ten-year-olds (22.6%) and 44 children older than ten years (45.5%). Complications after a liver echinococectomy after a long time period were observed in 12% of the cases.

Thus, the main causes of the complications was the inappropriate choice and low efficiency of the AR with Delbet's and N.F. Berezkin's methods or the lobe of the diaphragm which was the reason to abandon the previously described ARTs.

Duplication of the relaxed diaphragm reduces the space between the liver and the diaphragm which makes the drainage of the subdiaphragmatic area needless. An appropriate surgical approach when dealing with liver echinococcosis is an entire transverse laparotomy and, if required, additional widening of the wounds along the VIII or IX intercostal space up tp the mid-axillary line. For small and medium-sized EC that are

peripherally located the ART is invagination of the FC into the antrum. For centrally located EC of medium, large and vast size the most effective way to remove the antrum is cutting lobes out of the FC cyst. In case of a relaxed diaphragm the duplication of the diaphragm employed.

REFERENCES

1. ABDURAKHMANOV B.A. Surgery of liver echinococcosis with subdiaphragmatic localization: Dr. Med. – Tashkent, 1993.
2. ABDUFATAEV T.A. Method of determination of static compliance and elasticity of the lungs and the degree of their reduction: method. recommendations. Dushanbe, 1994.
3. BOYMURADOV C. Surgical treatment of echinococcosis of the liver in children: Dr. Med. Tashkent, 1996.
4. KARIMOV S.I.// The problem of echinococcosis in Uzbekistan – achievements and prospects. Proc. International Symposium. Surgery Echinococcosis. – Khiva, 1993, p. 1–5.
5. MUBOROKSHOAEVA M.A. Age norms of children respiratory function in Tajikistan: Method. Recommendations. Dushanbe, 1983. p. 1–8.
6. PULATOV A.T. // Surgery echinococcosis in children. ML, 1983.
7. PULATOV A.T. A method of reducing the antrum's width for deep echinococcectomy of the liver in children: Plowing one edge of the wound on the other. Rationalization proposal adopted by TGMI №154 from 21–2. 1980 // 30 years of pediatric surgery in Tajikistan. - Dushanbe, p. 436.

REHABILITATION OF CHILDREN WITH NEPHROLITHIASIS ASSESSMENT OF THE RESPIRATORY FUNCTION IN CHILDREN WITH AMBILATERAL UROLITHIASIS IN COMBINATION WITH CHRONIC KIDNEY FAILURE

T.Sh. Ikromov, H. I. Ibodov, N.S. Ibodov, S.K. Asadov

*Institute of Postgraduate Health Education
of the Republic of Tajikistan*

RELEVANCE

The development of a chronic inflammatory process in the kidneys is a serious medical and social problem since it may lead to disability of the affected children. The inflammation caused by pyelonephritis seems to be limited to one single organ: the kidney. The results of our research prove that every disease, even at an early stage, does damage to various body functions such as the respiratory function. An early discovery of these disorders is of great importance for the choice of a specific treatment and the prognosis of the course of the disease [1,3,4]. Chronic renal failure that develops as a result of nephrolithiasis and can be detected in a complex set of clinical manifestations that are caused by changes of the organs in the human body [5]. Damage of the respiratory system of patients with nephrolithiasis is not sufficiently discussed in literature. Therefore, a detailed study of respiratory function and blood circuit of these patients is required for making a correct diagnosis, choice of appropriate analgetics, prevention of various intra- and postoperative complications and, in first place, detection of existing functional resources and the development and prescription of appropriate medication [1,2,4].

A significant part of the contemporary anesthetic practice is the applied physiology of respiration. Therefore the effect of the most common inhalational anesthetics depends on its absorption and elimination in the lungs. The main side effects of these anesthetics are associated with the process of breathing. Muscle relaxants, the unfamiliar position on the operating table and some special factors have a profound influence on the patient's breathing process [1,2,3,4].

Purpose of the study. Determine the most significant sources of irritation of the breathing process of children with ambilateral nephrolithiasis in combination with chronic kidney failure.



MATERIAL AND METHODS

Analyzed were the results of the examination and treatment of 187 children suffering from nephrolithiasis at the age of six months to 18 years. There were 38 (20%) patients at the age of six months to six years, 4-7 years – 54 (28%), 8-11 years – 57 (31%) and 12-18 years – 40 (20%). 128 (68.5%) of them were male and the rest, 59 (31.5%) were females. In 116 (62.2%) cases one side of the kidney was affected, both sides in 47 (24.8%) cases and 24 (13%) of the children had numerous kidney stones.

Single stones were found in 126 (67.4%) children and accumulations in 51 (32.6%). Each patient suffered from chronic calculous pyelonephritis (CP) and 35 (18.8%) of them were at an advanced stage. 44 (23.5%) patients had CP in stage I, 80 (42.8%) in stage II and 63 (33.7%) in stage III. In addition to this hydronephrosis was observed in 64 (32.4%) cases and 78 (41.7%) children out of 187 suffered from chronic kidney failure (CKF). 26 (33.3%) of these patients were in stage I, 35 (44.91%) in stage II and 17 (21.79%) in stage III. The respiratory function of 63 patients was analyzed.

To evaluate the respiratory function (RF), spirometry — ("Metatest-2", "Cosmed") was employed, the blood gases determined by oximetry, pulmonary shunt – capnography and the oxygen method, hypocoagulation and the detoxification function of the lungs (biochemical analysis of the blood flowing to and out of the lungs), central and pulmonary hemodynamics (through impedance and doppler pneumography).

The results of the study were evaluated in accordance with the modern standards of evidence-based medicine. The obtained data was worked on with the method of varying statistics with calculation of the mean (M), error ($\pm m$) and evaluation of the reliability of the data ($P \geq$). The data was collected and processed with MS Excel (Ver.5.0.).

RESULTS AND DISCUSSION

In order to assess the dysfunction of the lungs of patients suffering from ambilateral nephrolithiasis worsened by chronic renal failure we observed the respiratory function (RF) of 67 out of 187 patients at the age of six to 18 years. According to the obtained data, 56 out of 67 patients suffered from inadequate alveolar ventilation (IAV). IAV stage I was detected in 16 (28.59%) cases, stage II in 29 (51.81%) and stage III in 11 (19.6%) cases out of 56. The IAV was handicapping for 12 (21.43%) patients, limiting for 27 (48.21%) and with both impacts on the patient in 17 (30.36%) cases. Especially often IAV was found in patients with numerous stones on both sides of the kidney, ambilateral CP and CKF. IAV was detected concurrently with CP stage I and II. 11 (16.42%) of the patients suffered from an acute handicapping course of the disease. Every patient suffering from IAV was also diagnosed with stage II or III of hydronephrotical kidney transformations and signs of chronic intoxication (lag in physical development, anemia, fatigue, loss of appetite).

The stage I of IAV caused the tidal volume (TV), lung capacity (LC), respiratory minute volume (RMV), maximum voluntary ventilation (MV), indicators of pneumotachometry (IP) and the forced expiratory volume (FEV) to decrease to 70–80% of the standard values.

The effectiveness of the pulmonary ventilation as well as the accordance of the values of ventilation and volume of the pulmonary blood flow (ventilation-perfusion ratio) is assessed by the changes in the oxygen utilization (uO_2). The decline of the uO_2 rate indicates the dominance of the ventilation over the blood flow and its increase may be a sign of a lack of alveolar ventilation in relation to the pulmonary circulation. The decrease of uO_2 was observed in 21 (31.35%) cases, which shows the dominance of alveolar ventilation in relation to the pulmonary circulation. The decline of uO_2 was observed in 38 patients with CKF, which is associated with spasms or the contamination of the pulmonary capillaries with toxic metabolites of the organism. 24 (35.82%) patients suffering from CP in stage II and III had an increase in the uO_2 rate indicating a lack of alveolar ventilation in relation to the pulmonary circulation. These patients were also having latent bronchospasm which is associated with the contamination of the alveolar walls and the bronchioles through the toxic substances in the lungs.

31 (46.27%) out of 67 patients had a decreased oxygen intake (iO_2). These changes (decrease of the value $23 \pm 1.3\%$ in comparison to the standard) were detected in children with stage II or III of IAV and characterize respiratory failure with decreased respiratory resources.

Berotec and pneumotachometry were prescribed to patients with CKF and ambilateral CP to detect latent bronchospasm, which 25 (37.32%) patients were suffering from.

Normally, the lung volume and capacity values vary up to $\pm 20\%$.

Thus, 56.6% of the patients with ambilateral nephrolithiasm worsened by chronic kidney failure were

Table 1. Respiratory failure due to lack of ventilation of children suffering from ambilateral nephrolithiasis worsened by chronic renal failure.

Type of kidney disease, stage CP, CKF	Respiratory insufficiency								
	Handicapping type			Restrictive type			Mixed type		
	stage	stage	stage	stage	stage	stage	stage	stage	stage
CP I stage	I	II	III	I	II	III	I	II	III
		2			2	1	1		1
		1		1				2	
CP II stage	1		1	3		3		3	
CP III stage									
CKF I stage									
CKF II stage									
CKF III stage									

Stage II of IAV decreased the previously mentioned parameters to 60–70% and stage III to less than 60%.

proved to have varying degrees of respiratory failure that depend on the stage of CP and CKF. It should be

noted that these children did not show clinical manifestations of respiratory disorders.

Therefore, analyzing the respiratory function of patients with ambilateral nephrolithiasis worsened by chronic kidney failure plays an essential role in the preoperative preparation, choice of the method of pain relief and prevention of intra- and postoperative complications.

CONCLUSIONS

1. Monitoring and appropriately assessing respiratory dysfunctions of children with chronic kidney failure supports a sufficiently early mending of the dysfunctions and leads to a decrease of complications in the intra- and postoperative period.
2. Complex examinations of patients with CKF allows to detect clinical manifestations of latent bronchospasm and, based on the identified transformations, conduct preoperative preparations.

REFERENCES

1. T.A. ABDUFATOEV. Assessment of the operational and anesthetic risk of children with lung diseases. /T.A. Abdufatoev, H.I. Ibodov, A.A. Abdulaliev. Methodical recommendations. – Dushanbe, 2000. – 16 p.
2. I.G. DANYAH. About diagnostic value of jugular venography for determination of the hemodynamic condition of the minor blood circuit of patients with nonspecific chronic respiratory diseases. / Diseases of respiratory the organs (manual). I.G. Danyah, Ostrovskaya V.S., Burtzeva V.O. – M.: "Medicine", 1978. – P. 32–34.
3. A.P. ZILBER/ Diseases of the pulmonary organs (manual). A.P. Zilber. – M.: "Medicine", 1990. – P. 350–352
4. A.P. ZILBER/ Respiratory failure (manual). A.P. Zilber. – M.: "Medicine". 1989. – 512 p.
5. C. ZOCCALI/ Cardiorenal risk as a new frontier of nephrology: research needs for intervention. Nephrol. Dial. Transplant. 2002; 17 (suppl.2); P. 50–54

VASKULÄRE KOMPLIKATIONEN DURCH AUTOANTIKÖRPER GEGEN G-PROTEIN GEKOPPELTE REZEPTOREN BEI DEN VOLKSKRANKHEITEN DEMENZ UND TYP-2-DIABETES SOWIE DER BÜRGERSCHEN KRANKHEIT

P. Karczewski, P. Hempel, M. Bimmler

E.R.D.E. -AAK-Diagnostik GmbH
Biomedizinischer Forschungscampus Berlin-Buch
Berlin, Germany

EINLEITUNG

Eine spezielle Gruppe von Autoantikörpern gewann in den letzten Jahren in Forschung und Klinik zunehmend an Bedeutung aufgrund ihrer besonderen Wirkungsweise und ihres Vorkommens bei schwerwiegenden Erkrankungen. Diese Autoantikörper sind gegen bestimmte Rezeptoren in der Zelloberfläche gerichtet, den G-Protein gekoppelten Rezeptoren (GPCR). Der zahlreichsten und wichtigsten Familie von Membranproteinen, die extrazelluläre Signale in das Zellinnere übertragen. Schwerpunkt der vorliegenden Übersicht sind die bisherigen Arbeiten unseres Labors auf diesem Gebiet. Die Aktivitäten unseres Labors umfassen die Diagnostik eines Spektrums von krankheitsassoziierten agonistischen Autoantikörpern sowie Untersuchungen zu zellulären Wirkungsmechanismen dieser Antikörper.

G-PROTEIN GEKOPPELTE REZEPTOREN (GPCR)

Die Superfamilie der GPCR umfasst mehrere hundert Rezeptoren. GPCR kommen in allen Zelltypen menschlicher und tierischer Gewebe vor. Sie vermitteln die Wirkung einer Vielzahl von Signalstoffen des Organismus wie Hormone, Neurotransmitter und sogar Photonen. Von vielen GPCR sind die natürlichen Liganden bisher nicht bekannt. GPCR sind an der Regulation fast aller Körperfunktionen beteiligt. Sie kontrollieren viele physiologische Prozesse und spielen bei pathologischen Zuständen eine oft zentrale Rolle. Sie sind deshalb die wichtigste Zielstruktur für pharmakologische Therapieansätze. Alle GPCR bestehen aus einer unverzweigten Kette von Aminosäuren, die die Oberflächenmembran der Zelle siebenmal durchdringt (1). Auf der Zelloberfläche befindliche Domänen der Rezeptoren sind das N-terminale Ende sowie die drei extrazellulären Schleifen. Letztere bilden

durch Disulfidbrücken und Glykosylierungen hydrophobe Taschen, die als die Bindungsstellen für die physiologischen Agonisten identifiziert wurden. Die physiologische Aktivierung des GPCR erfolgt durch Bindung des jeweiligen Agonisten an die extrazelluläre Bindungsstelle und die nachfolgende intrazelluläre Verknüpfung zweier Rezeptormoleküle (Dimerisierung). Der intrazelluläre Teil des Rezeptormoleküls interagiert typspezifisch mit verschiedenen G-Proteinen, einer Klasse regulatorischer heterotrimerer Proteine, die rezeptorspezifisch eine Kaskade intrazellulärer Reaktionen einleiten. Neben der Spezifität der Agonistenbindungsstelle des GPCR-Moleküls für den physiologische Liganden, bestimmt die Interaktion mit bestimmten G-Proteinen die Art und Weise, wie die Zielzelle auf das Signal der Rezeptoraktivierung reagiert. Je nach Art der vom Rezeptor rekrutierten G-Proteine werden zelluläre Signalwege aktiviert oder gehemmt.

Eine Gruppe von GPCR, die die Aktivität des sympathischen Nervensystems regulieren, sind die adrenergen Rezeptoren (Adrenozeptoren). Hierzu zählen die α -adrenergen und β -adrenergen GPCR mit ihren Vertretern α_1 , α_2 und β_1 , β_2 , β_3 . Ihre natürlichen Liganden sind die im Nebennierenmark produzierten Neurotransmitter/Hormone Adrenalin und Noradrenalin. Neben anderen physiologischen Prozessen regulieren Adrenozeptoren die Herz- und Gefäßmuskulatur und sind als Zielstrukturen bei Erkrankungen des Myokards und Gefäßsystems wie Herzinsuffizienz und Bluthochdruck von immenser therapeutischer Bedeutung.

AGONISTISCHE AUTOANTIKÖRPER GEGEN G-PROTEIN GEKOPPELTE REZEPTOREN

Autoimmunerkrankungen sind relativ häufig. Sie unterscheiden sich nach der Art der betroffenen Gewebe und Organe sowie der Ausprägung der Symptome. Bestimmte Autoimmunkrankheiten sind gekennzeichnet durch das Auftreten von Antikörpern (agonistische Autoantikörper), die an GPCR binden und diese aktivieren. Der klassische Vertreter einer solchen Erkrankung ist die Gravesche Krankheit (Hyper-

thyroidismus), bei der erstmals GPCR aktivierende Autoantikörper als Krankheitsursache nachgewiesen wurden (2). Hier treten agonistische Autoantikörper auf, die den Thyroid-stimulierenden Hormonrezeptor (TSHR) langanhaltend aktivieren und so Symptome der Erkrankung auslösen. In den letzten zwei Jahrzehnten wurden von verschiedenen Arbeitsgruppen solche Autoimmungeschehen gegen GPCR bei einer wachsenden Zahl von unterschiedlichsten Pathologien beschrieben. Hierzu zählen schwerwiegende Erkrankungen wie die dilative Kardiomyopathie sowie Volkskrankheiten wie Hypertonie, Typ-2-Diabetes und Demenz (Tab 1). Ein Schwerpunkt unserer Arbeiten ist das Autoimmungeschehen zum α_1 -adrenogenen Rezeptor (α_1 -AR). Dieser GPCR ist an der Regulation der kontraktilen Myokardfunktion und des Glukosestoffwechsels beteiligt und ist für die Funktion der Gefäßmuskulatur von zentraler Bedeutung. Die Antikörperdiagnostik von Patientenserien zeigte ein auffälliges Auftreten von agonistischen Autoantikörpern gegen den α_1 -AR bei Erkrankungen mit prominenter Gefäßbeteiligung. Das legt den Schluss nahe, dass eine durch Autoantikörper verursachte unphysiologische Aktivität des α_1 -AR ein Pathomechanismus für vaskuläre Schäden sein kann, die bei schweren Erkrankungen wie den Volkskrankheiten Demenz und Typ-2-Diabetes eine wesentliche, wenn nicht sogar eine kausale Rolle spielen. Diese Hypothese war Anlass für unser Labor, Wirkungsmechanismen dieser Autoantikörper gegen den α_1 -AR und die pathologische Signifikanz dieses Immungeschehens für die Entstehung von Gefäßschäden näher zu untersuchen.

ZELLULÄRE WIRKUNGSWEISE. AGONISTISCHER AUTOANTIKÖRPER GEGEN G-PROTEIN GEKOPPELTE REZEPTOREN

Die Interaktion eines Antikörpers mit einem GPCR setzt dessen Bindung an eine auf der Zelloberfläche zugängliche Domäne des Rezeptors voraus. Alle bisher in Patientenserien identifizierten agonistischen Autoantikörper binden im Gegensatz zu den physiologischen Agonisten an der ersten oder zweiten extrazellulären Schleife des GPCR. In Untersuchungen an Präparationen von α_1 -AR-spezifischen Autoantikörpern aus Patientenserien verschiedener Krankheitsbilder konnten wir mit unterschiedlichen Techniken Werte für die halbmaximale Bindung (EC50-Wert) an Peptidsequenzen der ersten und zweiten extrazellulären Rezeptorschleife im Konzentrationsbereich von 50 nM finden (3, 4). Die Bindung des Antikörpers bewirkt durch die extrazelluläre Verknüpfung zweier Rezeptormoleküle eine funktionelle Dimerisierung, die zu einem Agonisten-ähn-

lichen Effekt führt (5). Der Antikörper aktiviert den GPCR zwar nicht im Ausmaß wie der physiologische Agonist, wirkt aber durch die stabile Bindung an den Rezeptor und das Ausschalten zellulärer Schutzmechanismen (keine Rezeptordesensibilisierung) nahezu permanent auf die Zelle. Die Aktivierung des GPCR durch agonistische Autoantikörper löst in der Zelle rezeptorspezifische Reaktionen aus. Diese können, aber müssen nicht, identisch mit denen sein, die durch die physiologischen Agonisten aktiviert werden. Calciumionen sind die universellsten intrazellulären Boten und an den Signalwegen der GPCR beteiligt. Für eine Reihe von krankheitsassoziierten Autoantikörpern gegen unterschiedliche GPCR konnte nachgewiesen werden, dass sie ebenfalls das zelluläre Calcium erhöhen (6–8). Der α_1 -AR gehört zu den GPCR, die effektiv zum intrazellulären Calcium gekoppelt sind (9). Wir konnten zeigen, dass α_1 -AR-spezifische Autoantikörper aus Patientenserien, ebenso wie im Versuchstier hergestellte Antikörper, gegen bekannte Epitope des Rezeptors die Mobilisierung des intrazellulären Calciums bewirkten (3, 10). Diese Antikörper aktivierten so wichtige Signalmoleküle wie Proteinkinase C, induzierten die Phosphorylierung und somit eine Funktionsänderung von Regulatorproteinen der kardialen Calciumhomöostase und beeinflussten die Genexpression des L-Typ Calciumkanals. Die unphysiologische und langanhaltende Aktivierung von zellulären Prozessen, losgelöst von den aktuellen physiologischen Anforderungen an das Organ, wie sie durch agonistische Autoantikörper verursacht wird, führt zur Ausbildung von pathologischen Zuständen wie der Calciumüberladung der Zellen, dem Umbau von Zellstrukturen (Remodelling) bis hin zum Zelltod. Bedenkt man die Bedeutung des α_1 -AR für die Funktion der glatten Muskulatur, so ist eine entscheidende Rolle von agonistischen Autoantikörpern, die diesen Rezeptor attackieren, für die Entstehung von Gefäßschäden zwingend anzunehmen.

PATHOLOGISCHE SIGNIFIKANZ VON AGONISTISCHEN AUTOANTIKÖRPERN GEGEN G-PROTEIN GEKOPPELTE REZEPTOREN

Die Bedeutung von Autoimmungeschehenen gegen GPCR für die Entstehung und den Verlauf der betreffenden Krankheiten war lange Zeit unklar und wurde kontrovers diskutiert. Hier lieferten Tierversuche wertvolle Erkenntnisse zur Kausalität von rezeptorspezifischen Autoantikörpern für die Entstehung der Krankheit oder krankheitsrelevanter Symptome. Eine solche Kausalität konnte für β_1 -AR-Autoantikörper bei der dilativen Kardiomyopathie, dem bislang am umfassendsten untersuchten Autoimmungeschehen

gegen einen GPCR, für Autoantikörper gegen den Angiotensin 1-Rezeptor (AT1-R) bei Schwangerschaftsbedingtem Bluthochdruck (Präeklampsie) sowie renaler Transplantatabstoßung tierexperimentell nachgewiesen werden (11–13). Das gefäßschädigende Potential von Antikörpern, die gegen den α_1 -AR gerichtet sind, wurde erstmals in Ratten gezeigt, die mit den entsprechenden Rezeptorpeptiden immunisiert wurden (14). Die immunisierten Tiere entwickelten Antikörper gegen den α_1 -AR und zeigten pathologische Veränderungen in peripheren Gefäßen wie Aorta und Mesenterialarterien (Abb. 1).

Um die Relevanz eines Autoimmungeschehens gegen den α_1 -AR, das von uns bei Patienten mit vaskulärer Demenz und Alzheimer Demenz nachgewiesen wurde, für die Entstehung von Gefäßschäden im Gehirn zu klären, untersuchten wir an einem Tiermodell den Einfluss von α_1 -AR-Antikörpern auf die Makro- und Mikrovaskulatur des Rattenhirns mittels MRT-Techniken. Nach einem Zeitraum von acht Monaten zeigte sich in der Magnetresonanztomographie (MRA) eine signifikante Reduktion der Durchblutung von Makrogefäß in den Antikörper-exponierten Tieren (15, Abb. 2). Bestimmungen des zerebralen Blutvolumens durch Magnetresonanz Imaging (MRI) mit dem Kontrastmittel Ferumoxytol zeigten ebenfalls eine reduzierte Durchblutung der kleinen Gefäße im Cerebrum und in Gehirnbereichen wie dem Cortex und dem Hippocampus (16). Mit Immunfluoreszenzmikroskopie konnte eine signifikante Abnahme der Gefäßdichte in Schnitten des Cortex nachgewiesen werden (Abb. 3). Ebenfalls wiesen die Virchow-Robinschen Räume der behandelten Tiere eine höhergradige Dilatation auf (Abb. 4). Eine übermäßige Dilatation der Virchow-Robinschen Räume gilt als Indikator für das Vorhandensein von Mikroangiopathien. Somit konnten wir nachweisen, dass Antikörper gegen den α_1 -AR Schäden sowohl im makrovaskulären als auch im mikrovaskulären Gefäßsystem des Rattenhirns induzieren. Weitere mikroskopische Analysen der Gewebepräparate dieser Tiere zeigten, dass die durch Antikörper ausgelösten Gefäßschäden nicht auf die Hirnregion beschränkt waren, sondern auch in der Niere aufraten. Diese Befunde implizieren eine generelle Signifikanz der α_1 -AR-Autoantikörper für die Pathogenese und Progression von Krankheiten mit einer ausgeprägten Gefäßkomponente wie Demenz und Typ-2-Diabetes.

Therapeutische Optionen Therapeutische Ansätze können auf zwei verschiedenen Prinzipien basieren:

- Funktionelle Ausschaltung des agonistischen Autoantikörpers

— Entfernung des agonistischen Autoantikörpers aus dem Blutkreislauf

Funktionelle Ausschaltung des agonistischen Autoantikörpers

Ziel eines solchen Ansatzes ist es, die Interaktion des Antikörpers mit dem betroffenen GPCR zu verhindern. Das kann pharmakologisch durch Rezeptorantagonisten erfolgen, von denen bekannt ist, dass sie durch Konformationsänderungen des Rezeptormoleküls die Bindung des Autoantikörpers schwächen und diesen dadurch vom Rezeptor ablösen können. Zu den meisten krankheitsrelevanten GPCR existieren bereits Rezeptorantagonisten, die klinisch eingesetzt werden. Diese Option ist kostengünstig und für eine große Patientenzahl anwendbar. Nachteilig ist, dass diese pharmakologischen Substanzen mit erheblichen Nebenwirkungen behaftet sein können und natürlich auch die physiologische Rezeptorfunktion beeinflussen.

Ein anderes Prinzip nutzt die Spezifität des Antikörpers für sein Antigen. Die Bindungsepitope am Rezeptor, z.B. die betroffene extrazelluläre Schleife, sind für eine Reihe krankheitsassozierter Autoantikörper aufgeklärt worden. Hier können niedrigmolekulare Verbindungen entwickelt werden, naheliegend sind Peptide und deren Modifizierungen, die spezifisch an die zirkulierenden Autoantikörper binden und diese funktionell neutralisieren. Solche Ansätze wurden für Autoantikörper gegen den β_1 -AR beschrieben, die bei Patienten mit dilatativer Kardiomyopathie auftreten (17, 18). Diese Verfahren befinden sich jedoch im Entwicklungsstadium und sind noch nicht für die klinische Praxis verfügbar.

Entfernung der agonistischen Autoantikörper aus dem Blutkreislauf

Apherese-Techniken zur extrakorporalen Blutreinigung werden im großen Maßstab bei den verschiedensten Indikationen eingesetzt. Das bekannteste Verfahren ist die Dialyse bei der das Apheresesystem als künstliche Niere fungiert. Die Immunapherese entfernt Bestandteile des Immunsystems aus dem Blutkreislauf und ist eine effiziente Therapieoption bei Autoimmunerkrankungen. Eine Reihe von Autoimmunerkrankungen sind medikamentös nicht oder nur unzureichend behandelbar. Hierzu zählt das Autoimmungeschehen bei dilatativer Kardiomyopathie. Bei dieser Herzerkrankung spielen agonistische Autoantikörper gegen den β_1 -AR eine fatale Rolle. Die therapeutische Immunapherese wurde hier erstmals mit großem Erfolg bei einem Autoimmungeschehen eingesetzt, das gegen einen GPCR gerichtet ist (19). Die Entfernung der Antikörper resultierte in einer

Tab. 1. Spezifität und Prävalenz agonistischer Autoantikörper gegen G-Protein gekoppelte Rezeptoren (GPCR)

Erkrankung	GPCR	Prävalenz
Dilatative Kardiomyopathie	β_1 -AR	70%
Dialysepatienten	α_1 -AR, AT ₁ -R	25%
Nierentransplantatabstoßung	AT ₁ -R	
Bluthochdruck	α_1 -AR, AT ₁ -R	30%
Typ-2-Diabetes-assoz. vask. Erkr.	α_1 -AR, AT-R, ETA-R	70%
Alzheimer / vaskuläre Demenz	α_1 -AR, β_2 -AR	59%
Prostataktumor	α_1 -AR	40%
Bürgersche Krankheit	α_1 -AR, AT ₁ -R, ETA-R, PAR	82%

Die angegebenen Prävalenzen basieren auf Daten aus der Antikörperdiagnostik von E.R.D.E. GmbH

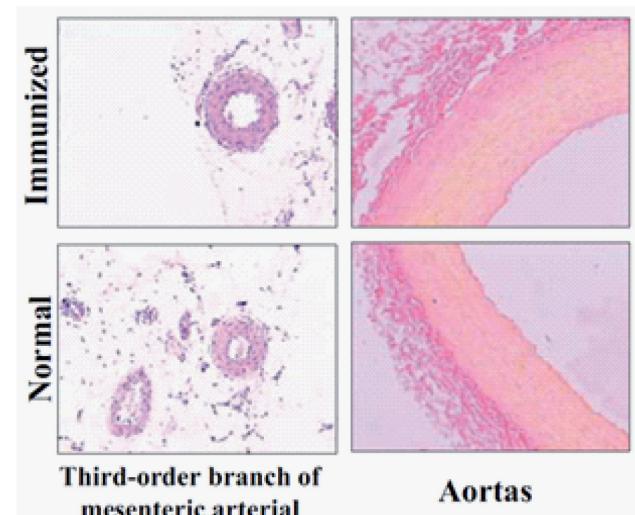


Abb. 1. Pathologische Veränderungen in Mesenterialarterie und Aorta von immunisierten Ratten, in denen Antikörper gegen den α_1 -Adrenozeptor induziert wurden. Die verdickten Gefäßwände sind Resultat einer verstärkten Zellhyperplasie. Abbildung aus (15).

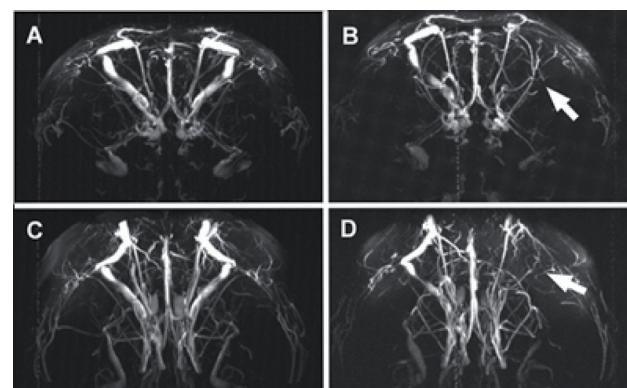


Abb. 2. TOF-MRA des Rattenhirns. Dreidimensionale Darstellung der koronaren Ansicht eines frontalen Hirnsegments. Angiographien des selben Tieres wurden zu Beginn der Behandlung mit einem α_1 -AR-spezifischen Antikörper (A, C) und 8 Monate später (B, D) aufgenommen. C, D zeigen die selben Hirnsegmente wie A, C um 45° vertikal gedreht. Die Pfeile markieren die massiven Läsionen nach 8 Monaten Antikörperbehandlung (B, D).

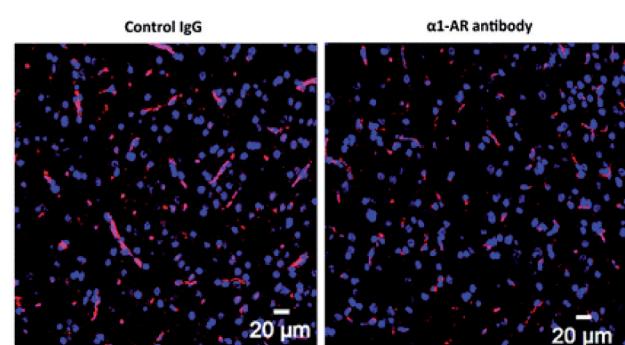


Abb. 3. Immunofluoreszenzfärbung der Blutgefäße in Schnitten des Rattenhirns mit Antikörpern gegen CD31. Die CD31-Signale (rote Färbung) waren stark reduziert im Cortex der Tiere, die mit dem α_1 -Adrenozeptor (α_1 -AR)-Antikörper behandelt wurden. Die Zellkerne sind mit DAPI (4',6-diamidino-2-phenylindol) blau angefärbt.

signifikanten und in den meisten Fällen langzeitlich stabilen Verbesserung der Herzleistung (20). Die Verbesserungen der Myokardfunktion und Myokardmorphologie waren bei einigen Patienten so umfassend, dass auf eine Herztransplantation verzichtet werden konnte. Interessanterweise kommt es in den meisten Fällen zu keiner Neubildung der Autoantikörper.

AUTOANTIKÖRPER ASSOZIIERTE KRANKHEITEN

Demenz

Alzheimer-Demenz und vaskuläre Demenz stellen die Hauptformen der Demenzerkrankungen dar. Durchblutungsstörungen aufgrund von Schädigungen des zerebralen Gefäßsystems sind die Ursache der

vaskulären Demenz und werden zunehmend auch für die Entstehung und Progression der sporadischen, genetisch nicht determinierten Alzheimer-Demenz als mögliche Ursache diskutiert (21).

2010 publizierten wir erstmals, dass in einer Kohorte von 54 Patienten mit Alzheimer- und vaskulärer Demenz bei 59% der Patienten agonistisch wirkende Autoantikörper gegen den α_1 -AR nachgewiesen wurden (4). Einige Patienten wiesen zusätzlich einen Autoantikörper gegen den β_2 -AR auf. Am häufigsten trat der α_1 -AR-Autoantikörper in Kombination mit dem Autoantikörper gegen den β_2 -AR auf. Untersuchungen der Eigenschaften des α_1 -AR-Autoantikörpers ergaben, dass dieser selektiv an die erste extrazelluläre Schleife des α_1 -AR bindet. Der Autoantikörper mobilisierte rezeptorspezifisch das intrazelluläre Calcium in einer klonalen Zelllinie. Wie oben bereits beschrieben, konnten wir im Tiermodell die gefäßschädigende Wirkung des α_1 -AR-Autoantikörpers nachweisen. Verbesserungen der diagnostischen Techniken unseres Labors versetzten uns in die Lage, eine größere Zahl von Patientenseren und ein breiteres Spektrum von agonistischen Autoantikörpern zu analysieren. Inzwischen beläuft sich die Kohorte auf 350 untersuchte Patienten mit Demenz vom Typ Alzheimer und vaskuläre Demenz. Zeitlich parallel zu den oben behandelten tierexperimentellen Untersuchungen wurden in einer kleinen Studie den Patienten die agonistischen Autoantikörper durch eine unspezifische Immunapherese entfernt. Die Entfernung der agonistischen Autoantikörper erfolgte in der Charité Berlin und der Universitätsklinik Jena mit den Adsorbern Immunosorber/Globaffin der Firma Fresenius Medical Care GmbH über einen Zeitraum von 4/5 Tagen. Um in diese Studie eingeschlossen zu werden, war ein kognitiver Status des Patienten von einem MMSE (Mini-Mental State Examination) zwischen 20 und 27 Voraussetzung. Bei uneingeschränkter kognitiver Funktion liegt der MMSE-Wert im Bereich von 28–30. Die Nachbeobachtungszeit betrug 12–18 Monate.

Am Beispiel eines 70-jährigen Patienten soll der Effekt der Immunadsorption veranschaulicht werden. Der Ausgangswert des MMSE betrug 21 Punkte. Dabei wurde das Plasmavolumen täglich 2 bis 2,5 fach prozessiert. Nach einem Beobachtungszeitraum von 12 Monaten betrug der MMSE-Wert des Patienten 23. Die Abb. 5 veranschaulicht die Fortschritte des Patienten in seiner kognitiven Leistung anhand einer beim MMSE-Test verwendeten Aufgabe, dem Zeichnen zweier ineinander verschrankter Fünfecke. Nach Angaben der Familie unterhält sich der Patient in geselliger Runde, liest wieder den Spiegel und beteiligte sich an der Hausarbeit, kocht und bügelt. Allerdings

kann er die Standuhr der Familie nicht immer richtig stellen. Der behandelnde Arzt berichtete, dass es dem Patienten nach der Immunadsorption subjektiv und objektiv deutlich besser geht. Die früheren psychotischen Symptome (paranoide Ängste) sind seit der Apherese nicht mehr aufgetreten. Die Medikamente (Memantine und Rivastigmin) sind reduziert worden auf Exelon 4,5 Pflaster und Memantine 10 mg täglich.

Die Nachbeobachtung über 18 Monate der behandelten Patienten dauert noch an. Die Ergebnisse werden voraussichtlich im Sommer 2015 publiziert. Ebenfalls für 2015 ist eine neue Studie mit Ärzten der Charité Berlin geplant.

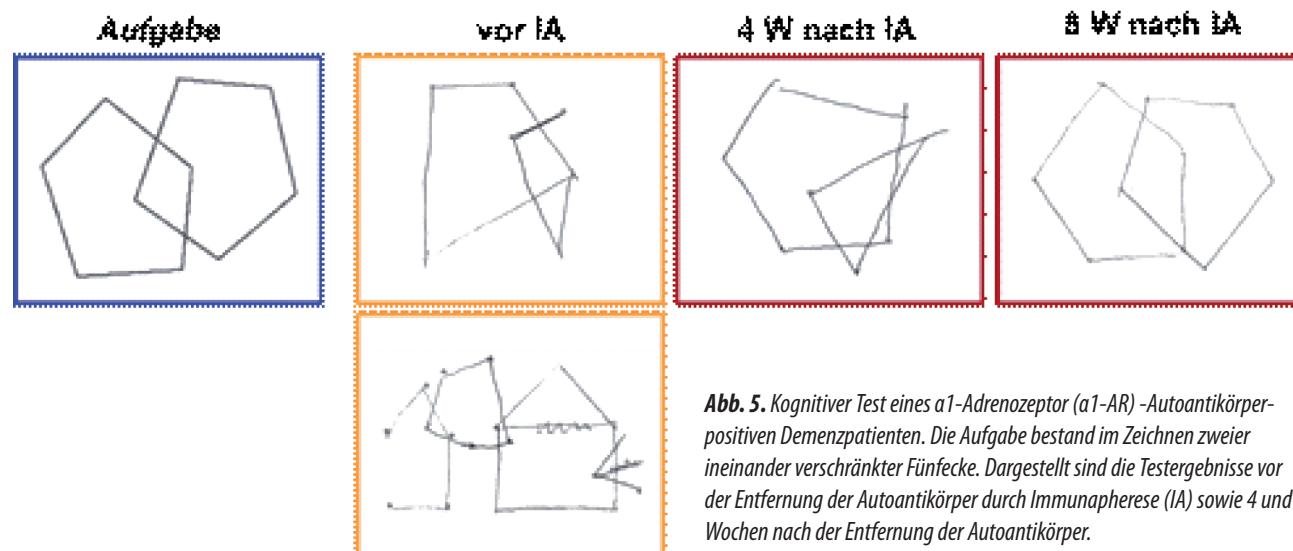
Typ-2-Diabetes

Die bei weitem häufigste Form der Volkskrankheit Diabetes ist der Typ-2-Diabetes. 90% der Menschen mit Diabetes leiden daran und nur etwa 5–10% sind dem Typ-1-Diabetes zuzuordnen (22). Bei den als diabetische Komplikationen bezeichneten Begleit- und Folgeerkrankungen sind vaskuläre Schäden besonders prominent. Diabetiker werden häufig auch als Gefäßkranken charakterisiert.

Unsere erste Untersuchung der Serumproben von Typ-2-Diabetikern aus deutschen Diabeteszentren zeigte, dass bei 53% der Diabetiker agonistisch wirkende Autoantikörper nachweisbar waren (23). Die nähere Klassifizierung der positiven Proben ergab, dass 36 % davon nicht nur einen sondern mehrere agonistisch wirkende Autoantikörper enthielten. 80% der positiven Proben wiesen agonistische Autoantikörper gegen den α_1 -AR und den AT₁-R auf. In unserer jüngsten Untersuchung legten wir genaueres Augenmerk auf die beim Patienten diagnostizierten Folgeerkrankungen (u.a. Retinopathie, Nephropathie, Neuropathie, makroangiopathische Veränderungen wie Bluthochdruck, Schlaganfall, Myokardinfarkt, koronare Herzerkrankung). Wir untersuchten 41 Patienten mit Typ-2-Diabetes und einer Diabetesdauer von mindestens 20 Jahren von denen 20 keine und 21 alle Folgeerkrankungen aufwiesen (24). Während in der Diabetikergruppe mit Folgeerkrankungen 100% der Patienten Bluthochdruck hatten, waren in der Gruppe ohne Folgeerkrankungen 80% der Patienten hyperton. Die Prävalenz agonistisch wirkender Autoantikörper lag in der Gruppe mit Folgeerkrankungen bei 90% und bei der Diabetikern ohne Folgeerkrankungen bei 70%. Insbesondere agonistische Autoantikörper gegen den α_1 -AR in Kombination mit agonistische Autoantikörper gegen den Endothelin A-Rezeptor (ETA-R) und / oder den AT₁-R waren nachweisbar.

Bei genauerer Betrachtung zeigte sich, dass bei Retinopathien, Nephropathien und Neuropathien keine signifikanten Unterschiede in der Häufigkeit von ago-

nistisch wirkenden Autoantikörpern zwischen beiden Untersuchungsgruppen auftraten. Ganz anders bei den makroangiopathischen Erkrankungen. Hier zeigten sich deutlichere Unterschiede. Patienten mit hypertensiver Herzkrankheit wiesen mit 92% deutlich häufiger Autoantikörper auf als Patienten ohne (59%). Patienten mit KHK hatten zu 83% mindestens einen positiven agonistischen Autoantikörper vs. 66% der Patienten ohne KHK. Patienten mit Myokardinfarkt zeigten zu 100% agonistische Autoantikörper auf im Vergleich zu 66% der Patienten ohne Myokardinfarkt. Auch hier waren Kombinationen der agonistischen Autoantikörper eher zu finden als der Nachweis eines einzelnen.



Unsere Ergebnisse zeigen, dass beim Krankheitsbild Typ-2-Diabetes und seinen Folgeerkrankungen agonistisch wirkende Autoantikörper insbesondere gegen den α_1 -AR in Kombination mit agonistischen Autoantikörpern gegen den ETA-R und / oder AT₁-R von Bedeutung sind. Die frühzeitige Diagnose des Spektrums agonistischer Autoantikörper bei Typ-2-Diabetikern ist nach unserer Erkenntnis eine entscheidende Voraussetzung für die Prävention der Diabetes-typischen Begleiterkrankungen. Durch medikamentöse Intervention oder durch die extrakorporale Entfernung (Immunapherese) kann die Wirkung der agonistischen Autoantikörper reduziert oder nachhaltig ausgeschaltet werden. So profitierten in einer klinischen Studie zur dilatativen Kardiomyopathie 68% aller Patienten von der Entfernung der Antikörper durch Immunapherese, jedoch 93% der Diabetiker mit dilatativer Kardiomyopathie (Abb. 6) (25). Die Analyse des Autoantikörperspektrums durch unser Labor ergab, dass 93% dieser Diabetiker positiv für den gefäßschädigenden α_1 -AR-Autoantikörper waren.

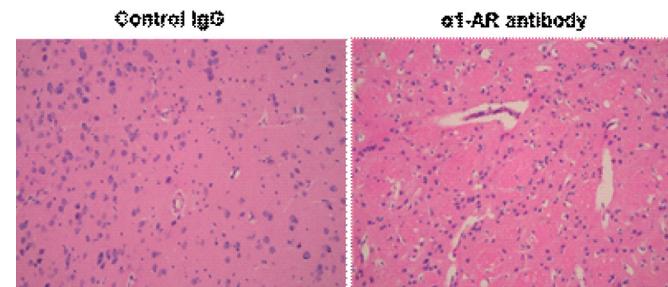


Abb. 4. Lichtmikroskopie von Hämatoxylin-Eosin gefärbten Schnitten des Rattenhirns. In Hirnschnitten der α_1 -Adrenozeptor (α_1 -AR)-Antikörper behandelten Tieren war eine deutlich verstärkte Dilatation der Virchow-Robinschen Räume feststellbar.

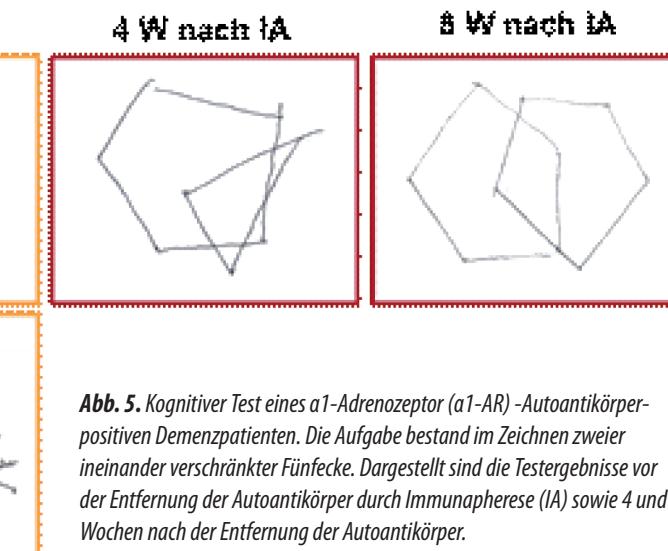


Abb. 5. Kognitiver Test eines α_1 -Adrenozeptor (α_1 -AR) -Autoantikörper-positiven Demenzpatienten. Die Aufgabe bestand im Zeichnen zweier ineinander verschrankter Fünfecke. Dargestellt sind die Testergebnisse vor der Entfernung der Autoantikörper durch Immunapherese (IA) sowie 4 und 8 Wochen nach der Entfernung der Autoantikörper.

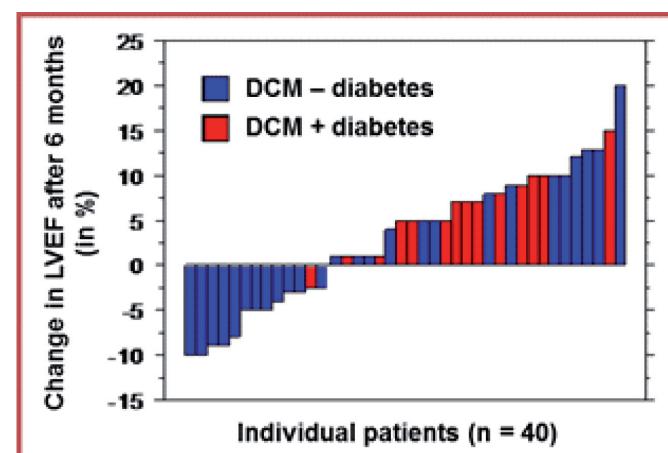


Abb. 6. Veränderung der Herzleistung (Linksventrikuläre Ejektionsfraktion LVEF) von Patienten mit dilatativer Kardiomyopathie (DCM) 6 Monate nach einer Immunapherese. Dargestellt sind Patienten mit Diabetes (rote Säulen) und Patienten ohne Diabetes (blaue Säulen). Von den 14 Patienten mit Diabetes profitierten 13 von der Immunapherese (93%), während von 26 Patienten ohne Diabetes 14 mit einer verbesserten LVEF reagierten (54%). Daten modifiziert aus (25).

Bürgersche Krankheit (Thromboangiitis Obliterans)

Bei dieser Erkrankung handelt es sich um eine Vaskulitis, die meist in den unteren Extremitäten auftritt. Die Entzündung betrifft kleine und mittelgroße Arterien und Venen. Als mögliche Ursachen werden unter anderem auch Autoimmunprozesse diskutiert. In einer ersten kleinen Patientenkohorte im Helios Klinikum Berlin Buch wurden die Seren der TAO Patienten auf die Anwesenheit von agonistisch wirkenden Autoantikörper untersucht (26). Bei 9 von 11 Patienten wurden agonistisch wirkende Autoantikörper nachgewiesen. Auffällig war dabei, dass bei 73% der Patienten ein agonistischer Autoantikörper gegen den α_1 -AR und 55 % der Patienten zusätzlich ein Autoantikörper gegen den ETA-R gefunden wurden. Dabei trat der Autoantikörper gegen den ETA-R nie allein, sondern immer als Cluster mit dem α_1 -AR spezifischen Autoantikörper auf. Bei 3 der 11 Patienten wurden Autoantikörper gegen den AT1-R und bei 2 von 11 Patienten Autoantikörper gegen den Proteinase-aktivierten Rezeptor (PAR) nachgewiesen. Die Entfernung der agonistisch wirkenden Autoantikörper erfolgte durch Immunadsorption mit dem Adsorber Globaffin der Firma Fresenius Medical Care GmbH. Bei 82% aller Patienten wurden nach einer 5-tägigen Behandlung keine agonistischen Autoantikörper mehr nachgewiesen.

FAZIT

Die hier behandelten Beispiele von Autoantikörper-assoziierten Erkrankungen sind gegenwärtige Schwerpunkte der Diagnostik unseres Labors. Ein gemeinsamer Nenner dieser Krankheiten ist die vaskuläre Komponente. So stehen die Volkskrankheiten Typ-2-Diabetes und Demenz in enger Beziehung zueinander. Es gilt als gesichert, dass Diabetiker ein erhöhtes Risiko aufwiesen, langfristig an Demenz zu erkranken (27, 28). In beiden Krankheiten, wie auch in der Gefäßerkrankung Bürgersche Krankheit, konnten wir vaskulär wirksame agonistische Autoantikörper vor allem gegen den α_1 -AR, sowie gegen den AT₁-R und den ETA-R nachweisen. Die prominente Stellung des α_1 -AR-Autoantikörpers in den von uns untersuchten Erkrankungen bestätigt uns in der Auffassung, dass dieser agonistische Autoantikörper ein Indikator für das Risiko der Entwicklung von Gefäßschäden ist.

Diese durch den α_1 -AR-Autoantikörper gegebene Verbindung zwischen verschiedenen Erkrankungen mit vaskulärer Komponente darf bei der Abschätzung von Folgerisiken der eigentlichen Grunderkrankung nicht unberücksichtigt bleiben. Bei den meisten Patienten fanden wir überwiegend Kombinationen dieser Autoantikörper, seltener ein singuläres Vorkommen eines einzelnen. Die Diagnostik des Spektrums

an agonistischen Autoantikörpern des Patienten ist deshalb essentiell für einen individuellen, optimierten Therapieansatz. Insbesondere für die Wahl, ob ein funktionelles Ausschalten des Autoantikörpers durch die Applikation von Rezeptorantagonisten oder dessen Entfernung durch Immunapherese in dem jeweils konkreten Fall indiziert ist. Eine möglichst frühzeitige differentielle Diagnostik des Autoantikörperspektrums ermöglicht eine schnellere und somit wirksamere individualisierte Therapie der Grunderkrankung und verbessert die Chancen der Prävention von Folgeerkrankungen für deren Entstehung vaskuläre Komplikationen eine signifikante Rolle spielen.

LITERATUR

- ROSENBAUM DM, RASMUSSEN SGF ET AL. The structure and function of G-protein-coupled receptors. *Nature* (2009) 459, 356–363
- DAVIES TF, ANDO T, LIN RY ET AL. Thyrotropin receptor-associated diseases: from adenomata to Graves disease. *J Clin Invest* (2005) 115, 1972–1983
- WENZEL K, HAASE H, WALLUKAT G ET AL. Potential functional relevance of α_1 -adrenergic receptor autoantibodies in refractory hypertension. *PLoS ONE* (2008) 3, e3742
- KARCZEWSKI P, HEMPEL P, KUNZE R ET AL. Agonistic autoantibodies to the α_1 -adrenergic receptor and the β_2 -adrenergic receptor in Alzheimer's and vascular dementia. *Scand J Immunol* (2012) 75, 524–530
- MIJARES A, LEBESGUE D, WALLUKAT G ET AL. From agonist to antagonist: Fab fragments of an agonist-like monoclonal anti- β_2 -adrenoceptor antibody behave as antagonists. *Mol Pharmacol* (2000) 58, 373–379
- THWAY TM, SHLYKOV SG, DAY M-C ET AL. Antibodies from preeclamptic patients stimulate increased intracellular Ca^{2+} mobilization through angiotensin receptor activation. *Circulation* (2004) 110, 1612–1619
- ZHU F, SUN Y, LIAO Y ET AL. Agonistic AT1 receptor autoantibody increases in serum of patients with refractory hypertension and improves Ca^{2+} mobilisation in cultured rat vascular smooth muscle cells. *Cellular & Molecular Immunology* (2008) 5, 209–217
- BKAILEY G, EL-BIZRI N, BUI M ET AL. Modulation of intracellular Ca^{2+} via L-type calcium channels in heart cells by the autoantibody directed against the second extracellular loop of the α_1 -adrenoceptors. *Can J Physiol Pharmacol* (2003) 81, 234–246
- HEIN P, MICHEL MC. Signal transduction and Regulation: Are all α_1 -adrenergic receptor subtypes created equal? *Biochem Pharmacol*. (2007) 73, 1097–1106
- KARCZEWSKI P, HAASE H, HEMPEL P ET AL. Agonistic antibody to the α_1 -adrenergic receptor mobilizes intracellular calcium and induces phosphorylation of a cardiac 15-kDa protein. *Mol Cell Biochem* (2010) 333, 233–242

11. JAHNS R, BOIVIN V, HEIN L ET AL. Direct evidence for a β_1 -adrenergic receptor-directed autoimmune attack as a cause of idiopathic dilated cardiomyopathy. *J Clin Invest* (2004) 113, 1419–1429
12. ZHOU CC, ZHANG Y, IRANI R ET AL. Angiotensin receptor agonistic autoantibodies induce pre-eclampsia in pregnant mice. *Nat Med* (2008) 14, 855–862
13. DRAGUN D, MÜLLER DM, BRÄSEN JH ET AL. Angiotensin II type 1-receptor activating antibodies in renal-allograft rejection. *N Engl J Med* (2005) 352, 558–569
14. ZHOU Z, LIAO Y, LI ET AL. Vascular damages in rats immunized by α_1 -adrenoceptor peptides. *Cell Mol Immunol* (2008) 5, 349–356
15. KARCZEWSKI P, POHLMANN A, WAGENHAUS B ET AL. Antibodies to the α_1 -adrenergic receptor cause vascular impairments in rat brain as demonstrated by magnetic resonanceangiography. *PLoS ONE* (2012) 7, e41602
16. POHLMANN A, KARCZEWSKI P, KU M-C ET AL. Cerebral blood volume estimation by ferumoxytol-enhanced steady-state MRI at 9.4 T reveals microvascular impact of α_1 -adrenergic receptor antibodies. *NMR Biomed* (2014) 27, 1085–1093
17. MÜNCH G, BOIVIN-JAHNS V, HOLTHOFF HP ET AL. Administration of the cyclic peptide COR-1 in humans (phase I study): ex vivo measurements of anti- β_1 -adrenergic receptor antibody neutralization and of immune parameters. *Eur J Heart Fail* (2012) 14, 1230–1239
18. HABERLAND A, WALLUKAT G, BERG S ET AL. Neutralization of pathogenic betal-receptor autoantibodies by aptamers in vivo: the first successful proof of principle in spontaneously hypertensive rats. *Mol Cell Biochem* (2014) 393, 1–2
19. WALLUKAT G, REINKE P, DÖRFELL WV ET AL. Removal of autoantibodies in dilated cardiomyopathy by immunoabsorption. *Int J Cardiol* (1996) 54, 191–195
20. MÜLLER J, WALLUKAT G, DANDEL M ET AL. Immunoglobulin adsorption in patients with idiopathic dilated cardiomyopathy. *Circulation* (2000) 101, 385–391
21. DE LA TORRE. Alzheimer disease as a vascular disorder: nosological evidence. *Stroke* (2002) 33, 1152–1162
22. HEIDEMANN C, DU Y, SCHUBERT I, RATHMANN W ET AL. Prävalenz und zeitliche Entwicklung des bekannten Diabetes mellitus – Ergebnisse der Studie zur Gesundheit Erwachsener in Deutschland (DEGS1), *Bundesgesundheitsblatt* (2013) 56, 668–677
23. HEMPEL P, KARCZEWSKI P, KOHNERT K-D ET AL. Sera from patients with type 2 diabetes contain agonistic autoantibodies against G protein-coupled receptors. *Scand J Immunol* (2009) 70, 159–160
24. MÜLLER N, BIMMLER M, HEMPEL P ET AL. Prävalenz agonistischer Autoantikörper gegen G-Protein gekoppelte Rezeptoren bei Patienten mit Typ 2 Diabetes mit und ohne Folgeerkrankungen. *Diabetologie und Stoffwechsel* (2013) 8, P 217
25. DOESCH AO, MUELLER S, KONSTANDIN M ET AL. Effects of protein A immunoabsorption in patients with chronic dilated cardiomyopathy. *J Clin Apher* (2010) 25, 315–322
26. KLEIN-WEIGEL PF, BIMMLER M, HEMPEL P ET AL. G-protein coupled receptor auto-antibodies in thromboangiitis. A obliterans (Buerger's disease) and their removal by immunoabsorption. *Vasa* (2014) 43, 347–352
27. UMEGAKI H. Type 2 diabetes as a risk for cognitive impairment: current insights. *Clin Interv Aging* (2014) 9, 1011–1019
28. WINKLER A, DLUGAJ M, WEIMAR C ET AL. Association of diabetes mellitus and mild cognitive impairment in middle-aged men and women. *J Alzheimer's Disease* (2014) 42, 1269–1277

DETERMINING TREATMENT TACTICS OF INFANTS OF 0-2 MONTHS WITH CONGENITAL HIP DISLOCATION

**V.M. Krestyashin, K.N. Darinskiy, L.U. Darinskaya,
I.V. Krestyashin, A.O. Domarev, O.U. Liteneckaya**

*N.I. Pirogov Russian National Research Medical University,
Moscow, Russia*

ABSTRACT — 248 children of age from 10 days to 12 months were treated in 2002–2012 at Outpatient surgical center of N.F. Filatov's City Children's Clinic in Moscow. The therapy included regular methods (such as expanding splint, cast bandage), and therapy progress was verified by X-ray scanning. Roentgenograms were rated with standard plans (H. Hilgenreiner plan) and additional index (K and L). Evaluating the results of the therapy a method has been developed to determine treatment tactics for infants with congenital hip dislocation revealed before 2 months of age.

Congenital hip dislocation — one of the most prevalent impairments of our locomotor apparatus. This malformation appears in hypoplasia of all coxal joint elements and in dislocation between hip and acetabulum.

Due to the facts the impairment can be found in 2–6 cases among every 1000 newborns, the defect is difficult to be found timely and the therapy can be provided lately or be incorrect – it is important to diagnose and to start treatment as early as possible.

When hip dislocation is figured out the therapy starts immediately, and firstly means in applying a special legs expanding splint.

When the defect is found out parents often want to learn about the way and time limits of the therapy. And it is hard to answer these questions momently because the depth of the pathological process differs and that causes the wideness of terms of the therapy.

Hip dislocation treatment includes the mono-therapy and a complex of several methods as well. First means legs expanding splint. Complex of methods additionally includes cast bandages, limb traction system and also invasive or noninvasive dislocated hip reduction. Terms of the treatment in this cases can exceed 15 months.

Timely found hip dislocation allows to use commonly the mono-therapy method that can observably decrease the treating time.



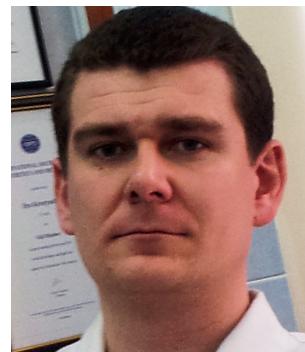
Vladimir Krestyashin,
MD, Professor



**Kirill Darinskiy, trauma
and orthopedic surgeon**



**Lubov Darinskaya, trauma
and pediatric orthopedic
surgeon**



**Ilya Krestyashin, MD,
assistant professor, full member
of ISPO, RAPS, Ponseti
International**



**Andrey Domarev, MD, full
member of ISPO, RAPS, Ponseti
International**



**Olga Liteneckaya, MD,
assistant professor, trauma and
orthopedics pediatric surgeon**

For this reason the list of methods concerning coxal joint impairments diagnostic enlarged, and earlier developed methods were upgraded and improved.

One of the most proved diagnostic method that is practiced in Russia and other countries is ultrasonic scanning. But the most available scan method in Russia is still X-ray – it allows to examine bone and cartilage condition in various phases of the treatment. So the X-ray scanning is yet the most reliable and trustworthy method to examine coxal joint defects, and ultrasonic scanning is used additionally but doesn't substitute the X-ray.

Due to newborns anatomic specialties during first months of their life it is rather hard to explore pelvis shape, its dimensions and edges, dimensions and location of femur proximal part and its relative position to the pelvis, and anatomic points ratio of the pubic. So we discovered new differential and diagnostic features to assess volume of movements in child's coxal joint which in addition with x-ray picture improve our selection of cure tactics and specify the treatment duration.

The way we suggest improves us picking our tactic to treat congenital hip dislocation among 0–2 months newborns by adding new roentgenogram marks to the previously discovered to provide more clear diagnostic rating.

Standard medical survey to find out hip dislocation includes x-ray scan of newborn's coxal joints in his age of 3 months. In uncertain cases the scan can be provided anytime and doesn't depend on child's age. Appreciation of the roentgenogram can be complicated because the femur proximal part is generally built of cartilage, moreover its hard to set child's proper position for the x-ray scanning.

Features used in H. Hilgenreiner plan do not allow doctor to forecast surely he will pick mono-therapy or a therapy complex. But significantly important to tell child's parents the most precise plan and period of the therapy we apply. So our roentgenological marks we're talking about are able to help us choosing the treating way more clearly and already in the beginning of our therapy help us to collect the group of newborns we are able to treat by expanding splint only.

Here I try to reveal our method (patent for invention №2495624 "Way for determining tactics of treating babies with congenital hip dislocation diagnosed in age up to 2 months" dated 20 oct. 2013).

A newborn is examined in age up to 2 months. On the roentgenogram of his coxal joints we mark a horizontal line that runs through both Y-shaped cartilage and we detect next:

- **a** — acetabular angle (see Fig. 1)
- **b** — perpendicular line (goes from the top of femur diaphysis up to the horizontal line) (see Fig. 1)

- **d** — distance between Y-shaped cartilage and perpendicular h (see Fig. 1)
- **K** — index counted out of the ratio between acetabulum width and width of the femur proximal part (see Fig. 2)
- **L** — interval from acetabulum osseous edge till the line that connects the iliac spine to the Y-shaped cartilage (see Fig. 2).

First X-ray scanning is made momently after first signs for congenital hip dislocation are noticed. If $K=0.7-0.8$, $L=0-1\text{ mm}$, $\alpha=37-42^\circ$, $h=7-8\text{ mm}$ and $d=16-19\text{ mm}$ — therapy with the expanding splint only is assigned.

Second x-ray scanning is performed 1.5 months later. If we see K index approaches 1.2, L is up to 3–4mm, acetabular angle (α) is now 34–36°, $h=9-10\text{ mm}$ and $d=13-14\text{ mm}$ — expanding splint is considered effective and the therapy proceeds.

If the K index on the first X-ray scan is below 0.7, α widens over 42°, $h=3-5\text{ mm}$ and $d=25-27\text{ mm}$ — cast bandage is needed additionally with expanding splint. Making the second x-ray survey if K increases up to 1.2, $L=3-4\text{ mm}$, α angle lowers to 34–36°, $h=9-10\text{ mm}$ and $d=13-14\text{ mm}$ — cast bandage can be removed. If all index during second scan stay constant or change slightly ($\alpha=38-40^\circ$, $h=4-6\text{ mm}$, $d=22-24\text{ mm}$) — double-therapy with expanding splint plus cast bandage is continued.

Determining the described tactic is based on results of treating 248 children with congenital hip dislocation from 10 day up to 1 year aged at outpatient surgical center located in N.F. Filatov's City Children's Clinic of Moscow in the years 2002–2012. Among 248 children there were 198 girls and 50 boys — so the ratio of girls to boys is 5 to 1. Concerning one-sided impairment 103 of 172 children had trouble in their left coxal joint and 69 in right joint. 76 children had their both coxal joints affected.

X-ray scanning was applied in 147 (of all 248 — 59.3%) cases during first 2 months of baby's life. On the roentgenogram according to H. Hilgenreiner plan there were acetabular angle, length of "h" and "d" to be measured. Then we count extra index "K" and length of "L" (see Fig. 2).

Treating the hip dislocation with expanding splint only (mono-therapy) among children in age of first 2 months of living was effective in 48 cases (32.6%). Initial x-ray scanning was performed when first signs child has his hip dislocated are observed — and we had the results: $K=0.7-0.8$, $L=0-1\text{ mm}$, $\alpha=37-42^\circ$, $h=7-8\text{ mm}$, $d=16-19\text{ mm}$. At next scanning in 1.5 months we saw K index increased to 1.2, L — to 3–4mm, α angle was 34–36°, $h=9-10\text{ mm}$ and

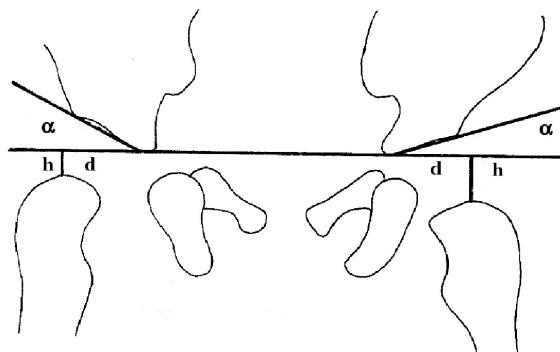


Fig. 1. H. Hilgenreiner plan

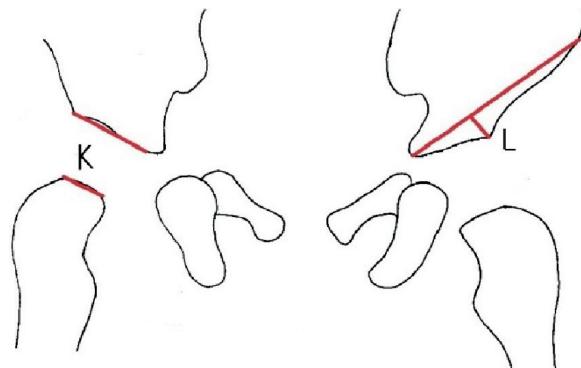


Fig. 2. K and L index

$d=13-14$ mm. That made us conclude the expanding splint therapy is positive. Hip dislocation reduced in time of 4–6 weeks since the treatment started. The total time lapse of splint fixation depends on the grade coxal joint is hurt, on child's age and on acetabulum regeneration activity, particularly in its external osseous ledge. It was 4.5 months on average. And treating the children of first 2 months living is positively predicted.

99 (67.4% of all) children when scanned first time on their roentgenogram had index: $K < 0.7$, $L=0-1$ mm, $\alpha > 42^\circ$, $h=3-5$ mm, $d=25-27$ mm — double-therapy with expanding splint and cast bandage was used. During next x-ray checkup we observed $K=1.2$, $L=3-4$ mm, $\alpha=34-36^\circ$, $h=9-10$ mm, and 53 children (35.7%) had index d decreased to 13–14 mm — further therapy was kept on with splint only saved. 26 (17.9%) children showed their rates permanent. And last 20 (13.8%) children had their rates changed weakly ($\alpha=38-40^\circ$, $h=4-6$ mm, $d=22-24$ mm) — we continued the therapy using both expanding splint and cast bandage (spica cast was applied twice). Hip dislocation became reduced in 4–6 weeks. The time child stays fixed by splint and cast bandage is considered 8–10 months as average.

This is how we believe our method to serve us choosing proper treating tactics and terms for children with congenital hip dislocation during first 2 months of their life.

REFERENCES

1. V.M. KRESTYASHIN. «A practical guide to outpatient pediatric orthopedics». Moscow 2013 – p. 232
2. V.M. KRESTYASHIN, A.I. GUREVICH, O.U. VASILEVA, A.O. DOMAREV, O.U. LITENETSKAYA, U.I. LOZOVARA. «New diagnostic capabilities for children's congenital hip dislocation» – partials of the III Russian outpatient surgery congress, journal «Ambulatory technologies. Outpatient surgery» 2009 vol. 35–36 №3–4 p. 95.

3. V.M. KRESTYASHIN, O.U. LITENETSKAYA, U.I. LOZOVARA. «A new look at diagnostic and treatment of children's congenital hip dislocation», journal «Problems in biology and medicine» 2010 vol. 59 №4 p. 79–80.
4. A.B. GUREVICH, K.V. VATOLIN, E.V. SHMITKOVA, T.I. TIKHONENKO, U.I. LOZOVARA. «Modern techniques of coxal joint scanning among healthful children». Journal «Medical displaying». №2, 2011 p. 79–85.
5. A.B. GUREVICH. «Radiodiagnosis of children's coxal joint malformations», dissertation abstract. Moscow 2001.
6. U.M. RUSTAMOVA. Dissertation «Congenital hip dislocation and subluxation among children of first 3 years of life – radiology scanning importance in diagnostics, treatment selection and predicting the therapy outcome». Tashkent 1991. p. 140.
7. O.U. LITENETSKAYA «Early diagnosing and treating congenital hip dislocation among children of first 6 months age», dissertation abstract. Moscow 2004. 23 pages.

ROLE OF THE IMMUNE DRUGS IN THE TREATMENT OF ACUTE LYMPHOBLASTIC LEUKEMIA IN CHILDREN

Z.N. Nabiev, M.D. Murodov, M.M. Egamberdiev

Republican Research-Clinical Center of Pediatrics and Pediatric Surgery

ABSTRACT — Authors on the basis of study of clinical laboratory data, hemodynamic indices, data on infectious complications in patients with acute lymphoblastic leukemia after Viferon use in complex therapy have achieved positive results. Chemotherapy and long-term antibiotic treatment bring to intestinal dysbiosis and application of Viferon provides the normalization of intestinal flora, reducing Candida genus fungi. Out of the 41 children patients, whose therapy course included Viferon, by the end of the 1st week positive dynamics observed, bowel passage restored, leveled down bloating, decreased endogenous intoxication syndrome.

KEYWORDS — Viferon, complex therapy, comprehensive treatment, intestinal microflora, prebiotics, lymphoblastic leukemia, children.

RELEVANCE

To date, the primary means of prevention and treatment of infectious complications of disease is antibiotic therapy. However, in some cases, it does not achieve the desired effect, prompting the search for new drugs and change tactics such patients.

At present, there are insufficient data on the state of intestinal microbiota in children with leukemia in different periods of the disease, and the effect of cytostatics on cross-species interaction on a modern cytostatic therapy [1, 3]. There is lack of information on clinical efficacy of immune drugs (Viferon) in the complex treatment of patients during the clinical and hematological deployed pattern for correction of intestinal microflora and preventive treatment of infectious complications in children with acute lymphoblastic leukemia (ALL).

Among the other interferon drugs special attention deserves Viferon containing, along with interferon alpha 2b recombinant human vitamins E and C [1].

Impact of Viferon components can significantly reduce the course doses and duration of antibiotic and hormone therapy [1, 2].

There are numerous studies that indicate the feasibility of using Viferon in children with infectious



Zohir Nabiev



Murodov Mahmadqul



Maksud Egamberdiev

process, who frequently get sick after surgery in obstetrical practice. However, administration of this drug in patients with acute lymphoblastic leukemia after chemotherapy to prevent suppurative complications and improve intestinal dysbiosis in adjuvant therapy in the available literature is not reflected. Therefore, to improve the results of treatment in these patients we have studied the application of Viferon [2,4].

OBJECTIVE

The purpose of this study was to explore the clinical and bacteriological aspects of disorders of the intestinal flora and to determine the effectiveness of using Viferon in complex therapy in children with acute lymphoblastic leukemia.

SUBJECTS AND METHODS.

Work carried out on the basis of a comprehensive treatment of 76 children with acute lymphoblastic leukemia. During the period 2009–2012, the children were under hospital treatment of pediatric hematol-

ogy National Medical Center of the Republic of Tajikistan.

Microbiological examination was carried out in children with acute lymphoblastic leukemia of both sexes between the ages of 3 to 17 years. All the children came to the hospital during the expanded clinical and hematological picture (Table 1).

Among the examined there were 43 (56.5%) boys, 33 girls (43.5%). Of all patients 54% were urban dwellers (Table 2).

In 35 (46%) of 76 patients with observed adverse somatic background of: underweight from 10 to 25% — 11 (31.4%), chronic infection hearth (dental caries, tonsillitis, pyelonephritis) 17 (48.5%), retarded physical development in 7 (20.0%) children.

Diagnosis was based on complaints, clinical examination, laboratory and instrumental examination that included blood tests, urine and feces, myelogram, spinal fluid test, immunophenotyping, and chest X-ray, endoscopy with biopsy tissue and seeding microflora, ECG, ultrasound (liver, gall bladder, spleen, kidneys, adrenals, thyroid, testes, heart). According to the testimony consulted specialists - ophthalmologist, neurologist, endocrinologist, gastroenterologist, nephrologist, genetics, ear-nose-throat doctor, dentist.

To study the state of intestinal microbiocenosis and infectious complications 76 children with acute lymphoblastic leukemia were examined. A control group comprised 15 healthy children, who underwent the work-up of intestinal microbiota using the methods described above.

To determine the effect of cytostatics on bakteriocinogenic activity of *E. coli* used a modified method of determining bakteriocinogenic activity [3].

Assessment of the state of intestinal microbiocenosis by degrees carried out in accordance with the classification of I.B. Kuvaeva and K.S. Ladodo [2, 3].

In order to prevent infectious complications children with acute lymphoblastic leukemia were divided into 2 groups randomly assigned to the major groups: 41 children received a combined therapy of probiotic lactoflor and Viferon suppositories 1 time per day, 35 children received standard therapy without immune correction.

Viferon administered to children simultaneously with the start of treatment with cytostatics protocol ALL BFM 90.1. Group received comprehensive treatment (+ Viferon lactoflora) for 4 weeks, then the two groups of children have been re-examined using bacteriological methods. [4] The effectiveness of the drug used was assessed by the dynamics of intestinal microbiota disturbances, level of bactericidal activity and persistent properties of *E. coli*, the clinical course of infection seen in a catamnesis for 12 months.

RESULTS AND DISCUSSION

We analyzed the medical history, clinical and functional parameters obtained from long-term (2-3 years) observation of 41 children with acute lymphoblastic leukemia.

Revealed that $69,3 \pm 7,9\%$ of children with ALL manifestation of the disease was observed in age from 1 to 7 years. Established family history of cancer pathology in the family at $24 \pm 2,7\%$ of children. Analysis of anamnestic data revealed that intestinal dysbiosis in the first year of life (before disease in acute leukemia) was observed in 26 children ($66,7 \pm 7,6\%$). Of these, a violation intestinal microbiota degree I-II was detected in 23 people ($88,5 \pm 10,1\%$), III-IV degree — in 3 ($11,5 \pm 1,2\%$). Intestinal dysbiosis is more common in children whose mothers during pregnancy suffered anemia, toxemia I and II half, obstructed labor ($p < 0,05$). These children are more likely than children who did not have the manifestations of intestinal dysbiosis in the first year of life, there were frequent colds ($15,3 \pm 1,7\%$, $p < 0,05$), violations of the chair ($80,7 \pm 9,2\%$, $p < 0,01$), abdominal pain ($26,9 \pm 2,9\%$, $p < 0,05$).

At the same time there is a significant increase in the level of B-lymphocytes (SD19) — the absolute amount of $0,7 \text{ t/l}$, relative - $24,8 \pm 2,7\%$ ($p < 0,05$). In the leucocyte count showed a sharp decline in the number of neutrophils: segmented neutrophils accounted for $10,4 \pm 1,1\%$ ($p < 0,01$), eosinophils — $0,6 \pm 0,1\%$ ($p < 0,01$). All children showed a significant reduction in monocyte — average - $0,4 \pm 0,1\%$ ($p < 0,001$), indicating a pronounced inhibition of cells that perform phagocytic function. Phagocytic index (FI) was reduced and reached $40,8 \pm 4,6\%$ ($p < 0,05$).

In children with acute lymphoblastic leukemia in first acute period revealed significant changes in indicators immunograms as a reduction in the total number of white blood cells, neutrophils and monocytes, as well as reducing AF. These changes indicate a high risk of infectious complications in children with acute lymphoblastic leukemia during the expanded clinical-hematological picture.

It should be noted that in the context of chemotherapy and prolonged antibiotic therapy is disrupted intestinal dysbiosis and application Viferon provides the normalization of intestinal flora, reducing the fungi of the genus *Candida*. Of the 41 patients of the main group of children whose therapy included Viferon, by the end of the 1st week, there was a positive dynamics, restore intestinal passage, leveled bloating, decreased endogenous intoxication syndrome.

Thus, in children inclusion of Viferon in the complex treatment of acute lymphoblastic leukemia in comparison with traditional treatment was accompanied by a reduction in the length of exacerbations of

Table 1. The distribution of patients by age and sex (in absolute terms and as a percentage)

Sex	Age				Total (%)
	3-7	7-10	10-14	14-17	
Boys	12	14	10	7	43 (56.5)
Girls	6	8	8	11	33 (43.5)
Total	18	22	18	18	76 (100)

Table 2. The distribution of patients by age and comorbidity

№	Nosology	Age			
		3-7	7-10	10-14	14-17
1	Pneumonia	3	1	-	-
2	Bronchitis	3		2	1
3	Tonsillitis	1	4	3	1
4	Pyelonephritis	3	1	1	3
5	Dental caries	6	1	1	1

1.5 times, longer remission in 2.0 times, reducing the number of relapses per year by 1.5 times.

REFERENCES:

1. AVZALETDINOV B.K. Features of intestine biocenosis in acute leukemia in children. The Abstract of Ph.D. 2004; 21c.
2. ARDATSKAYA M.D. Modern diagnostics violation of microflora in diseases of the gastrointestinal tract and ways of correction / M.D. Ardatskaya // GastroNews- layn. - 2006, -№1.-S.5-7.
3. BUTOROVA L.I. The value of lactulose in the regulation of intestinal microflora / L.I. Butorova A.V. Kalinin // Clinical prospects of gastroenterology, hepatology- 2002.-№6.- S. 21-26.
4. NABIEV Z.N. Intestinal microflora disorders in children with acute lymphoblastic leukemia. Pediatrics and Pediatric Surgery, Tajikistan, Dushanbe - 2013. - №2. -C. 7-15.

THE STATE OF LIPID PEROXIDATION AND ANTIOXIDANT DEFENCE SYSTEM IN PATIENTS WITH CHRONIC CALCULOUS CHOLECYSTITIS

Y.Y. Peresta, S.M. Dzhupyna, O.V. Dulo, V.V. Vayda

Uzhgorod National University, Uzhgorod, Ukraine

Gallstone disease or cholelithiasis is one of the most common diseases in gastroenterology. According to different authors, the gallstone disease incidence among the population of the developed countries is within 8–15%. Gallstone disease is more often occurs among inhabitants of Europe, North and South America, less often – among inhabitants of Asia and Central Africa. In Ukraine almost 300 thousand people are registered annually with the disease, about 12–15 thousand cholecystectomies are made.

Predictors for course of the gallstone disease are age over 40 years, female gender, multiple pregnancies, genetic predisposition, lipid and carbohydrate metabolism disturbance, hyperadiposis, inflammatory processes in the gallbladder.

MATERIALS AND METHODS

In our case 60 patients with gallstone disease took part, aged 24 to 68 years, among them 11 (22%) men and 49 (78%) women. Duration of disease was from 2 months to 20 years. The diagnosis was determined as per complex clinical laboratory and instrumental methods of examination, according to the Clinical protocol of provision of care delivery for patients who have gallstone disease, approved by the Ministry of Health of Ukraine No. 271 of 13.06.2005.

For the reference basis of biochemical and immunological findings the data of the Laboratory of Immunology and Biochemistry of the Scientific and Practical Association "Rehabilitation" of Ministry of Health of Ukraine were taken.

The measures of lipid peroxidation and antioxidant defence were diagnosed in patients: isolated double bonds content in blood, diethenoid conjugate, malondialdehyde, catalase, superoxide dismutase. Mathematical treatment of the results was carried out using standard software packages Microsoft Windows XP, Microsoft Office.



Y.Y. Peresta



S.M. Dzhupyna



O.V. Dulo



V.V. Vayda

RESULTS AND DISCUSSION

During the clinical course of gallstone disease the following features were evidenced: general weakness, loss of appetite, esthesia of bitterness in the mouth, sicchasia, periodic occurrence of pain syndrome in the right hypochondrium, often associated with diet breaking. During objective examination the subicteritiousness of sclera, tongue plaque, moderate disease in the right hypochondrium were noticed.

As per results of ultrasound examination of the abdominal cavity organs of patients, thickening of the walls of the gallbladder, in some cases its deformation, the presence of concretions in the gallbladder was noticed. The increase echolucency of the liver, pancreas and increase of their size was inspected.

During endoscopic examination in most patients coexisted esophagus and gastroduodenal abnormality

was observed: reflux esophagitis, erythematous and erosive gastropathy, duodenogastric reflux, stomach ulcer.

Double bonds content was $5,67 \pm 0,10$ U.rd.g/ml ($p < 0,05$), which was for 2,18 times above the norm ($2,61 \pm 0,14$ U.rd.g/ml). The concentration of diethenoid conjugate was equal to $2,62 \pm 0,18$ U.rd.g/ml ($p < 0,05$), which exceeded the norm ($1,27 \pm 0,08$ U.rd.g/ml) in 2,06 times. The ketodyens rate was $1,37 \pm 0,07$ U.rd.hg/ml ($p < 0,05$), exceeding the rate of $0,62 \pm 0,05$ U.rd.g/ml in 2,21 times. The increased concentrations of malondialdehyde was noticed - $7,54 \pm 0,25$ nmol / l ($p < 0,05$) — in 2,16 times higher compared to the norm ($3,49 \pm 0,21$ nmol / l). Reduction of antioxidant protection was observed: catalase activity was below of the normal rate ($72,2 \pm 0,8\%$) in 2,1 times and was $31,26 \pm 0,1\%$, the concentration of superoxide dismutase was equal to $1,88 \pm 0,4$ U/mg Hb, which is in 1,9 times lower than the normal rate ($4,14 \pm 0,36$ U/mg Hb).

SUMMARY

The clinical presentation of the patients with gallstone disease was characterized by asthenovegetative, diarrheal and pain syndrome, often accompanied by abnormal changes of the liver, pancreas, esophagus and gastroduodenal abnormality.

The measures of lipid peroxidation proved the enhancement of lipid peroxidation, which was characterized by the growth of double bonds, diethenoid

conjugate, ketodyens, and malondialdehyde. At the same time catalase and superoxide dismutase activity reduction was noticed, which may be evidence of antioxidant defense system wasting in patients with chronic calculous cholecystitis.

The results of studies show the need for a complex approach to treatment and preoperative assessment of patients with gallstone disease using antioxidant medication, but it is subject to further treatment and research.

REFERENCES

1. ELWOOD D.R. Cholecystitis / D.R. Elwood // Surg. Clin. North. – 2008. – V. 88, No 6. – P. 1241–1252.
2. GEROK W. Hepatologie (2 Auflage) / W. Gerok. – Munchen: Urban – Schwarzenberg, 1995. – 165 p.
3. MIZAUS B. Diagnosis and treatment of cholecystitis / B. Mizaus, P.E. Kulchi // Ves. Im. I. I. Grek. – 2004. – No 123 (8). – P. 48–51.
4. NESLAND J.M. Chronic cholecystitis / J.M. Nesland // Ultrastruct. Pathol. – 2004. – V. 28. – P. 121 – 123.
5. PAPI C. T., CATARCI M., AMBROSIO L. D. ET AL. Timing of cholecystectomy fo acute calculous cholecystitis: A meta-analysis // Am. J. Gastroenterol. 2004. Vol. 99. P. 145–147.
6. UCHIAMA K. Long-term prognosis after treatment of patient with choledocholithiasis / K. Uchiama, H. Onishi, M. Tani // Ann. Surg. – 2008. – Vol. 238 (1). – P. 97–102.

THE WOUND INFECTION IN CHILDREN WITH THE SEVERE THERMAL TRAUMA

S.P. Sakharov¹, A.A. Zhidovinov²

¹ Tyumen State Academy Medicine,
Tyumen, Russia,

² Astrakhan State Medical University,
Astrakhan, Russia



Sergey P. Sakharov, PhD
(Medicine), Department of
Pediatric Surgery



Alexei A. Zhidovinov, Professor,
Head of the Department of
Pediatric Surgery

ABSTRACT — The analysis of 262 microbiological studies from the surfaces of burn wounds in children aged 6–17 has been carried out in the centre of burns in the Tyumen regional hospital N1 for 2007–2012. The associated microflora was determined in 56% of cases on the burning surface in children. *S. aureus* and *S. epidermidis* were marked in 39.3% of cases, and *P. aeruginosa* was in 10.3% of cases, *E. coli* was in 2.7% of cases. All microorganisms mentioned above have an ability to form biofilms that is why it is necessary to determine the presence of biofilms on the surface of burns for the long course of the infectious process. It is also determined that the generalized infectious process with the septic outcome was being developed in the concentration of 10^{10} of microbe cells in 1 gr. of the burn tissue.

KEYWORDS — burn, wound, microbe picture

INTRODUCTION

The thermal burns in children are very serious medical, social and economic problems in the health-care (7). The main reason of the lethal outcome in the extensive deep burns is the development of the associated infection on the burn wound surface resulting in the death in 75% of patients (1).

The moist coagulated biological tissue with constantly increasing reserve of diffused plasma nutri-tion substances is formed on the surface of burn wounds but the temperature of a person gives optimal conditions for the intensive microorganism reproduction. The probability of the microorganism invasion into the near-by tissues and the blood circulatory

system increases due to the bacteria reproduction. As soon the microorganisms reach the blood flow the infectious foci can appear in any body places and tissues which are not connected with the primary infectious focus but the constant bacteria reproduction on the burn wound surface create conditions for sepsis development resulting in the organism immunological reactivity decrease (9, 12).

Electromicroscopy of burn wounds showed that 60% of biopsies taken from the patient's wound surface had biofilm-forming bacteria (14). The biofilms found in the wound are light and gel-formed (13). They stimulate the inflammation, increase vessels permeability and both wound exudates and fibrinous scab forming. The presence of the scab can show the presence of the biofilm in the wound. The microbes being in the biofilm have noncultivated features in 6–12 hours, become resistant to antibiotics, chemotherapeutic preparations, anticeptics and disinfectant solutions as the result of extracellular polysaccharides forming. (3,10).

O.V.Rybalchenko et al. (6) consider that the wound treatment will be effective in 24 hours concerning the planctone bacteria fraction as well as bacteria covered with the biofilm.

Thus, the burn surface is an optimal medium for many bacteria reproduction and cultivated bacteria are released from the burn wound surface using common microbiological methods as well as noncultivated biofilm-forming bacteria covered by polysaccharide

matrix. The favourable conditions for microbe population growth and the reproduction are created. So, the study of burn wound microflora is actual from the point of effective therapy administration as well as the prognosis of the infectious process development caused by microbe associations being in biofilms.

The objective of the present study is to analyze the microbe picture of the burn wounds in children with the severe thermal trauma and reveal its influence on the infectious process outcome.

MATERIALS AND METHODS

The analysis of 262 microbiological studies of samples from the burn wound surface in 103 patients aged 6–17 treated in the Tyumen regional hospital N1 has been carried out for 2007–2012. 66 boys (64%) and 37 girls (36%) having the burn II–IIIAB–IV with the injury area from 7 to 70% of the body were examined. The burn was got with hot liquids in 79.6% and it was because of flame or electrical current in 20.4% of cases. The patients were at the reanimation and the intensive care department where the antibacterial, infusion and transfuse, respiratory therapy, the nutrition, anesthesia and the local wound treatment were carried out.

The microbiological study of the wound release was carried out according to the law requirements of MH RF N535 "About the unification of microbiological (bacteriological) methods of the investigation used in the clinical and diagnostic laboratories at the medical and preventive institutions".

The statistical analysis of samples was carried out using a computer program Statistica 6.0 using arithmetical mean taking into consideration a mean error ($M+m$).

STUDY RESULTS AND DISCUSSION

As a rule, local and common signs of the wound infectious process development are unspecific that is why it is necessary to develop specific methods of the laboratory diagnostics in the dynamics of the infectious process development. To improve the microbiological diagnostics it is necessary to develop innovative technologies for revealing biofilmforming bacteria at this stage.

The analysis of the microbe picture of burn wounds showed that bacteria *Staphylococcus* spp. (42.7%) and *Enterococcus* spp. (18.7%) were more often revealed on the wound surfaces. *S.aureus* and *S.epidermidis* comprised 39.3%. Epidermal *Staphylococcus* in the burn wounds was 22.5%. It is obvious that *S.epidermidis* is a specimen of a man's normal skin and mucosa microflora. The skin is a primary defensive barrier against an infection. Being injured the skin surfaces with the thermal agent *S.epidermidis* dissemina-

tion occurred on the burn surface from near-by tissues. In our opinion the burn wound was infected with these bacteria.

Bacteria *Enterococcus* spp. were revealed in 18.7% of cases. It is known that *Enterococcus* spp. is a conditional and pathogenic microorganism which can cause autoinfection. At the same time *Enterococci* have a high resistance to the influence of disinfectant solutions used in the burn centre and they can result in exogenous wound infecting in their sufficient accumulation. The presence of the extensive wound surface resulted in it too.

Among nonenzyme gram-negative microflora *P.aeruginosa* was revealed in 10.3% of cases. *Pseudomonas aeruginosa* infection on the children burn surface caused long wound healing and created unfavorable conditions for healing of skin parts after donor skin transplantation.

E.coli on the burn wound surface was in 2.7% of cases.

The analysis of literature showed that bacteria *S.aureus*, *S.epidermidis*, *P.aeruginosa* and *E.coli* have biofilmforming activity (2,4,11).

It is known that infecting of burn surfaces is occurred by different ways such as through air and domestic articles, due to its own conditional and pathogenic microflora, medical personnel and visitors' bacteria carriers as well as in medical procedures (1).

The fungus infection and difteroids comprise 6.5% of all investigations of burn wounds. *Candida* spp. release was 3.8%, *Bacillus* spp. was 4.9%. *Candida albicans* were revealed in one patient with the burn IIIAB which resulted in sepsis and then to the lethal outcome.

Microbe associations on burn wound surfaces were revealed in 56% of cases. 2–4 different microorganisms were released in patients. The monoculture was found in 44% of examined patients. The mixed infection including 2 types of bacteria was in 44% of cases, 3 types were in 13.3% of cases, 4 types were 2.7% of cases. The carried analysis showed that the microflora in microbe associations was senseless to antibiotics in 60%. The microbes were senseless to oxycyclin, hentamycine, ciprofloxacin, ceftazidine and etc.)

The microbe concentration on the burn wound surfaces influenced on the generalized infectious process development. In 1965 R.B.Lindberg et al. carried out an investigation to study the influence of the bacteria concentration in the burn wound surfaces on the infectious process and the prognosis of the burn disease course. It was determined that the generalized infectious process was developed in the burn wounds in the amount of 10^{10} microbe cells in 1 g. of the tissue.

The results of 115 studies from burn wound surfaces showed that the bacteria concentration in the

burn wounds was 10^{-10} in 50.4% of cases, it was 10^{-10} in 25.2% of cases. The bacteria concentration being higher than 10 was registered in 24.4% of cases. Bacteremia and the generalized infectious complication (sepsis) were marked in children having the bacteria concentration of 10^{-10} microbe cells in 1 g of the studied tissue.

The analysis of the lethal outcome in 83 children with the severe thermal trauma showed that bacteremia caused by biofilm-forming bacteria was observed in 50.6% of cases. *P. aeruginosa* was marked in 30.9% of cases and *S. aureus* was in 23.8% of cases. Probably noncultivated bacteria *P. aeruginosa* and *S. aureus* being in patients organism turned into the cultivated state.

So, according to the results of the microbiological investigations it was determined that the associated microflora was determined on the burn surface in children with the severe thermal trauma in 56% of cases. *S. aureus* and *S. Epidermidis* were released in 39.3% of cases. *P. aeruginosa* was in 10.3% of cases and *E. coli* was in 2.7 of cases. A specimen of the man's normal microflora (*S. epidermidis*) was a prevalent microorganism on the burn wound surfaces (22.5%). All microorganisms mentioned above have an ability to form biofilms, that is why it is necessary to determine the presence of biofilms on the burn wound surfaces in long course of the infectious process. It was also determined that bacteremia and the generalized infectious process with sepsis were marked in children having the bacteria concentration of 10^{-10} the microbe cells in 1 g. of the studied tissue.

CONCLUSIONS

1. The associated infection including 2–4 different microorganisms was in 56% of cases in children aged 1–17 having the burn trauma II–IIIAB with the injury area from 7 to 70% treated in the burn centre of the Tyumen regional hospital N1. In the microbe associations the bacteria were senseless to different groups of antibiotics in 60% of cases.
2. Epidermal *Staphylococcus* had the most percentage (22.5%) from gram-positive microflora but *Pseudomonas aeruginosa* was from gram-negative microflora.
3. The generalized infectious process with the septic outcome was in 25.2% of cases in the concentration of microbe cells 10^{-10} in 1 g. of the burn tissue.
4. The received results of the analysis of the burn wound microbe picture show the necessity of the development of methods for bacteria biofilms diagnostics being on the burn wound surfaces.

REFERENCES

1. ALEXEEV A.A., KRUTIKOV M.G., YAKOVLEV V.P. The burn infection. Etiology, pathogenesis, diagnostics, prevention and treatment. – M.: Higher school book, 2010. – 41 p.
2. AFINOGENOVA A.G., DAROVSKAYA E.N. Microbe biofilms RAS: The state of the issue // Traumatology and orthopedics of Russia. – 2011. – N3. – P.119–125.
3. BEKHALO V.A., BONDARENKO V.M., SYSOLYATINA E.V., NAGURSKAYA E.V. Immunological features of the bacterial cells being in the composition of "medical biofilms" // Microbiology. – 2010. – N4. – P. 97–107.
4. VINNIK Yu.S., PERYANOVA O.V., ONZUL E.V., TEPLYAKOVA O.V. Microbebiofilms in surgery: mechanisms of forming, resistance to medical preparations, ways of solving these problems // News in surgery. – 2010. – V.18. – N6. – P.115–125.
5. MAYANSKY A.N. Pathogenetic microbiology: Nizhniy Novgorod: Nizhniy Novgorod state med. Academy, 2006. – 124 p.
6. RYBALCHENKO O.V., BONDARENKO V.M., DOBRITS SA V.P. Atlas of ultrastructure of microbiota of a man's intestine. – SPb.: SRC VMA, 2008. – 112 p.
7. SAKHAROV S.P. Epidemiology of children burn trauma // Children surgery. 2013. – N2. – P.29–31.
8. SAKHAROV S.P., IVANOV V.V., SHEN N.P., SUCHKOV D.V. Lethal outcomes of burn disease in children: 18-year work experience // Emergency. 2011. – N11. – P. 52–57.
9. BELBA M., BELBA G. Acute Renal Failure In Severe Burns. Conclusions After Analyses Of Deaths During 1998 // Annals of Burns and Fire Disasters. – vol. XIII – n.2 – June, 2000.
10. BESTER E., KROUKAMP O., WOLFAARDT G.M., BOONZAAIER L., LISS S.N. Metabolic differentiation in biofilms as indicated by carbon dioxide production rates // Appl. Environ. Microbiol. – 2010. – Vol. 76, N 4. – P. 1189–1197.
11. VOROBIEV E.S., VORONKOV A.S., VINNIKOV A.I. Bacterial biofilm. Quorum sensing – «feeling quorum» of bacteria in biofilm // Bulletin of Dnipropetrovsk University. Biology. Ecology. – 2012 – Vol. 20, v. 1. – P. 13–22.
12. GANG R.K., SANYAL S.C., BANG R.L., MOKADDAS E., LARI A.R. Staphylococcal septicaemia in burns // Burns. – 2000. – 26, № 4. – P. 359–366.
13. HURLOW, J., BOWLER P.G. Clinical experience with wound biofilm and management: a case series // Ostomy Wound Manage. – 2009. – Vol. 55, N 4. – P. 38–49.
14. JAMES G.A., SWOGER E., WOLCOTT R., PULCINI E. L., SECOR P., SESTRICH J., COSTERTON J.W., STEWART P.S. Biofilms in chronic wounds // Wound Repair Regen. – 2008. – Vol. 16, N 1. – P. 37–44.
15. MONCRIEF J.A., SWITZER W.E., ORDER S.E., MILLS W.JR., LINDBERG R.B. The successful control of burn wound sepsis // J. Trauma. – 1965. – Vol. 5. – P. 601–616.

PATHOGENETIC OPTIONS OF TREATMENT OF THE KNEE OSTEOARTHRITIS

A.N. Serova¹, M.A. Kurbatov¹, A.A. Gerasimov²

¹ Medical Center "Help", Nizhny Novgorod, Russia

² Ural State Medical University, Ekaterinburg, Russia

ABSTRACT — This article is devoted to the pathogenesis of osteoarthritis with primary impairment of blood circulation in the subchondral bone and secondary infringement of diffuse nutrition of the cartilage and its subsequent disorder. The pathogenetic treatment stopping degeneration of cartilage tissue has been offered.

KEYWORDS — intratissual electric stimulation, gonarthrosis, pathogenetic treatment, knee joint, synvisc.

The problem of the treatment of the knee joint osteoarthritis of the recent years has not decreased but increased. The involutive gonar gonarthrosis is recorded in the majority of the population over 60 years old. The medication therapy based on symptomatic action is commonly used.

In recent years, hyaluronic acid started increasingly to be used for administration in joints. Hyaluronic acid in the existing formulations according to the literature data has two functions: lubricating and increasing of activity of chondrocytes.

Another important issue of the treatment is the activation of metabolic and reparative processes in hyaline cartilage, the ability to influence the nutrition of matrix and the functional activity of chondrocytes. Possibility to influence the amplification of these processes occurs through the diffuse nutrition of hyaline cartilage, which is performed only from the bone tissue. The name "osteoarthritis" refers to a dominant role of the bone in the disease occurrence. You should not consider the processes occurring in the cartilage without the root causes – the impairment of circulation in the bone tissue adjacent to the joint. The pathological process "bone-cartilage" is single and it should be treated by the methods affecting both tissues.

Pathophysiological and functional changes may be detected long before the occurrence of pain and radiological changes.

In recent decades owing to physiologists and anatomists enough data have been accumulated to



A.N. Serova
Doctor of Medicine, professor



A.A. Gerasimov
Professor, Doctor of Medicine



M.A. Kurbatov
Doctor of Philosophy in Medicine

confirm that the source of the pain is the bone itself with its osteoreceptors. Innervation of bone, periosteum and their receptors is performed by the sympathetic nervous system only. From the works of G.A. Yankovskiy it is known that the representation of bone receptors in the brain is more than from skin and muscle coverings.

Pathogenesis of formation of the pathology in the joint may be represented as follows. The initial changes in osteoarthritis occur first in the bone tissue in the places of attachment of capsule of the joints or ligaments. These places bear a heavy load and a limited blood supply (bradytroph zones). In the bone tissue first small areas of local osteoporosis with destruction of bone trabeculars appear, they gradually increase, and against this background in the microcavities stagnation of venous blood and increase of intraosseous pressure occur. Bone tissue is rich in osteoreceptors, their irritation occurs with a decrease of the partial pressure

of oxygen in the bone vessels, i. e. during the hypoxia caused by circulatory disorders with venous stasis. It has been proved that the worse the bone circulation, the more enhanced the pain intensity of pain is.

Pathology of bone tissue progresses gradually, often with the course of years. Henceforth, the changes cover the periosteum and joint capsule, their swelling and palpation tenderness occur. This stage can already be identified clinically. The impairment of circulation and bone hypoxia create pain syndrome - a bone pain syndrome.

The impairment of circulation in the bones is the primary link at degenerative phenomena in all joints. As far as is known, the nutrition of hyaline cartilage takes place by diffusion of the bone epiphyses. Even small blood circulation disorders of the adjacent bone lead to a sharp decrease in diffusion processes of the nutrients into the cartilage matrix. The impairment of this nutrition is the basis for the occurrence of biochemical abnormalities and later of degenerative phenomena in the hyaline cartilage of the joint.

The existing treatment methods do not solve the problem of bone and cartilage degeneration. It is known the basic methods of conservative treatment: medication, vascular therapy and physiotherapy, unfortunately, they do not affect the circulation of the bone. The insufficient effect is explained by the absence of response of the vascular wall in the bone vascular to antispasmodic medications.

Physiotherapy treatment is ineffective, since the electric current is attenuated by skin by 200–500 times. The attenuated current entered the body does not actually reach the bone. The bone is covered by the endplate having a high resistance.

We have tried the intraosseous administration of various drugs, but have not obtained a lasting effect. It has been determined experimentally that a specific electric current improves the blood circulation by affecting the osteoreceptors and activation of trophic function of the sympathetic nerves. We have developed a method of the bone pain treatment.

We have developed an electric current which is close to the physiological characteristics. This is a low-frequency difficultly-modified pulse current. Standard physiotherapy devices have high-frequency components of pulses and have a damaging effect on the myelin sheath of nerves. This treatment has been named the intratissual electrical stimulation.

TREATMENT METHOD

An electrode needle is introduced into a skin at a depth of the contact with the painful area of the periosteum into the places of attachment of the joint capsule. The needle is supplied with the current within

5–10 minutes. In one procedure 3–5 pain points of the joint may be treated. The course of treatment depends on the stage and severity of osteoarthritis inflammation. These criteria increase the number of pain points in the joint area. Typically, the course consists of 3–6 procedures.

The objective of the study is to determine the effectiveness of the intratissual electric stimulation treatment (ITES) in comparison with the traditional combined treatment and optimization of the treatment with intra-articular synvisc injections.

STUDY MATERIAL

A comparative evaluation of the treatment results in the two homogeneous enough groups of patients with gonarthrosis at the age of 51–68 years has been performed. The traditional conservative complex has been used in 23 patients of the control group (physiotherapy, medication, intra-articular injection of corticosteroids). In the treatment group of 32 patients the method of intratissual electric stimulation (ITES) has been used only. The choice of treatment has been made by the blind envelope method. The patients have been allocated roughly equally according to the stages of the process.

Evaluating the effectiveness of the treatment has been performed based on the complex of the objective criteria. A positive result has been evaluated at the gain of motion in the joint, the complete absence of pain, the positive dynamics at the biomechanical examination in statics and when walking, a significant decrease in muscle tone at rest.

The satisfactory result has been evaluated at improving of the joint motions; pain relief has been evaluated according to the visual analogue scale (VAS) at 10 points, improving of single factors of the combined biomechanical study, a slight decrease in hypertension of joint muscles. The unsatisfactory result has been evaluated in the absence of any positive dynamics of the clinical picture and additional study methods.

Positive results at electric stimulation have been observed 2.5 times more often, and unsatisfactory results 3 times more rarely than at the traditional complex (see table 1). The unsatisfactory results during the ITES have been observed in patients with stage IV of the disease, and during the traditional treatment such results have been observed with stages II–IV of gonarthrosis.

During the ITES the amplitude of motions has increased in all patients, without exception, who had painful contractures, and after the traditional treatment - only in half of the patients. The latter had the increase of the amplitude at stage II–III by 2 times less than after the ITES treatment.

Table 1. Comparative evaluation of the results of treatment of the patients with gonarthrosis

Treatment method	Treatment results, %			Total, %
	positive	satisfactory	unsatisfactory	
Traditional complex	8–33	12–54	3–13	23–100
Intratissual electric stimulation	25–78	5–16	1–4	32–100

Before the treatment, the pain intensity according to the visual analog scale (VAS) in both groups was identical of 5–8 points. After the ITES the complete pain management mostly occurred at the early stages of up to 1–2 points. At stage III the pain management achieved in 25% of patients. After the traditional complex the pains remained in the patients almost in all cases and all stages of the disease (the pain score according to VAS decreased down to 2–5). The comparison of the radiographs produced before the start and after the ITES treatment has shown that the changes in the X-ray pattern have not occurred.

Therefore, a comparative analysis of the data of clinical and biomechanical studies has shown the solid benefits of treatment of the patients with gonarthrosis by the method of intratissual electric stimulation (ITES).

The important medical and economic indicator of the treatment effectiveness is the treatment duration. The duration of treatment by a traditional complex was equal to 25.3 ± 3.2 days, during the ITES the term was 11.6 ± 2.4 days ($p < 0.05$).

The possibility of recurrence after the electric stimulation in the first 2 years has been reduced by 2.5 times. Any complications from use of the electrical stimulation have not been observed.

In order to study the effect of intratissual electric stimulation on the tissue local blood circulation in 20 patients, polarographic and rheographic studies of the bone, periosteum and soft tissues of the joint have been conducted with needle electrodes before and after the treatment. In 5–7 days after the ITES treatment there has been a significant acceleration of latency delivery periods (from 29.2 to 11.3 ± 5.7 with $p < 0.05$) and oxygen uptake (from 60 ± 6.9 to 23.8 ± 7.3 with $p < 0.05$) compared with those before the treatment. The correlation analysis of the pain syndrome degree, the processes of oxygen uptake and blood circulation intensity has shown that in addition to management of the pain syndrome, the electrical stimulation enhances the oxidative processes of the periosteum and tissues adjacent to the joint. Blood circulation and microcirculation in bone recover, the processes of energy metabolism strengthen, which is consistent with the literature data [15]. Taking into account that

the impairment of blood circulation is one of the main causal factors in the development of gonarthrosis, the method of intratissual electric stimulation may relate to pathogenic therapy.

Thus, the intratissual electric stimulation (ITES) is a rapid and highly effective method for treatment of the patients with stage I–II of gonarthrosis of joints, completely eliminating the clinical symptoms. The ITES facilitates the rapid management of the pain syndrome and elimination of clinical and biomechanical disorders of the extremities. At arthritis of stage III the ITES method brings a significant improvement, but the symptoms and disorders may partially remain. The treatment terms of the patients are reduced by 2 times and are equal to 11.6 days. A positive effect is achieved in 83% of cases, with the traditional methods — in 32%.

Intra-articular injections. To improve the results of treatment of the patients with satisfactory and unsatisfactory results in both groups, the treatment with intra-articular injections synvisc has been continued. The course consisted of three injections of 2.0 ml per 1 week.

In the group treated with the ITES the introduction of synvisc was performed in four patients with stage III and IV of osteoarthritis, and after the traditional methods — in six persons with stage III and two persons with stage IV. In the group after the ITES management of pain senses reached after two procedures in all patients. The motion range in the joint and dynamics of movement increased slightly. At long dates the complaints of pain occurrence were observed in two persons after 6 months, and in two persons with stage III there was no pain within 1 year of the follow-up.

In the group of patients treated with the traditional combined method the pain senses in four patients decreased down to 2–4 points according to the VAS. Two persons achieved a complete pain management. The motion range in the joint and dynamics of movement were not improved. Recurrence of pain was noticed in three patients in 4–6 months, and in two patients in 7 months.

Therefore, to obtain a positive and long-lasting effect the intratissual electric stimulation (ITES) in

combination with intra-articular injection of hyaluronic acid medications (synvisc) should be used. This is a preliminary analysis of the results of such treatment, the studies are being continued.

This combination has a major advantage: the treatment methods creating a synergy to each other due to the influence from different sides of the cartilage have been used. Synvisc acts inside the joint cartilage creating a lubricating function as an implant of synovial fluid, and a therapeutical function reducing the dystrophy process.

The intratissual electric stimulation affects the blood circulation of the bones adjacent to the joint. Improvement of blood circulation, especially of microcirculation, activates a diffuse nutrition of the hyaline cartilage and thereby restores the biochemical proc-

esses in the cartilage. Therewith, the recovery effect occurs from the bone side.

CONCLUSIONS

1. The combination of intratissual electric stimulation and intra-articular injection of synvisc is effective at all stages of the disease, even at stages III–IV and may completely manage the pain syndrome. Such combination may be an alternative to surgical treatment, especially in the cases with contraindications to surgery.

2. The combination of intratissual electric stimulation (ITES) and intra-articular injection of synvisc is an effective pathogenetic therapy. Both methods affect different pathogenic mechanisms, increasing the effect of each other.

NON-INVASIVE DIAGNOSIS OF VASCULAR LESIONS OF THE LOWER EXTREMITIES IN DIABETIC PATIENTS BY LASER DOPPLER FLOWMETRY IN CONJUNCTION WITH POLYMAGNETOTHERAPY

**K.A. Tatzhikova, L.A. Gurkina,
L.I. Naumova, M.I. Shikunova**

Astrakhan Medical State University, Astrakhan, Russia

Vascular lesions of the lower limbs (ischemic and mixed form of diabetic foot syndrome) is one of the most severe complications of diabetes mellitus (DM), the cause of infringement of quality of life and high mortality of patients with this pathology. Growing rate of emergency admissions — more than 90%, indicates the lack of effective outpatient care these patients. This makes any attempt to improve current diagnosis and treatment of angiopathy, especially with the use of non-invasive techniques very essential.

The processes of plasma exudation and their soaking, basal membrane damage precapillaries, capillaries and venules, basal membrane thickening precapillaries due to the accumulation in them Schick-positive glycoproteins and mucopolysaccharides neutral are the basis of the morphological changes of the walls microvascular diabetic angiopathy. Desquamation of vascular endothelium proliferation of endothelium and peritellum euroconnector, formation of aneurysmal expansion of the walls of capillaries is observed.

Severity and consequences of tissue ischemia are determined by hemodynamic impairment (impaired microcirculation) and developing tissue damage. The methods of diagnosis allowing to assess the state of microhemodynamics are of particular interest. The resolving ability of existing ultrasonic devices does not allow direct visualization of microvascular. Laser Doppler flowmetry (LDF) use allowing indirectly but objectively assess the microhemodynamics state in superficial tissues, rhythmic activity of microvasculature is effective in this case.

The study was conducted in the form of non-randomized prospective observation of 82 patients with diabetic foot syndrome, diabetic angiopathy vessels of the lower limbs and chronic arterial insufficiency of I-III A stage for Fontain-Saveliev. Microcirculation in the tissues of the lower limbs was evaluated during



Kristina Tatzhikova
Assistant, Department of Pharmacology



Larisa Gurkina
Assistant, Department of Histology and Embryology



Lyubov Naumova
Professor at Department of Histology and Embryology



Marina Shikunova
Doctor at Polyclinic Department

the LDF with a laser analyzer LAK-01 ("LAZMA", Moscow) with one transcutaneous sensor under standard conditions at two points with different structural features of the microvasculature: in the inner ankle (zone with a strong network of arteriovenous anastomoses) and on the dorsum of the foot in the first interdigital spaces (anastomoses are practically absent). Obtained by analyzing data LDF perfusion parameters and amplitude-frequency characteristics of the MC are shown in Table 1. Reliably determined that patients with diabetic foot syndrome KHAN I-IIIA stage reduced microcirculation index. Moreover, this decrease is more pronounced in the first interdigital

spaces on the dorsum of the foot than in the inner ankle. Relatively more intense perfusion at the ankle there is most likely due to increased tone of precapillary sphincters and smooth muscle cells in the wall of microvessels, the opening of arteriovenous shunts and shunt in the venous bed, bypassing the capillary network. This phenomenon, referred to as just "steal syndrome" is a criterion specific nature of diabetic vascular lesions associated with the parallel development of diabetic polyneuropathy. Changes in myogenic activity, FLACSO and neurogenic microvascular tone in the same match the specified violations of microcirculation.

To assess the functional reserve of microcirculation limbs in our study as a load test very physiotherapy procedure of polymagnetotherapy was used. PMT is a method of influencing energy-running pulsed magnetic field (BIMP) and the background magnetic field. In conducting the PMT in order to optimize the impact the biosynchronization principle is used: control algorithm synchronizes the rhythmic characteristics of created magnetotherapeutic environment with normal rhythmic activity of the lower limbs microvasculature of a healthy person according to LDF (the resonance effect).

Real growth in the level of perfusion during PMT was 102.4% in the inner ankle and 203.6% in the dorsum of the foot, the increase in value of the myogenic activity indicator amounted to 46.2% in the inner ankle and 32% on the rear surface and an increase in the coefficient variation was respectively 37.5% and 50.5%. The increase in the amplitude vasomotions, indicating that maintaining the ability to actively reduce microvascular was marked (Table 2). The appearance and increase of the amplitude of the

pulse oscillation, which is a sign liquidation spasm of capillary sphincters, vasodilation and increased blood flow in the MC. The increase in pulse volume and blood flow in the microvasculature is possible in the case of maintaining sufficient functional reserve and mechanisms of tissue blood flow regulation, the presence of predominantly functional changes under the influence of MC polyneuropathy, not only in the area of arteriovenous anastomoses, but also at the level of true tissue capillaries. The results obtained in the study data show the feasibility and effectiveness of using LDF and PMT methods to adequately assess the nature and extent of the violation microhemodynamics, predicting possible outcomes of the process and the selection of the most efficient treatment program. Timely (to the lack of critical ischemia) application of PMT BIMP enables to improve microcirculation and to compensate for ischemic disorders in these patients.

Table 1. Data of a laser Doppler fluogramm in normal state and at a chronic arterial insufficiency with a diabetes mellitus, ($M \pm \sigma$), $p=0,05$

Data of a laser Doppler fluogramm	Internal anklebone		Interdigital interval	
	Healthy people (n=30)	Patients with CAI (n=82)	Healthy people (n=30)	Patients with CAI (n=82)
M (perfuzion units)	6,623±0,923	4,132±0,2497*	11,849±2,601	2,279 ±0,2277*
σ (perfuzion units)	0,95±0,321	1,59±0,088	2,12±1,013	1,77±0,101*
ALF/M*100%	209,3±63,51	202,9±30,22*	271,7±98,26	304,6±15,60
$\sigma/ALF*100\%$	6,87±0,498	15,69±1,444*	5,67±1,115	18,83±2,293*

* — reliable distinctions at the level of significance $p=0,05$

Table 2. Change of an indicator of microcirculation (M), coefficient of variation (Cv) and miogenny activity (ALF/M) during sessions of polymagnetotherapy, ($M \pm \sigma$), $p=0,05$

Data of a laser Doppler fluogramma	The tested area		
	Internal anklebone	Foot sole	
M (perfuzion units)	input data	4,11±0,108	2,20±0,244*
	during sessions	8,32±0,156	6,68±0,192*
ALF/M*100%	input data	211,6±3,67	315,7±4,72*
	during sessions	309,4±4,11	416,8±49,0*
Cv	input data	22,75±8,675	21,94±8,081*
	during sessions	31,27±6,327	33,02±2,852*

* — reliable distinctions at the level of significance $p=0,05$

REFERENCES

1. NEUMARK M.I. Intensive Care "complicated" diabetic foot / Neumark M.I., Kalinin A.P. // Problems of Endocrinology. – 2000. – №4. – P. 14–19.
2. MIKULSKI E.G. The use of LDF in medical practice / Mikulski E.G., Burov Y.A., Somov I.A. and others. // Materials III All-Russia Symposium. – 2000. – Ed. VI. – 163 p.
3. GRACHEV O.A., SMIRNOVA O.N., NOSENKO E.M. Peripheral vascular disease in diabetic patients // Kremlin medicine. Clinical vestnik. – 2003. – №1. – P. 36–40.
4. CHUR N.N. Etiology, pathogenesis, classification and surgical treatment of diabetic foot syndrome / Chur N.N. // Hirurgiya. – 2003. – № 4. – P. 42–46.



Moderne Krebsbehandlung

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Bei der Schlüssellochchirurgie, auch „minimal invasive Chirurgie“ genannt, wird mit sehr kleinen Schnitten schonend im Bauchraum operiert. Die minimal invasive Chirurgie stellt einen besonderen Schwerpunkt unserer Klinik dar. Die Vorteile dieser Technik sind vielfältig. Patienten brauchen deutlich weniger Schmerzmittel und erholen sich schneller.

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- Gallensteine
- Blinddarmentzündung
- Divertikelerkrankung des Dickdarms
- Bösartige Erkrankungen des Darms
- Chronisch entzündliche Darmerkrankungen
- Refluxerkrankung
- Kleine Magentumoren
- Speiseröhrenkrebs
- Leberkrebs

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Prof. Dr. Guido
Schumacher,
Chefarzt

POINT-OF-CARE DIAGNOSTIK VON KEIMEN IN DER AUSATEMLUFT VON PATIENTEN BEI INFJEKTIONSKRANKHEITEN

**Gunther Becher^{1,2}, Jörg Schulz³, Stephan Heymann³,
Roman Purkhart¹, Rolf Graupner¹, Werner Schüler⁴**

¹ Graupner medical solutions GmbH, Geyer

² BecherConsult GmbH, Bernau

³ ICP HealthCare GmbH, Berlin

⁴ STEP Sensortechnik, Pockau, Germany

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

Bei langsam wachsenden Keimen wie Mycobacterium tuberculosis und atypischen Mycobakterien (Mycobacterium avium paratuberculosis (MAP)) dauert eine Kultur 6 bis 8 Wochen zum sicheren Befund, wobei mit positiver Kultur der Keim noch zu differenzieren ist.

Mit der Ionenbeweglichkeitsspektrometrie ist es möglich, flüchtige Produkte des durch Bakterien im Wirtsorganismus oder auf der Kultur ausgelösten Stoffwechsels sehr frühzeitig und sicher nachzuweisen. Die Methode basiert auf der spektrometrischen

Messung von volatilen Peaks und einer patentierten Auswertung zur Differenzierung der Stichproben nach dem Auftreten oder Fehlen von Peaks in den Messungen. Die tatsächliche chemische Identität der Peaks muss dazu nicht bekannt sein. Unbekannte Messungen konnten den vorher differenzierten Lernstichproben mit 100%iger Spezifität zugeordnet werden.

Am Beispiel von MAP-Kulturen wurde mit der Methode ein signifikanter Befall schon nach 3-6 Tagen nachgewiesen, mit Möglichkeit der Differenzierung verschiedener Stämme.

Durch Einbeziehung weiterer Cluster ist eine Differenzierung und Sicherung des Ergebnisses möglich.

Die Methode ist auch geeignet, einen Keimnachweis aus Ausatemluft, Abstrichen aus Rachen und Nase, Sputum oder anderen biologischen Proben zu sichern. Andere schnellwachsende Keime wie E. Coli, Staphylococcus aureus u. a. sind auch detektierbar. Der erwartete Vorteil der Methode besteht darin, dass neben einer schnellen Erkennung des Wachstums an sich (Sensitivität) gleichzeitig eine Keimdifferenzierung erfolgen kann (Spezifität).

Für noch nicht validierte Erkennung von einem Keim ist eine spezifische Methode mit der selbstlernenden Software jederzeit beim Anwender selbst erstellbar.

MORPHOLOGY OF CHRONIC PROCESS IN LUNGS DUE TO LONG INHALATION OF LOW CONCENTRATION OF GAS CONTAINING HYDROGEN SULFIDE

**I.J.Chekunova, L.I. Naumova, T.A. Shishkina,
I.S. Davlatova, M.I. Shikunova**

Astrakhan Medical State University, Astrakhan, Russia

Long negative impact of natural gas on respiratory organs creates conditions for development of a chronic inflammation. Standard protective reactions include processes of a proteolysis of connective tissue of a stroma of lungs and its active regeneration. As a result of the progressing proliferation of connective tissue irreversible destruction develops in structures of lungs.

The progressing course of chronic diseases of organs of respiratory system is caused by development of irreversible morphological changes in all departments of airways and a parenchyma of lungs. Relevance of a problem of early diagnostics and prevention of chronic bronchitis dictates necessity of studying of mechanisms of synchronization of pathological process.

The purpose of an experimental research was the study of dynamics of chronic pathological process development in lungs in the conditions of a long inhalation of the natural hydrogen sulfide containing gas of the Astrakhan field.

Experiment was carried out on 320 laboratory not purebred pubertal rats by weight 180–220 g, affected by the hydrogen sulfide containing gas in concentration 3mg/m³ on hydrogen sulfide within 4 hours, 5 days per a week. All animals were divided into 5 groups, one of them control. The others were formed according to duration of inhalation effect for periods of 1, 2, 3 and 4 months.

MATERIALS AND METHODS

Studying of a condition of structural components of lungs and bronchial tubes is carried out by means of morphological and morphometric methods. Structural components of lungs are painted hematoxylin – eosin and on Van Gizon. Following histochemical methods were used: coloring strong green on protein content, CHIC reaction on existence of a glycogen in tissues. Change of vascular permeability was investigated by means of 0,3% of solution of acridine orange and luminescent microscope of LYMMAM-IZ.

RESULTS

Within the first month of inhalation effect it is observed: hyperplasia of goblet cells with accumulation of Schiff-positive secretory granules in their cytoplasm, strengthening cellular infiltration of extravascular, peribronchial spaces and interalveolar partitions. In lungs there are limited sites of atelectasis.

Thickness and cellular infiltration of a vascular wall increases. Nuclei of smooth muscle cells are getting rounder and closer forming unbreakable chains. Nuclei of endotheliocytes stick out in a vessel gleam. The luminescence of contrast substance is clearly defined in walls of vessels and extravascular area.

In the second month of experiment the cellular infiltration accrues, lightness of structural components of lungs decreases. Among zones with atelectasis the alveoluses changed by emphysema



with the thinned walls appear. The folds of mucous bronchial tubes are broken. The muscular cover loses homogeneity of coloring and an regularity of arrangement of smooth muscle cells nuclei. In a gleam of bronchial tubes there are deposits of mucin, infiltrated by leucocytes. In peribronchial interstitium cellular infiltrates become more dense, reminding lymphoid follicles.

A number of vessels become empty, in others erythrocytes stasis develops. Thickness of a vascular wall increases at the expense of a cellular infiltration and stratification of muscular cells as a result of hypostasis. In interstitial (extravascular) compartment, an enhanced intensity of strong green as well as luminescence of contrast agent were revealed.

Within the third month the quantity of sites with emphysema increases. Many bronchial tubes are deformed, have a star-shaped form on a section and contain congestions of mucin, infiltrated by cells. Mucosa of bronchial tubes forms protrusions, similar to polyps. Process of an atrophy of a muscular cover of bronchial tubes progresses that is expressed in reduction of its volume and increase in intermuscular connective tissue.

The tendency to permeability strengthening remains, on the course of vessels numerous narrowings, expansions are formed. In the external cover of vessels and extravascular space collagen deposits are well seen. When coloring strong green walls of vessels visually lose the integrity, in them the "emptiness" corresponding to intermuscular stratifications and cellular infiltrates are formed.

The fourth month of experiment is characterized by rough destructive changes. The number of the deformed bronchial tubes with protrusions of walls similar to sacks, characteristic for bronchiectasia increases. Atrophic processes in a bronchial wall are caused by growth and hypostasis of intermuscular connecting tissue. Lightness of lungs increases with increase of volume of the parenchyma, which has changes in a type of emphysema.

In a vascular wall the muscular cover is exposed to processes of an active collagen deposits. Intensive diffusion coloring of extravascular space by fuchsin shows an increase in collagen deposits with distribution of process to a surrounding parenchyma. Thickness of a vascular wall is increased, the clearness of its contours is lost due to plasmatic treatment and a cellular infiltration. The described changes in a vascular wall in luminescent microscopy are followed by significant increase in its permeability.

In a weak Schiff-positive stromal connective tissue of bronchial tubes presence of intensively painted fibers which appearance is connected with simultaneous of a proteolysis and formation of collagen is recorded. Intermittence and a disorientation of these fibrous structures, especially in the field of massive cellular infiltration is noted.

CONCLUSIONS

Long influence of the damaging factor accounts for development of chronic pathological process. Inhalation of low concentration of the hydrogen sulfide containing gas within the first month of experiment is followed by changes of functional character. Long inflammatory process causes a perversion of compensatory reactions that leads to destruction of lung parenchyma and activation of proliferative reactions. The developing deficiency in stromal connective tissues affects the structural organization of lungs and promotes further progressing of pathological process.

REFERENCES

1. SHISHKINA T.A. Condition of elements of connective tissue in lungs of laboratory animals at chronic influence of natural gas / T.A. Shishkina, L.I. Naumova, A.A. Osipov, I.J. Chekunova// Morphology. – 2009. – No 4. – P. 157.
2. KUZ'MINA L.P. Biochemical and moleculo-genetic mechanisms of development of professional pulmonary pathology / L.P. Kuzmina// Pulmonology. – 2008. – No 4. – P. 107–110.
3. NEKLYUDOVA G.V. Morfo-functional changes of vessels of system of a pulmonary artery at the secondary pulmonary hypertension caused by CODL / G.V. Neklyudova, A.L. Chernyaev, A.V. Chernyak, M.V. Samsonova, I.J. Tarasenko, A.V. Byicanova, G.K. Naumenko// Pulmonology. – 2006. – No 4. –P. 21–25.

THE PATHOLOGY AND MORFOLOGY OF LESION IN MICE BRAIN CORTEX UNDER INFLUENZA VIRUS A (H3N1 1/62) INFECTION

Liana Gogiashvili, Zurab Tsagareli

*A. Natishvili Institute of Morphology,
Iv. Javakhishvili Tbilisi State University
Tbilisi, Georgia*

The pathology caused by so-called "non neurotropic" virus infection, is not well understood. The urgency of the problem is not just the nature of the epidemic and pandemic influenza with enormous human and economic troubles but the frequency lesion, if CNS damages is the second after respiratory.

There are a number of features in the CNS contributing to the persistence of the virus. In addition to

the above mentioned these include: 1) mostly humoral factors of immune protection; 2) existence of special cells of mononuclear phagocytic system-microglial cells; 3) low capacity to develop interferon. So far, the question remains – what are the qualitative differences in morphological and pathogenetic entity lesion in viral influenza infection.

Our own examinations, performed in the period from 1996, have shown a direct cytopathic effect of influenza A virus (H3N1, H3N2, Yong Kong 1/68) on nuclei of medulla oblongata, parasympathetic nervous system with its primary damage. The neural transport of viruses from the periphery to the CNS is not well investigated but we and other authors have demonstrated on the CBA mice models that n. vagus, nuclei of m. oblongata and brain stem are most affected.

The aim of study is to reveal pathologic changes of brain cortex nervous elements in influenza A virus infection in experiment and to clarify neural disturbance by analyzing their ultra structural findings in

mice under experimental influenza virus infection in first 16 days of experiences.

All experiments using live A Hong Kong H3N1 viruses were performed in a biosafety level-3 laboratory approved for use by Georgian Disease Control Center.

Ultra structural and histological appearance also volume fraction of neurons from parieto-temporal cortex in 6-week-old mice were carried out after 24, 48-72 hours and 5-16 days of intranasal inoculation of influenza virus A (H3N1 1/62) Hong Kong.

Nerve cells in layer V of the cerebral cortex of mice respond to infection with influenza virus by complex changes: acute swelling, chromatolysis, vacuolization, shrinkage and neuronophagia.

Quantitative changes in the "acute" phase of infection up to 72 hours to testify of cortex cytoarchitectonic in the form of lower differentiation and higher monotony size of neurons with their polarization from very small cells to large, hypertrophied, which is unusual for the "intact" model of brain.

THE STUDY OF MYOCARDIUM REMODELING AFTER INTERVENTIONAL TREATMENT OF ATRIAL FIBRILLATION IN PATIENTS WITH ISCHEMIC HEART DISEASE AND ARTERIAL HYPERTENSION

**D.V. Dedov^{1,2}, S.A. Masyukov¹, I.Y. Yevtyukhin¹,
A.N. Kovalchuk³, M. Asisova¹, T. Yarakhmedova¹**

¹ Tver State Medical University of Health Care Ministry of the Russian Federation, Tver, Russia

² Tver Regional Clinical Cardiologic Dispensary, Tver, Russia

³ Hospital of the Ministry of Defense of the Russian Federation, Tver, Russia



Dmitry Dedov

cardiologist of Regional Clinical Cardiological Dispensary, Candidate of Medicine, assistant professor of Tver State Medical Academy, 170036 Russian Federation, Tver, P. Saveljeva street, 15-2-22.
e-mail: dedov_d@inbox.ru

OBJECTIVE

To study of electrical myocardium remodeling after interventional treatment of atrial fibrillation (AF) with patients with ischemic heart disease (IHD) and arterial hypertension (AH).

MATERIAL AND METHODS

The research was done according to the plan of research works of Tver State Medical University (Tver). Overall, on the basis of Regional Clinical Cardiologic Dispensary and Hospital of MD RF in Tver 88 patients (average age $58,6 \pm 7,4$) with IHD were examined. IHD showed itself in the attacks of stable angina of II–III functional classes with the accompanying paroxysmal form of AF. According to Declaration of Helsinki, the patients gave informed consent for the study. The criteria for inclusion into the study were: age not more than 72, verification by previous clinical and anamnestic and instrumental examination of IHD and AH, availability of electrocardiogram (ECG) and/or ECG of AF paroxysm documented during Holter monitoring [6] and radiofrequency ablation (RFA) of increased automatism focuses performed at Federal medical centres (Moscow). All the patients underwent clinical and anamnestic and instrumental examination. We monitored the rhythm to be sinus and as its criterion we considered the availability of P-wave of equal morphology constantly preceding the QRS complex and positive in I-II standard leads. Initially and 24 months after that the examined people were inspected with regard to such factors of P-wave as maximum and minimum in milliseconds (ms) (Pmax and Pmin respectively). We calculated P-wave dispersion – Pdis (in ms). This factor was calculated according to the formula: $Pdis = Pmax - Pmin$. PQ(R) and QT-intervals were calculated in the similar way as P-wave analysis [4]. The analysis of P-wave length and dispersion, PQ(R) and QT intervals was performed initially before radiofrequency ablation (RFA) and 24 months after intervention.

RESULTS AND DISCUSSION

As a whole, men and women with IHD and AH 24 months after successfully performed RFA had P-wave dispersion and QT interval values lower than before the intervention (by 47.3% and 27.7%, 14.3% and 11.8% respectively; all $p < 0.05$). Besides, women showed PQ(R) dis decline (by 31.1%; $p < 0.01$). The study shows that its effectiveness was more than 72.7%, which is in agreement with the data of the leading arrhythmological centres of the world [1, 8, 12]. Development and progression of IHD and AH is connected with availability of general atherosclerotic process, emergence of left ventricular hypertrophy, heart rhythm disorders and the appearance of clinically apparent chronic heart failure (CHF) [1, 5, 14, 15]. In turn, this is aggravated by the presence of risk factors with a patient. We must assume that the same reasons lie at the basis of pathophysiological mechanisms of AF developing, causing, fatal cardiovascular events. In-

cluding sudden cardiac death [7, 9, 10, 11]. It is known that the basis of most pathophysiological processes with patients with IHD and AH is a defect of heart ultrastructure. The authors consider P-wave dispersion as a predictor of AF paroxysmal form [2, 3, 4, 5, 10, 14]. On the other hand, reduction of Pdis values after RFA foci of increased automaticity might show reverse atrial myocardium remodeling [3, 8, 11, 12, 13]. It is interesting to note that after RFA that supposes some impact on atria structure positive changes also take place in ventricular myocardium. It is known that QT interval represents the duration of the total electrical activity of the heart, and QT lengthening - delayed and asynchronous ventricular myocardium repolarization. The authors connect the increase in QT duration with the risk of the development of ventricular tachycardia paroxysms like pirouette — «torsade de pointes» [7]. Our study shows that patients with IHD and AH accompanied by AF, who underwent RFA, have parameters of ventricular conduction improving. It is believed that in the postoperative period favorable changes are observed not only in atria, but in ventricular myocardium. Apparently, based on the data we can talk about regression mechanisms of arrhythmogenesis after RFA [1, 8].

CONCLUSIONS

72.7% of patients with IHD and AH who underwent interventional treatment of AF had arrhythmia attacks ceased. At the same time, both men and women had decreased values of P-wave dispersion and QT interval. Thus, the given figures can be considered as predictors of reverse electrical myocardium remodeling.

REFERENCES

- ARDASHEV V.N., ARDASHEV A.V., STEKLOV V.I. Treatment of heart rhythm disorders. – Moscow: Medpraktika Publishing House, 2005. – 228p.
- DEDOV D.V., IVANOV A.P., ELGARDT I.A. Influence of electromechanic heart remodeling on the development of atrial fibrillation with patients with IHD and arterial hypertension. Russian Cardiological Journal. – 2011. – №4. – P. 13–18.
- DEDOV D.V., IVANOV A.P., ELGARDT I.A. Clinical and functional features and prognosis with patients with atrial fibrillation of various etiologies after radiofrequency ablation. Cardiology and Cardiovascular Surgery. – 2011. – Vol. 4. – №5. – P. 54–58.
- DEDOV D.V., IVANOV A.P., ELGARDT I.A., ROSTORTSKAYA V.V. Predictors of poor prognosis with patients with atrial fibrillation, according to Holter monitoring of ECG and pulse oximetry. Bulletin of arrhythmology. – 2011. – №63. – P. 22–26.
- MILLER O.N., BELYALOV F.I. Atrial fibrillation. Tactics of patients treatment at pre-hospital, hospital

- and outpatient phases. Russian Journal of Cardiology. – 2009. – №4. – P. 94–111.
6. RYABIKINA G.V., SOBOLEV A.V. ECG monitoring with the analysis of heart rhythm variability. – Moscow: Medpraktika, 2005. – 222 p.
 7. ANTZELEVITCH C. Ionic, molecular, and cellular of QT – interval prolongation and torsade de pointes. Europace. 2007; №9(4): P. 4–15.
 8. ARORA S., MOOKADAM F., SRIVATHSAN K. Interventional management of atrial fibrillation. Expert Rev. Cardiovasc. Ther. 2010; №8(7): P. 949–958.
 9. CENTURIÓN O.A. Clinical implications of the P wave duration and dispersion: relationship between atrial conduction defects and abnormally prolonged and fractionated atrial endocardial electrograms. Int. J. Cardiol. 2009; Vol. 1, № 134(1): P. 6–8.
 10. DILAVERIS P.E., GIALAFUS J. E. P wave dispersion novel predictor of paroxysmal AF. Ann. Noninvasive Electrocardiol. 2001; №6: P. 159–165.
 11. DOGAN A., AVSAR A., OZTURK M. P-wave dispersion for predicting maintenance of sinus rhythm after cardioversion of atrial fibrillation. Am. J. Cardiol. 2004; № 93(3): P. 368–371.
 12. LÁBROVÁ R., SPINAR J., HONZÍKOVÁ N. Radiofrequency ablation in treatment of atrial fibrillation. Physiol. Res. 2010; № 59, Suppl. 1: P. 43–49.
 13. RASCHI E., BORIANI G., DE PONTI F. Targeting the arrhythmogenic substrate in atrial fibrillation: focus on structural remodeling. Curr. Drug Targets. 2011; №12(2): P. 263–286.
 14. STIELL I.G., MACLE L. Canadian Cardiovascular Society atrial fibrillation guidelines 2010: management of recent-onset atrial fibrillation and flutter in the emergency department. Can. J. Cardiol. 2011; №27(1): P. 38–46.
 15. YILMAZ R., DEMIRBAG R. P-wave dispersion in patients with stable coronary artery disease and its relationship with severity of the disease. J. Electrocardiol. 2005; №38(3): P. 279–284.

INTRAKORPORALE HARNABLEITUNG BEI DER ROBOTERASSISTIERTEN RADIKALEN ZYSTEKTOMIE (RARC) — ERGEBNISSE UND ERFAHRUNGEN NACH 50 PATIENTEN

S. Edeling, S. Pokupic

*da Vinci-Zentrum Hannover,
Vinzenzkrankenhaus Hannover gGmbH, Hannover*

Die roboter-assistierte Zystektomie (=RARC) wird seit 2005 zunächst in den USA und nun auch in Europa durchgeführt. Erste onkologische Daten bezüglich positiver Absetzungsränder, Anzahl der entfernten Lymphknoten und 5-Jahre-Überleben zeigen keine Unterschiede zur offenen Operation. Vorteile bestehen in der niedrigeren Komplikationsrate, einem verkürzten Krankenhausaufenthalt und einem geringen intraoperativen Blutverlust. Obwohl die Durchführung einer intrakorporalen Harnableitung möglich ist und sich erst durch diese die vollen Vorteile der minimalinvasiven Chirurgie ergeben, werden zur Zeit noch knapp 80% der RARCs mit einer extrakorporalen Harnableitung durchgeführt.

Wir berichten über unsere Erfahrungen bei der Durchführung einer RARC mit intrakorporalem Ileumconduit und intrakorporaler Neoblase und vergleichen die Outcomes.



*edeling@vinzenzkrankenhaus.de,
0511-950-19356,
pokupic@vinzenzkrankenhaus.de,
0511-950-19355,*

COMPARATIVE STATE OF LOCAL AND SYSTEMIC INDICATORS OF CELLULAR, HUMORAL IMMUNITY AND CYTOKINE PROFILE IN PATIENTS WITH PEPTIC ULCER BLEEDING

J.N. Hajiyev, V.A. Allahverdiyev, E.M. Klimov*, N.J. Hajiyev

Azerbaijan Medical University, Baku, Azerbaijan
and Institute of General and Emergency Surgery NAMSU, Kharkov*

INTRODUCTION. The generally accepted efficiency of modern anti-ulcer agents also did not solve the problem of gastric and duodenal ulcer, the number of patients with peptic ulcer bleeding is increased from year to year. The immune status of the organism also plays an important role in pathogenesis of gastroduodenal ulcer.

However, in patients with peptic ulcer bleeding, both local and systemic immunity, including cytokine profile was not fully studied.

THE PURPOSE OF THE STUDY. The study of some local and systemic indicators of cellular and humoral immunity and cytokine profiles in patients with peptic ulcer bleeding.

MATERIALS AND METHODS. On admission to the hospital in 154 patients with peptic ulcer bleeding (gastric ulcer — 37, duodenal ulcer — 111 and gastroduodenal ulcer — 6) was determined the content of cellular (CD3+, CD4+, CD8+ — lymphocytes) and humoral (CD19+ — lymphocytes, Ig A, M, G, circulating immune complexes (CIC) indicators of immunity and cytokine profile (TNF α , IFN γ , IL-1, 2, 6, 8 and anti-inflammatory IL-4, 10 of cytokines) in blood serum. In 107 patients local immunity were evaluated by studying lysozyme levels and IL-6 in gastric juice, and Ig A, M, G — in duodenal juice.

RESULTS AND DISCUSSION. In study of cellular immunity in patients with peptic ulcer bleeding were revealed a statistically significant decrease — in CD3+ — lymphocytes up to 32.9%, CD4+ — 32.5%, CD8+ — 13.3%, CD4+/CD8+ — 23.2% and phagocytic index (PI) — 18.9% than in healthy individuals. Also it was established disturbances in humoral immunity: a statistically significant increase of CD19+ — lymphocytes by 58.8% and CIC — 2.3 times, decrease of concentration of Ig A, M, and G respectively 16.5%, 15.8% and 10.7% ($p<0.05$).

On background of this, there was a statistically significant increase in concentration of serum TNF α — 5.7 times, IFN γ — 5.4 times, IL-1 — 9.9 times, IL-2 — 8.7 times, IL-4 — 6.2 times, IL-6 — 12.8 times, IL-8 — 2.5 times, and decrease in IL-10 — 45.2% compared with the normal. The content of IL-6 in urine was 8.2 times ($p<0.001$) more than in healthy individuals.

In stomach mucose the content of IL-6 by 37.5% ($p<0.001$) and lysozyme by 38.3% ($p<0.001$) was lower in comparison with the control group. In duodenal content was revealed decrease of Ig A, M and G respectively by 72.0% ($p<0.001$), 55.1% ($p<0.001$) and 37.6% ($p<0.001$) relative to normal indicators.

CONCLUSION. Thus, studies have shown that in patients with peptic ulcer bleeding immunosuppression is observed in cell immunity with increasing levels of CD19+ cells and disbalance of immunoglobulins and cytokine status at the local and systemic level.

FORTSCHRITTE IN DER ADJUVANTEN THERAPIE DES DIABETES MELLITUS TYP 2 MIT MINERALIEN

S. Heymann¹, J. Schulz¹, O.G. Nikolaev², S.V. Fomchenkov³

¹ ICP HealthCare GmbH, Berlin,

² Woronescher Vereinigung der Endokrinologen und Diabetologen,

³ 000 Nitrozdav, Moskau

Bei Diabetikern des Typs II wird der insulin-abhängige Stoffwechselweg zur Energiegewinnung aus Glukose entlastet, wenn ein Teil der aufgenommenen oder der aus Stärke bzw. Disacchariden freigesetzten Glukose durch käfigförmig strukturierte Alumino-silikate (Zeolithe) isomerisiert wird [S. Saravana-

murugan et al., J. Am. Chem. Soc. (2013), 135 (4), S. 5246–5249]. Die dreiwöchige Einnahme von Zeolithen im Bestand spezieller diätetischer Lebensmittel senkt die Blutzuckerkonzentration erheblich, wie kontinuierliche Tagesverlaufsmessungen der Blutzuckerkonzentration beispielhaft zeigen (Abb.1).

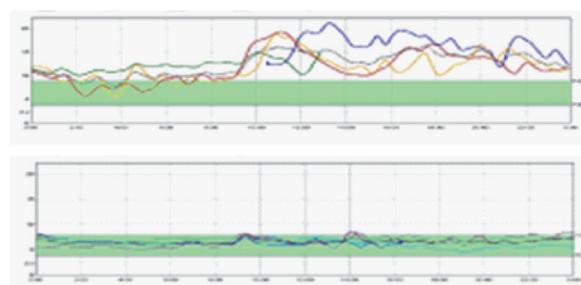


Abb. 1. Tagesverlaufskurven des Blutzuckerkonzentration bei einer Patientin mit mittelgradigem Diabetes Typ II vor (oben) und nach (unten) dreiwöchiger Einnahme von Nanovit® Metabolic. Die verabreichten Kapseln entsprechen einem Zeolithgehalt von 270 mg pro Tag. Medikation und Ernährungsgewohnheiten der Person haben sich über die Mess- und Einnahmezeiträume nicht verändert.

Von besonderer Bedeutung ist eine zweite Beobachtung: Die oft lebensgefährliche Unterzuckerung in den späten Nacht-/frühen Morgenstunden wird ebenfalls normalisiert (Abb.2).



Abb. 2. Tagesverlaufskurven des Blutzuckerkonzentration bei einem an sich gut eingestellten DM II Patienten mit Neigung zu nächtlicher Unterzuckerung vor (oben, Pfeile) und nach (unten) dreiwöchiger Einnahme von Nanovit® Metabolic.

COMPLEX RADIO-DIAGNOSTIC FEATURES OF COMPLICATION PREDICTORS AFTER CORONARY ARTERIES STENTING

Khachatryan G.H., Karapetyan A.G., Kamalyan N.S., Khondkaryan K.V.

Science Center of Radiation Medicine and Burns, Ministry of Health of the Republic of Armenia, Yerevan, Republic of Armenia

The work was aimed to study complex radio-diagnostic parameters as predictors of complications after percutaneous coronary intervention (PCI).

The survey involved 131 male patients aged 20–75 years with multiple coronary arteries lesions and exposed to PCI. Total number of stents was 333, including 164 (49%) with drug emitting coverings (DEC), 169 (51%) — without DEC. As to concomitants diseases, there were 28% patients with diabetes mellitus.

Multi-factorial analysis of 57 quantitative parameters of radiation diagnostics was performed using 3 methods: coronarography, echocardiography, SPECT-tomography (perfusion).

Reasons of repeated referrals for relapses of angina pectoris, arrhythmia, myocardial infarction were analyzed.

The following results were obtained and considered complication predictors:

1. Left coronary artery lesion with the ongoing worsening of end diastolic volume.
2. Ongoing worsening of ejection fraction (EF): of both general and local contractility.
3. Aortic disruption with right heart failure.
4. Combination of lesions of the left coronary arterial trunk and the right ventricle.
5. At the second visit to physician, 26 patients had myocardial infarction. At the first referral, 3 significant parameters were recorded; at the second referral the combined ongoing worsening of EF with lesions of left coronary artery was revealed to be accompanied by impairment of end-diastolic volume (EDV), end-systolic volume (ESV), aggravation of perfusion, and added

- right parts: the number of parameters increased from 3 to 6.
6. In case of drug eluting stents in group of patients with myocardial infarction at the second visit to doctor the most reliable in hypokinesis was impairment of anterior left descending part (distal area): $p = 0.03$
 7. Patients with diabetes mellitus most frequently visited the physician: in case of drug eluting stents by the second year, while similar patients with stents without drug eluting coverings presented by the fourth year ($p = 0.002$).

COMPLEX DIAGNOSIS OF NOSOCOMIAL PNEUMONIA IN SURGICAL PATIENTS — ROLE OF CLARA CELL PROTEIN AND SURFACTANT PROTEIN D

A. Kuzovlev, V. Moroz, A. Goloubev

V.A. Negovsky Scientific Research Institute of General Reanimatology,
Moscow, Russia

The objective of the investigation was to estimate the informativity of plasma Clara cell protein (CCP) and surfactant protein D (SPD) in the diagnosis of nosocomial pneumonia in surgical patients.

MATERIALS AND METHODS. The observational study in ICU ventilated septic patients with peritonitis (70%), pancreonecrosis (25%) and mediastinitis (5%) was done in 2010–2015. Nosocomial pneumonia was diagnosed according to the Russian National guidelines. ARDS was diagnosed and staged according to the V.A. Negovsky Research Institute criteria. Plasma CCP and SPD were measured on day 0, 3 and 5 by the immunoenzyme assay (BioVendor, USA). Patients were treated according to the international guidelines. Data were statistically analyzed by STATISTICA 7.0, ANOVA and presented as median and 25 to 75th percentiles (ng/ml); $P < 0.05$ was considered statistically significant. Areas under the receiver operating (ROC) curves were calculated.

RESULTS. 65 patients were enrolled (out of 312 screened). Patients were assigned into groups: NP + ARDS ($n = 43$, 43 ± 4.9 years old, M/F 39/4, mortality 23%); NP ($n = 22$, 40 ± 5.1 years old, M/F 20/2, mortality 18%); no NP ($n = 25$, 42 ± 5.1 years old, M/F 22/2, mortality 17%). Groups were comparable in APACHE II and SOFA scores on the baseline. In patients with NP caused by *Pseudomonas aeruginosa* plasma CCP was significantly lower at all points than in the patients with no *Pseudomonas aeruginosa* detected. Plasma CCP on day 0 had a good capacity for the diagnosis of *Pseudomonas aeruginosa* NP: CCP

on day 0 ≤ 17.5 ng/ml yielded a sensitivity of 92.7% and specificity of 72.0% (AUC 0.84; 95% CI 0.713 to 0.926; $P = 0.0001$). In the NP + ARDS group SPD was higher at all points than in the NP group. Plasma SPD on day 0 > 111.2 ng/ml yielded a sensitivity of 68.2% and specificity of 92.3% (AUC 0.85; 95% CI 0.684 to 0.945; $P < 0.0001$) for diagnosing ARDS in NP. P/F ratio on day 0 < 280 yielded a sensitivity of 94.1% and specificity of 76.9% (AUC 0.89; 95% CI 0.744 to 0.952; $P < 0.0001$) and EVLWI on day 0 > 8.3 ml/kg yielded a sensitivity of 94.1% and specificity of 92.3% (AUC 0.92; 95% CI 0.810 to 0.982; $P < 0.0001$) for the diagnosis of ARDS in NP. A complex ROC analysis (for SPD in the group of patients with P/F < 280 and EVLWI > 8.3) yielded a much better diagnostic accuracy of SPD: cutoff > 93.7 ng/ml, sensitivity 81.0%, specificity 100.0% (AUC 0.96; 95% CI 0.817 to 0.998; $P < 0.0001$).

CONCLUSIONS. A complex approach – CCP ≤ 17.5 ng/ml + [P/F < 280 , EVLWI > 8.3 , SPD > 93.7] presents as a sensitive and highly specific method for diagnosing NP and ARDS in surgical patients.

PROGNOSTIC INDICATOR FOR THE DEVELOPMENT OF INFECTIOUS COMPLICATIONS IN PATIENTS WITH SEVERE TRAUMA AND HYPOXIA

V.V. Moroz, E.A. Miagkova, A.K. Zhanataev,
D.A. Ostapchenko, A.D. Durnev, V.I. Reshetnyak

¹V.A. Negovsky Research Institute of General Reanimatology, Moscow, Russia

²V.V. Zakusov Research Institute of Pharmacology, Moscow, Russia

INTRODUCTION. Severe trauma and blood loss lead to compensatory release of leukocytes from the bone marrow and blood depots in response to significant tissue destruction. The increase of leukocytes in the blood plasma of the patients immediately after the trauma is directed to the removal of products of cell death in the damaged tissues and the prevention of infectious complications.

OBJECTIVE: to improve the accuracy of the prediction of infectious complications development in patients with severe trauma and severe hypoxia in the early stages after trauma.

MATERIAL AND METHODS. We examined 28 patients (15 men and 13 women, aged 35.3 ± 13.2 years (from 20 to 59 years) who underwent severe combined mechanical trauma. Patients were divided into two groups to assess the impact of hypoxia on DNA damage and death of white blood cells, based on the values of the 4 indicators, which reflect the presence or absence of hypoxia: pO_2 of the capillary blood, lactate level, pH and BE of blood plasma. Group 1st - "Hypoxia <+>" – 18 patients with all 4 indicators (pO_2 of the capillary blood, lactate level, pH and BE of blood plasma) on admission in to intensive care unit were changed and testified of hypoxia. Group 2nd — "Hypoxia <->" — 10 patients on admission in to intensive care unit with all 4 indicators were within normal limits. Each group was subdivided into two subgroups: infection <+> (13 patients in group 1st and 9 in the second group) and infection <-> (5 patients in group 1st and 1 in the second group). DNA damage in leucocytes, as well as indirectly apoptotic and necrotic leucocytes, were estimated using DNA comet assay method in alkaline and neutral versions. The analysis was performed by epifluorescence microscopy at magnification $\times 200$ – 400 . Obtained from micropreparations images of DNA-comets were analyzed using CASP 1.2.2 software. As a quantitative measure of

DNA damage the percentage of DNA in tail of DNA comets (% DNA in the tail of the total amount of DNA in the comet) was used. The data were statistically processed using Microsoft Excel (Microsoft Corporation, USA) and Statistica 6.0 (StatSoft Inc., USA) according to basic requirements for medical and biological data processing. Prediction of infectious complications was determined by logistic regression.

RESULTS. In patients with severe trauma and severe hypoxia were increased the processes of cell death hypothetically by apoptotic and necrotic pathway, which is accompanied by increase of level of DNA single-, double-strand breaks. In dynamic were noted that on the 3rd day after the trauma the change of these indicators in the 1st group of patients differ in subgroups without (infection <->) and with (infection <+>) infectious complications, which developed on the 5–7th day of observation. At 3 days after trauma in the group with hypoxia <+> infection <-> the level of necrotic [8.7 (2.3; 14.7) %] and apoptotic DNA comets [4.3 (2.5; 7.2) %], as well as DNA single-, double-strand breaks [27.3 (21.4; 32.5) %] was significantly higher than that in the group "hypoxia <+>" infection <+> [6.7 (4.5; 12.4) %; 4.3 (2.6; 7.2) %; 13.4 (10.2; 18.6) % respectively]. This data suggests that if the death of cells is more intensive in the first three days after trauma, that infectious complications are developed less likely. The death of cells by apoptotic and necrotic mechanism involving DNA single-, double-strand breaks in patients with trauma related, most likely, with the active participation of leukocytes in the prevention of infectious complications. In this connection, was made an attempt to sum of the values: necrotic DNA comets, apoptotic DNA comets and DNA single-, double-strand breaks on the third day after trauma with prognostic purpose. The ROC analysis of the integration index (necrotic DNA-comets+apoptotic DNA comet+DNA single, double strand breaks) obtained on day 3 after trauma in the group affected hypoxia <+> revealed: the value of the area under the ROC curve for total score at day 3 after trauma was 0.923 (sensitivity 100%, specificity –75.0%). The cut-off point was 47.3% in total score. The value of the integration index below 47.3% indicates a high risk of developing infectious complications in patients with trauma and severe hypoxia. The

total value of the index above 47,3% is a good prognostic sign, suggesting a low degree of probability of infectious complications development in these patients.

CONCLUSION: a method of early prediction of infectious complications development in patients with

severe trauma and severe hypoxia, which includes the identification of integration index (the percentage of apoptotic DNA-comets, necrotic DNA-comets and DNA single-, double-strand breaks of leukocytes) by DNA comet assay was suggested.

RECONSTRUCTIVE SURGERY FOR TUMOURS OF THE BONE SHOULDER AND KNEE JOINTS

V.V. Protsenko, B.S. Duda, O.S. Ilnitskyi

Institute of Traumatology and Orthopedics NAMS of Ukraine

Over the past 50 years in orthopedic oncology the concept of organ-treatment of bone tumours was introduced. All this was made possible due to improvements in surgical techniques, the use of new schemes of chemotherapy, radiation therapy, hormone therapy and immunotherapy and. The use of grafts and stents allowed some patients to perform organ-surgical treatment for tumour localization in the long bones.

THE AIM OF THE WORK. To show the advantages of organ-surgical treatment of tumours of long bones.

MATERIAL AND METHODS. 17 patients (21.5%) with tumours of the proximal humerus underwent surgical treatment. If it affects the bones of the shoulder girdle after resection Tihova-Limberg a reverse shoulder prosthesis in 13 patients was performed and arthrodesis of the shoulder joint using vascularized fibular autograft — in 4 patients. Knee arthroplasty was performed in 62 (78.5%) patients, of which after resection of the distal femur in 40 proximal tibia tumour — 22.

RESULTS AND DISCUSSION. After resection of the proximal humerus and shoulder joint arthroplasty

of the shoulder joint function restored in 13 patients with arthrodesis with vascularized fibular autograft from the shoulder joint function restored in 3 patients. After knee replacement, joint function restored in 59 (95,2%) patients. Postoperative complications were observed in 14 (22,6%) patients with a median follow-up of 36 months. Of these, in 8 patients infectious complications were identified, in 2 — broken leg prosthesis, in 4 — aseptic loosening of the prosthesis stem. In 11 cases revision cases were performed. In 3 cases, the prosthesis was removed and knee arthrodesis using external fixation devices was performed. Length regenerate formed from 10 to 25 cm. After knee arthrodesis limb supporting ability restored in 2 patients. Amputation were performed in 2 patients with recurrent tumours.

FINDINGS. Each type of reconstruction should be preceded by a thorough analysis of the particular case and selection of patients with the cancer and orthopedic aspects, as well as emotional and psychological status of the patient. Organ-surgical treatment for tumours of the bone helps to restore function and support ability of limbs and therefore improve the quality of life of these patients.

THE ANALYSIS OF MORTALITY CAUSES IN PREHOSPITAL AND HOSPITAL PERIODS IN SEVERE TRAUMATIC BRAIN INJURY

**D.M. Sabirov¹, R.N. Akalaev², K.I. Mahkamov²,
R.N. Mavlyan-Khodjaev¹, A.L. Rosstalnaya¹,
S.E. Khaydarova¹, F.O. Parpibaev¹**

¹Tashkent Institute of Postgraduate Medical Education

²Republic Research Center of Emergency Medicine
Uzbekistan, Tashkent

Traumatism in people of young and active adult age has particular social significance among numerous problems of modern clinical medicine. According to the data of Konovalov AN et al., 2001, Klevno et al., 2001 and Sabirov DM et al., 2011, severe traumatic brain injuries (STBI) are 40 up to 50% of all injuries and is in the leading position in the structure of general

traumatism. Mortality even in mild traumatic brain injury reaches 5–10%, while in severe injuries it ranges from 41 up to 85%. After performing comparative analysis, we can say that mortality has not decreased in last years despite of many researches in pathogenesis of primary and secondary injuries of the brain, development of modern diagnostic methods, treatment and rehabilitation of patients with STBI. The importance of the problem does not raise doubts as more than one third of injured people die on accident place before the arrival of emergency aid or during transportation to the hospital.

OBJECTIVE: reveal dominant causes of prehospital and hospital mortality in patients with severe traumatic brain injury.

MATERIALS AND METHODS. We have analyzed 362 medical cases of the patients with STBI admitted to Republic Center of Emergency Medicine in last 2 years. 80% was men and 20% was women. Glasgow coma score was 8±3. Among these patients 55 died in different periods after admission. Mortality was 15.2% and 73% of them were men.

In prehospital and hospital periods after getting trauma during the first day 12 patients died (21.8%), during the first week 25 patients died (45.4%) and in

later periods 18 patients died (32.7%).

RESULTS AND DISCUSSION. The cause of death in the first group patients (mean hospital stay duration was 18.7 ± 5.5 hours; GCS in admittance 5 ± 2) was cerebral edema because of brain contusion ($n=6$) with brain dislocation ($n=4$). In some cases edema was of destructive character and when brainstem was involved, the trauma was incompatible with life ($n=2$).

Mean hospital stay duration of patients of the second group was 45.6 ± 15.9 hours and GCS was 7 ± 3 . The morphology manifested with the initial stages of necrotized brain tissue resorption, occurrence of active vascular-mesenchymal and glial reaction to the injury and hemorrhage resorption.

In later posttraumatic periods of STBI (mean hospital stay duration – 249.6 ± 34.7 hours; SCG – 8 ± 3) morphological picture was diverse. It was progressive development of secondary infection resulted in cardiac-pulmonary failure (81%), rarely multiple organ failure (13%) and endotoxicosis (6%).

CONCLUSIONS. The outcome of treatment of patients with STBI substantially depends on degree and quality of medical aid in prehospital and hospital periods.

THE MECHANISMS OF BACK PAIN FORMATION AND PATHOGENETIC TREATMENT

A.N. Serova, M.A. Kurbatov, A.A. Gerasimov

Medical Center "Help" Nizhny Novgorod, Russia
Ural State Medical University, Ekaterinburg, Russia

ABSTRACT. The author describes a new version of the pathogenesis of pain in the spine where the pain occurs during stimulation of bone receptors in conditions of circulatory disorders of bone tissue. The method for the recovery of the microcirculation is developed by interstitial electrostimulation. The complete elimination of back pain was proved in 90 % of patients.

KEYWORDS: interstitial electrostimulation, back pain, pain pathogenesis, spinal osteochondrosis.

INTRODUCTION. Back pain is the most common complaint among adults. Thus, the duration of incapacity for work increases each year. This indicates

that the quality of treatment does not become better. The new methods of treatment are created, but they are based on the old approaches and are the analogues of existing ones. These methods do not create a significant improvement of quality care.

Modern radiation diagnosis often does not correspond to the clinical picture. However, pathophysiological and functional changes can be detected long before the appearance of pain. Reasons of pain appearance do not often associated with hernial protrusion.

Recent decades physiologists explored new important players in the pathogenesis of the disease. Previously it was believed that the source of pain was the compression of the nerves exiting the spine bone, then the tension of the muscles. Many believe that periosteum is the reason of the formation of reflexory pain syndrome. In recent years, a lot of data have been accumulated to argue that the source of pain is the bone itself with its osteoreceptors that belong to the sympathetic nervous system.

Pathogenesis of the nidus formation, both in spinal bone and trigger zones, can be represented by follows. The initial changes in degenerative diseases of the spine firstly happen in the bony tissue as a local osteoporosis with destruction of trabecula of bone, the stagnation of blood in the venous system and intraosseous pressure and increase. Bone tissue contains a lot of osteoreceptors and irritation of them occurs with poor blood circulation. They react to the decrease of the partial pressure of oxygen in the bone vessels. It is proved that the worse blood circulation in bones, the more pain intensity. Later, the changes cover the periosteum and the swelling occurs. Pathology in vertebral bone progresses slowly, often it takes over the years. Pain manifestations are localized in bones, causing pain on palpation. An important clinical feature of process progression is the involvement of muscles. The secondary reflex tension arises and muscular-tonic syndrome develops. The irritation of osteoreceptors increases progressively, and then through a sinuvertebral nerve it affects the spinal nerves. The process of pain spread on periphery is performed by sclerotomic part of the nerve, to vertebrae symptomatic nerves. As a result, it breaks the trophism of bones in the limbs in the affected area of the sclerotome, which causes structural changes and additional pain.

Poor blood circulation in the bones is the initial link both for dystrophic phenomena in the intervertebral discs and for all the joints. As it is known, the nutrition of hyaline cartilage takes place by diffusion from the bone tissue of the vertebral bodies. Even small disturbances of direct arterial blood supply of bone leads to a drastic reduction of diffusion process of nutrients in the cartilage matrix. Interruption of this nutrition is the basis for the emergence of biochemical abnormalities, and degenerative phenomena in the intervertebral discs.

We have revealed with the help of a needle-radiography and polarography that metabolic processes in the limb bones depend on the intensity of pain syndrome in spinal bone. Severe pain weakens blood circulation and microcirculation in the bones in the area of innervation of the vertebral nerve of the. Poor circulation is an important factor in the occurrence of bone pain.

According to the described pathogenesis, treatment should be aimed at improving the circulation in bone tissue. Attempts to apply the known medicines for cardiovascular therapy did not give a significant effect. This happened due to the slow perfusion of drugs into the bone, which lead to greater concentration of them in the soft tissues than in bone. The second reason for the insufficient effect was a weak response of the vascular wall of bone blood vessels on antispasmodic drugs.

Physiotherapy treatment according to the known data is also ineffective. The skin is a barrier to the pas-

sage of the different types of energy within the body. Thus, the electric current is attenuated by skin cover in 200–500 times. The weakened current does not reach the bone. The bone is covered with endplates with a high resistance. Therefore, the current bypasses the bone through the conductive paths.

Thus, the interruption of circulatory in bone tissue is an important pathogenetic link. Therefore, the aim of our work was to develop an effective method of treatment based on this pathogenesis.

METHODS OF TREATMENT. We have found experimentally that the electric current improves blood circulation in bone and is a good stimulus for bone receptors. In order for the electric current to reach the bone, a metallic conductor in the form of needle was used. Sterile needle is applied to the acantha of the affected spine bone and make a special electrical current. Current characteristics were developed taking into account the parameters of natural bioelectric current flowing through the nerves. Therefore, the developed electric current is close to the physiological characteristics. This is a low frequency and complex modulated pulse current. The new method of treatment is called as interstitial electrostimulation. The equipment provides interstitial electrical procedures. The procedure is painless and comfortable, and is used for adults and children. The absence of complications allows to use the method in outpatient practice.

Special needle (disposable) is introduced to the depth of the skin prior to contact with the acantha of affected spinal bone, the passive electrode is placed on the affected limb. The current is transferred through the needle for 15–20 minutes. The sequential treatment of two spine bones is possible. Course of treatment depends on the number of involved spinal bones and pain points on the limb bones. Usually, the course consists of 4–6 procedures.

RESEARCH MATERIAL. 324 patients with spinal osteochondrosis of different localizations (cervical, thoracic and lumbar) were examined and treated. Each of these categories of patients was divided into 2 groups. One of these groups was the principal, where the treatment was carried out using the method of interstitial electrostimulation. The other group was a control group with a traditional modern complex treatment (medicinal physiotherapy, massage, stretching, reflexotherapy). Selection of patients was performed by method of envelopes. The results were comprehensively analyzed in groups. All the patients underwent clinical examination, radiography, computer tomography, rheography and polarography of spine, ultrasonic Doppler examination, electrometric study of pain, biomechanical study of the functions of the spine and limbs.

RESULTS AND DISCUSSION. Full management of vertebrogenic pain syndrome is achieved in 85–90% of hospitalized patients and 92–95 % in ambulatory patients. Traditional methods of pain relief helped to manage pain syndrome in 36% and 39%. Remote results of treatment were studied. It is determined that the duration of remission for more than 3 times exceed the period of traditional complex treatment. Timing of treatment using interstitial electrostimulation are reduced by 2.5 times.

The application of intratissual electric stimulation helped to reduce the period of temporary incapacity up to $11,2 \pm 2,4$ days, for the control group with traditional treatment – $25,3 \pm 3,2$ days ($p < 0,01$).

Relapses within 2 years after intratissual electric stimulation were observed in 5% of cases in the control group in 16–19% of patients. Complications of treatment were not observed. The method proved to be effective not only for elimination of referred pain, but also for the recovery of peripheral nerves.

The underlying mechanisms of therapeutic action are explored. 1. Overall reflex mechanism is implemented through the central nervous system and

promotes the development of opiatelike analgesic substances. 2. Local action is to improve the blood circulation in bone tissue. Method of interstitial reography and polarography of bone tissue has proved that this effect leads to a local restoration of blood circulation and microcirculation in the affected vertebra and periosteum. 3. In this method, a new mechanism of action via peripheral nerves to the patient limb arises. We have proved that under physiological intratissual electric stimulation the current excites the nerve cell structures and restores impaired function as in nerve trunks so in synaptic connections.

CONCLUSION. Thus, an important basis of pain syndrome in the spine is the primary interruption of blood circulatory in bone tissue. Specially developed method of interstitial electric stimulation effectively improves blood circulation and microcirculation of the spine bones being a pathogenetic effect.

Elimination of pain syndrome at interstitial electric stimulation occurs over 90% of the cases, the term of remission increases by 3 times or more during the reduction of treatment period by 2,5 times. Complications were not observed.

CIRCULATORY DISTURBANCES IN THE SPINAL CORD OF ADULTS (INNOVATIONS IN SPINAL ANGIONEUROLOGY)

A.A. Skoromets, S.A. Dambinova, T.A. Skoromets

*I.P. Pavlov Saint Petersburg State Medical University,
Saint Petersburg, Russia*

OBJECTIVE. To analyse features of anatomy and hemodynamics of spinal circulation (arterial and venous systems), pathogenesis of its disturbances and clinical picture. Develop classification principles and diagnostic algorithm for radiculomyelosclerosis of cervical, thoracic and lumbosacral spinal cord segments, differential diagnosis criteria of vascular and demyelinating diseases of the spinal cord. Develop therapeutic strategy and tactics in the treatment of acute and chronic radiculomyelosclerosis. Determine therapeutic effectiveness of some vasoactive and neurocytoprotective drugs (mostly arterial or venous spinal cord blood flow). To clarify the role and possibilities of biomarkers evaluation in terms of spinal cord ischemia.

MATERIAL AND METHODS. A large series of architectonics studies on arterial and venous systems of the

spinal cord was conducted. They were conducted at all levels using a latex mixture injected into the blood vessels and subsequent photographing. An experimental model of arterial and venous ischemia of thoracolumbosacral spinal segments was created. Ischemia was caused by ligation or compression of abdominal aorta and its branches (simulation of aorta and paraaortic area surgery) as well as compression of dural sac at the lower lumbar segments caused by balloon catheter during the experiment with cats (herniated disc simulation). Simultaneous blood filling at different levels of the spinal cord (cervical, lumbar enlargement and thoracic segments) in the presence of administration of vasoactive drugs (aminophylline, dibazol, nicotinic acid, etc.) was investigated using the original method of myelography.

A detailed study of the neurological status of patients with circulatory disturbances in the spinal cord was conducted. More than 1,000 patients participated in this study. Clinical picture features related to myelosclerosis of various segments of the spinal cord were assessed. Natural model for clinical

research of myeloischemia of the bottom half of the spinal cord was identified. This model also referred to myeloischemia course in response to neurosurgical removal of low lumbar discal herniation and use of some vasoactive drugs increasing arterial blood flow or improving venous outflow from the thoracolumbosacral spinal segments. Role and possibilities of contrast myelography (mayodil and pneumomyelography), spinal selective arteriography and MRI of spine and spinal cord in radiculomyeloischemia diagnostics were assessed.

RESULTS. Study of anatomy and physiology of spinal cord vascular system allowed to review "classic" idea that the spinal cord was supplied by "anterior spinal artery" with a direct rostral-caudal bloodstream originating from intracranial vertebral artery branches (its anterior spinal branches) and moving in caudal direction along the spinal cord. Our experimental and clinical pathomorphological studies show that the anterior spinal artery is not a separate vessel. It is an anastomotic tract like cerebral arterial circle of the brain, exerted along the spinal cord. Blood pumps through several major radiculomedullary arteries (the most important are the artery of Adamkiewicz for lumbar enlargement and the artery of the cervical enlargement) which form the anterior spinal anastomotic tract. Directions of arterial blood flow at different segments of the spinal cord are contralateral. Magistral and loose types of blood flow to the spinal cord were shown for the first time (similar to the structure of the arterial, venous and nervous systems in the human limbs according to the definition of anatomist V.N. Shevkunenko). Pathogenic blood flow compensation syndrome in the cerebrospinal hemodynamic was identified for the first time (analogue of "steal" syndrome in the brain). Biphasic effect of vasoactive drug aminophylline on the spinal hemodynamics was demonstrated for the first time. Variants of myeloischemia clinical picture were studied for the first time. Their classification, based on ischemia territory in the context of spinal cord breadth and length, was proposed (transversal myeloischemia of the ventral half of the breadth (Preobrazhenskiy syndrome), transversal myeloischemia of the dorsal third of the breadth (Williamson syndrome), transversal myeloischemia of one-half of the spinal cord breadth (ischemic Brown–Sequard's syndrome), centromedullar ischemia (syringomyeloischemia), antero-cornual poliomieloishemiya (ALS syndrome) Stanilovsksiy–Tanon syndrome etc.). The classification also based on angio topical principle (anterior spinal artery and sulcal-commissural artery district, posterior spinal artery district and vasocorona district). Congestive radicular veins of cauda equina in case of diskal hernia were examined using MRI of

the spine for the first time. This allowed to monitor the effectiveness of venotonic drugs such as L-lysine aescinat. Chronization of spondylogenetic back pain as a result of reduced endorphin levels in spinal fluid was explained for the first time. Also therapeutic efficacy of Cortexin polypeptide improving the production of endorphins in the brain stem was shown.

CONCLUSION. A new chapter in neuropathology, referred to peripheral vascular diseases of the spinal cord and its roots, was created.



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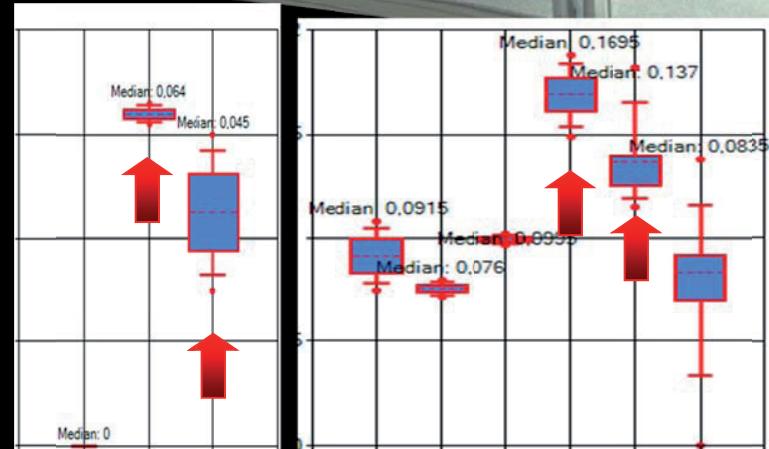
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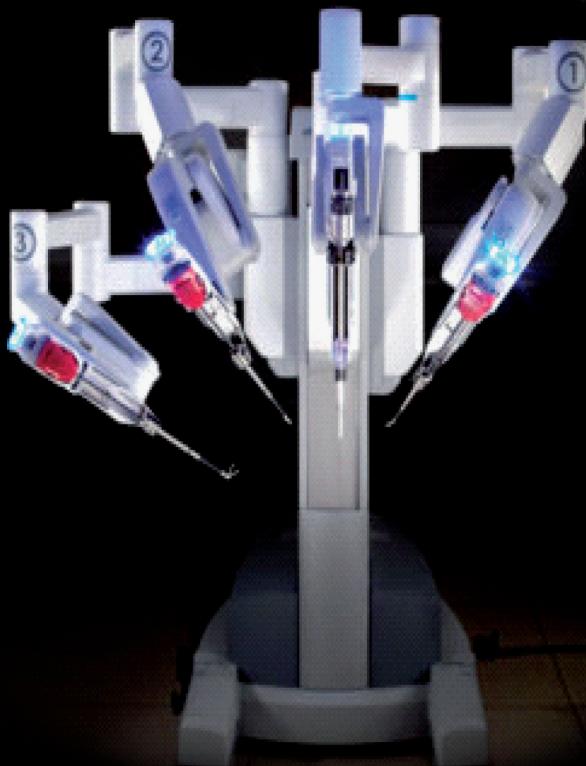
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