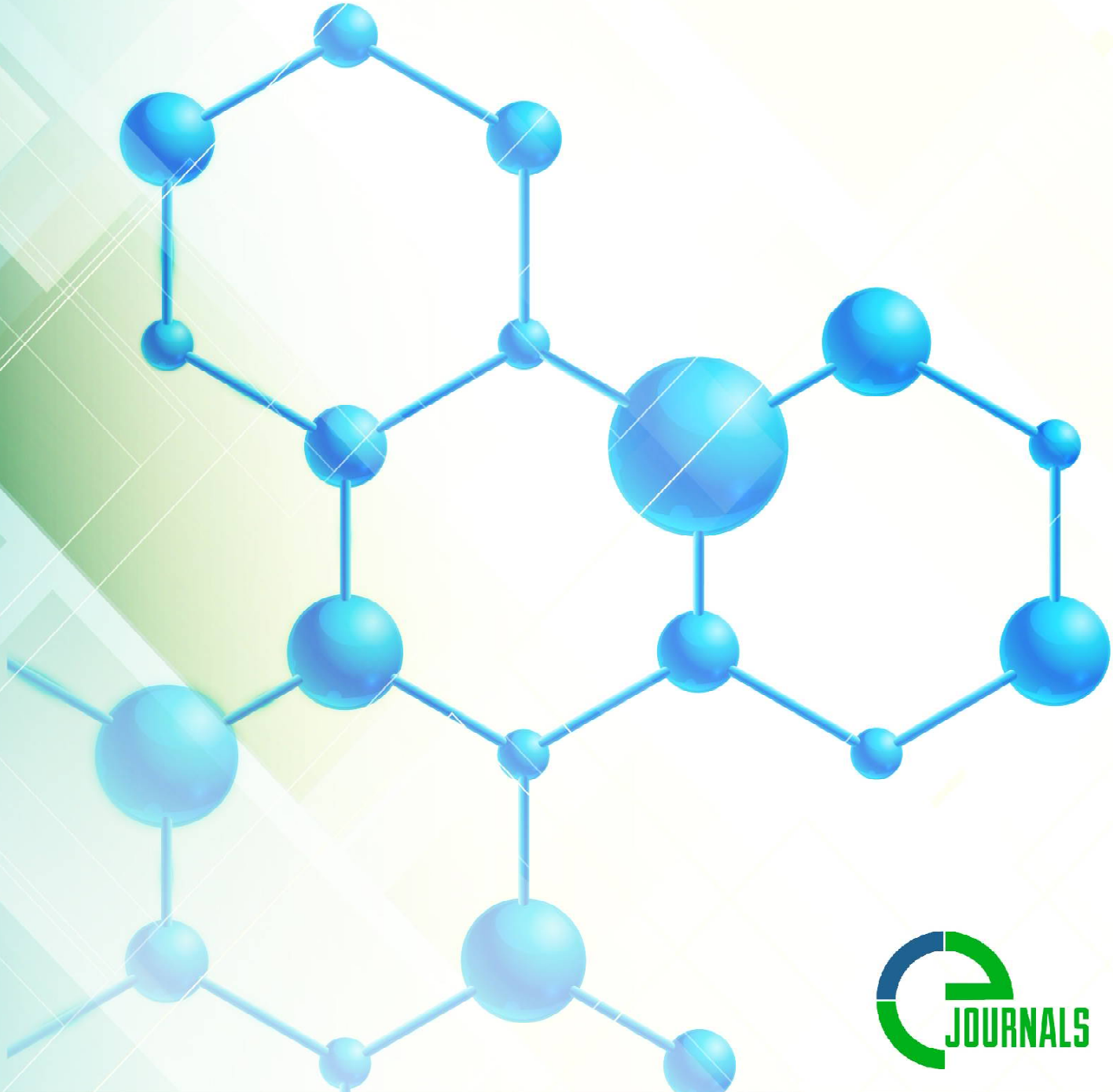
EUROPEAN JOURNAL OF

MOLECULAR MEDICINE



JOURNALS

European Journal of Molecular medicine
Volume 1, Issue 1, March 2021

Internet address: http://ejournals.id/index.php/EJMM/issue/archive
E-mail: info@ejournals.id
Published by ejournals PVT LTD
Issued Bimonthly
DOI prefix: 10.52325
Potsdamer Straße 170, 10784 Berlin, Germany

Requirements for the authors.

The manuscript authors must provide reliable results of the work done, as well as an objective judgment on the significance of the study. The data underlying the work should be presented accurately, without errors. The work should contain enough details and bibliographic references for possible reproduction. False or knowingly erroneous statements are perceived as unethical behavior and unacceptable.

Authors should make sure that the original work is submitted and, if other authors' works or claims are used, provide appropriate bibliographic references or citations. Plagiarism can exist in many forms - from representing someone else's work as copyright to copying or paraphrasing significant parts of another's work without attribution, as well as claiming one's rights to the results of another's research. Plagiarism in all forms constitutes unethical acts and is unacceptable. Responsibility for plagiarism is entirely on the shoulders of the authors.

Significant errors in published works. If the author detects significant errors or inaccuracies in the publication, the author must inform the editor of the journal or the publisher about this and interact with them in order to remove the publication as soon as possible or correct errors. If the editor or publisher has received information from a third party that the publication contains significant errors, the author must withdraw the work or correct the errors as soon as possible.

CONTENT

Daminov B., Raimkulova N., Ortiqboyev J.
CLINICAL CHARACTERISTICS OF ARTERIAL HYPOTENSION IN HEMODIALYSIS PATIENTS.....5
Shamukhamedova N., Kadirova G.
PLACE OF ENDOTHELIAL DYSFUNCTION IN THE FORMATION OF OBSTRUCTIVE PULMONARY DISEASE IN ARTERIAL HYPERTENSION....9
Kamalova M.I., Islamov SH.E.
MORPHOLOGICAL FEATURES OF ISCHEMIC AND HEMORRHAGIC BRAIN STROKES.....20
Akhmedov Yu.M., Akhmedov I.Yu.., Karimova G.S.
IS THE MEGAURETER THE PROBLEM OF YESTERDAY, TODAY OR TOMORROW?.....27
Rizaev J., Kubaev A.
PREOPERATIVE MISTAKES IN THE SURGICAL TREATMENT OF UPPER RETRO MICROGNATIA.....34

CLINICAL CHARACTERISTICS OF ARTERIAL HYPOTENSION IN HEMODIALYSIS PATIENTS

Botir Daminov
daminovbotirt@gmail.com
Narina Raimkulova
robertovnanarina@gmail.com
Jahongir Ortiqboyev
jakhongir2025@gmail.com
Tashkent Pediatric Medical Institute Republic of Uzbekistan.

Abstract: *There has been a steady increase in the number of patients with chronic kidney failure (CKD) worldwide. In CIS countries in the last decade chronic renal insufficiency has been registered with the frequency of 100-600 people per 1 million populations. Since the information on the prevalence of chronic renal failure (CRF) is based on circulating or dialysis center data, the true prevalence of CRF may be underestimated. The following substitution therapies are currently widely used to treat terminal stage chronic kidney disease (CKD): hemodialysis and permanent outpatient peritoneal dialysis, which can significantly prolong the lives of patients. [2, 8, 10]. Over the past five years, the number of patients in the world who are on kidney substitution therapy has increased by more than 25% and currently stands at over 2 million people. The largest growth in the number of such patients was recorded in developing countries (including Uzbekistan) - more than 50% in 5 years [5, 9]. A survey of 102 patients (59 women and 43 men) with CKD of stage 5 was conducted.*
Keywords: *sidial arterial hypotension, hemodialysis, chronic renal insufficiency, ultrafiltration.*

Introduction. Currently, the following replacement therapy methods are widely used to treat the terminal stage of chronic kidney disease (CKD): hemodialysis and continuous outpatient peritoneal dialysis, which can significantly extend the life of patients [3, 11].

Hemodialysis is a high-tech procedure associated with the use of multicomponent equipment, extracorporeal circulation, correction of water-electrolyte balance, changes in the acid-base state and osmolar equilibrium. In this regard, hemodialysis is accompanied by various complications. One of the most common complications is syndialytic hypotension (SDH) [6, 12]. According to various authors, LDH is detected in 25-55% of patients [4, 7, 13].

Arterial hypotension induced by the hemodialysis procedure increases the risk of vascular access thrombosis [4, 8, 10]. The presence of IDH episodes also affects the development of atrophy of the frontal lobes of the brain, which leads to functional neurological disorders and a deterioration in the quality of life [3, 5, 6]. Currently, there is no doubt the unfavorable prognostic value of SDH. Mortality in patients with SDH can reach 10-15% per year [13].

Purpose of the study. Determine the conditions for the occurrence of syndialytic arterial hypotension.

Materials and research methods: 102 patients (59 women and 43 men) with stage 5 CKD were examined. The average age of patients was 50.3 ± 2.4 years.

The criteria for inclusion in the study were the presence of stage 5 CKD according to the classification of the United States National Kidney Fund (NKF: K / DOQI Clinical Practice Guidelines for Chronic Kidney Disease, 2002) and renal replacement therapy with programmed hemodialysis for 1 year or more.

Exclusion criteria were acute myocardial infarction or acute cerebrovascular accident, paroxysmal cardiac arrhythmias, acute purulent-inflammatory and infectious diseases, diseases of the thyroid gland and adrenal glands, erosive and ulcerative lesions of the gastrointestinal tract and an indication of acute blood loss in history.

The development of chronic renal failure was due to: chronic glomerulonephritis in 51.0%, diabetic nephropathy in 13.7%, polycystic kidney disease in 8.8%, hypertension in 6.9%, congenital renal dysplasia in 5.9% , chronic pyelonephritis - in 3.9%, other diseases (renal amyloidosis, gouty nephropathy, bilateral renal artery stenosis, chronic tubulointerstitial nephritis, unspecified causes) - in 9.8% of patients.

Clinical and anamnestic data were studied in detail. The nature of drug therapy was evaluated. We analyzed the features of the hemodialysis procedure that can affect the likelihood of developing IDH (the frequency and duration of hemodialysis sessions, the composition of the dialysis solution, the type of dialyzer, the amount of ultrafiltration, etc.).

Measurement of blood pressure was performed before the start of the hemodialysis session, during the session (with an interval of 1 hour) and after it was completed, the relative (percentage) decrease in systolic and diastolic blood pressure was calculated for 1, 2, 3, 4 hours and for the entire duration of the hemodialysis procedure.

The IDH episodes were considered to decrease systolic blood pressure below 100 mmHg. or more than 20 mmHg. compared to the pre-dialysis level in case of clinical symptoms.

All patients underwent clinical and biochemical blood tests, additional instrumental studies and specialist consultations were conducted to exclude gastrointestinal diseases, endocrinological diseases and other possible causes of secondary arterial hypotension.

We also evaluated electrocardiography data in 12 conventional leads (to identify exclusion criteria) and echocardiography (to study the size of the heart chambers, its wall thickness and myocardial contractility).

Statistical processing was carried out using the Microsoft Excel software package (version 14.0). When conducting statistical processing, methods of parametric and nonparametric statistics were used.

Results of the study: Out of the 102 patients included in the study, episodes of SDH within 1 year were observed in 71 patients. Among them were 32 people with frequent episodes of SDH (on average, 6.59 ± 0.87 per month) and 39 people with relatively rare episodes of SDH (on average, 0.87 ± 0.14 per month). Patients without episodes of SDH (31 people) made up the control group.

Differences in the frequency of SDH in men and women were not statistically significant (2.2 ± 1.2 and 3.8 ± 0.9 episodes per month, respectively).

The results of the study showed that the most common episodes of SDH occur in patients with diabetic nephropathy. The relative risk of developing IDH in patients with chronic glomerulonephritis is 62% less, and in patients with polycystic kidney disease - 81% less.

The duration of hemodialysis treatment ranged from 12 to 288 months. The average duration of hemodialysis treatment was maximum in patients with frequent episodes of SDH, comprising group 2 (111.9 ± 12.6 months), and minimum in the control group (70.5 ± 14.8 months). The differences between these groups were statistically significant ($t = 2.14$; $p = 0.041$). The average duration of hemodialysis treatment in the group with relatively rare episodes of IDH was 83.7 ± 10.6 months.

The average levels of predialysis systolic and diastolic blood pressure for 1 month of observation were: in the group of patients with rare episodes of SDH - 136.8 ± 3.2 and 79.7 ± 1.8 mm mmHg., in patients with frequent episodes of SDH - 116.7 ± 4.4 and 70.8 ± 2.4 mmHg., in the control group (without episodes of SDH) - 148.5 ± 6.3 and 84.6 ± 3.1 mmHg., respectively. In the majority of patients in the control group, the figures of pre-dialysis blood pressure corresponded to arterial hypertension (mainly systolic).

When conducting a correlation analysis, we found that the pre-dialysis indicators of systolic blood pressure negatively correlate with the duration of hemodialysis treatment ($rs = -0.240$; $p = 0.017$) and the average monthly number of episodes of SDH ($rs = -0.399$; $p < 0.001$). Similar, but less powerful, correlation relationships were identified for indicators of diastolic, middle and pulse pre-dialysis blood pressure.

Analyzing the intradialytic indicators of blood pressure, we found that in most patients, episodes of SDH developed 3-4 hours after the onset of hemodialysis. The duration of the episode in 60.6% of cases did not exceed 1 hour, in 18.3% - from 1 to 2 hours, in 5.6% - from 2 to 3 hours, in 7.0% - more

The average values of systolic and diastolic blood pressure after 1 hour and 2 hours after the start of the hemodialysis procedure did not significantly differ from the corresponding indicators of pre-dialysis and post-dialysis blood pressure. Mean systolic blood pressure after 3 hours (112.3 ± 4.1 mm Hg) and 4 hours (103.8 ± 2.6 mm Hg) after hemodialysis started, as well as post-dialysis blood pressure (117.0 ± 4.2 mm Hg), were significantly lower than the pre-dialysis level - 145.0 ± 4.7 mm Hg. Art. ($p < 0.01$). Diastolic blood pressure after 3 hours (62.4 ± 1.8 mm Hg) and 4 hours (60.0 ± 1.5 mm Hg) after the start of the procedure were also below the pre-dialysis level - 76.3 ± 2.3 mmHg Art. ($p < 0.001$). Postdialysis diastolic blood pressure did not significantly differ from predialysis.

Averaged (according to hourly measurements) intradialysis indicators of systolic blood pressure correlated: negatively with the duration of hemodialysis treatment ($rs = -0.458$; $p = 0.042$) and intradialystic weight gain ($rs = -0.469$; $p = 0.037$).

In many patients, episodes of IDH were combined with arterial hypertension in the intradialystic period or during other hemodialysis sessions. Antihypertensive drugs were received by 68.6% of patients under observation. ACE inhibitors were most often prescribed, less commonly, β-adrenergic blockers and calcium channel blockers. 65.7% of patients received erythropoiesis stimulants. Significant differences in the frequency of prescription of erythropoiesis stimulants and the main classes of antihypertensive drugs between groups of patients with episodes of SDH and without episodes of SDH were not detected.

Most patients observed received hemodialysis 3 times a week. 5 out of 71 patients with episodes of IDH (7.0%) were on hemodialysis twice. The average monthly number of SDH episodes and relative changes in blood pressure during the hemodialysis procedure in these patients did not significantly differ from other patients, however, a correct comparison was not possible due to the small size of the group, as well as differences in age, body weight, and other clinical and laboratory parameters. In general, according to our data, the hemodialysis regimen did not have a significant effect on the incidence of SDH. However, we do not exclude that this factor may be relevant in situations where existing recommendations for determining the adequacy and dose of hemodialysis are not followed.

The intradialytic gain in body weight ranged from 0.8 to 5.3 kg. The absolute value of the increase in body weight did not correlate with the age of the patients, the duration of hemodialysis treatment, and pre-dialysis blood pressure. However, there was a statistical relationship with the average intradialytic values of systolic blood pressure ($rs = -0.469$; $p = 0.037$) and the relative (percentage) change in systolic and diastolic blood pressure for the entire hemodialysis procedure ($rs = -0.262$; $p = 0.012$ and $rs = -0.312$; $p = 0.002$, respectively).

The amount of ultrafiltration was closely associated with interdialysis weight gain ($rs = 0.795$, $p < 0.001$) and ranged from 0.1 to 4.9 liters. When conducting a correlation analysis, we found that in most cases the correlations of the main clinical data with the relative magnitude of ultrafiltration are of greater strength and statistical significance than correlations with the absolute indicator.

When studying laboratory data, it was found that patients with relatively rare episodes of SDH and with frequent episodes of SDH had lower hemoglobin compared with patients in the control group who did not develop SDH (108.3 ± 2.4, 107.2 ± 3.1 and 117.0 ± 2.2 g/l, respectively). Similar differences were also characteristic of the hematocrit level (31.5 ± 0.8, 31.9 ± 0.7 and 34.6 ± 0.8%, respectively). Significant intergroup differences in the average hemoglobin content in the erythrocyte, the average volume of red blood cells, the number of leukocytes, platelets and ESR were not detected.

An echocardiographic study was performed to identify left ventricular hypertrophy and assess myocardial contractility.

Left ventricular hypertrophy, diagnosed by MMILV, was observed in the vast majority of patients (91.2%). The main echocardiographic parameters had negative correlation with the average monthly number of IDH episodes and positive correlations with pre-dialysis and post-dialysis blood pressure, as well as with a relative change in systolic blood pressure over the entire hemodialysis session. Systolic dysfunction of the left ventricle was observed in less than a fifth of patients. An ejection fraction of less than 40% was not observed.

Conclusions:

1. The frequency of episodes of syndialytic hypotension was correlated with the duration of hemodialysis treatment and the nature of the underlying disease.

2. In patients with diabetic nephropathy, syndialytic hypotension was observed 2.6 times more often than in patients with chronic glomerulonephritis, and 5.3 times more often than in patients with polycystic kidney disease ($p < 0.01$).

3. The average monthly number of episodes of intra-dialysis hypotension negatively correlated with the average level of both pre-dialysis systolic ($rs = -0.399$; $p < 0.001$) and post-dialysis systolic blood pressure ($rs = -0.691$; $p < 0.001$).

4. The frequency of intradialytic hypotension in the absence of clinically significant heart diseases does not correlate with systolic dysfunction of the left ventricle.

References:

1.Stetsyuk EA. Sodium in dialysate. In: Stetsyuk EA, Lashu-tin SV, Chuprasov WB, ed. Dialysis almanac. Elby-SPb, SPb., 2005; pp.100-106

2.Suvorov AB, Zubeeva GN, Suslova OA, etc. Features of arterial hypertension in patients with end-stage chronic renal failure in the pre-dialysis and dialysis periods. Honey Almanac 2010; 4: pp.249-251

3.Fedorova Yu.Yu. Factors affecting the frequency of intradialysis hypotension in patients receiving treatment with programmed hemodialysis / Yu. Yu. Fedorova // Materials of the 16th All-Russian Medical and Biological Conference of Young Researchers “Fundamental Science and Clinical Medicine - Man and His Health”. - St. Petersburg, 2013 .--pp. 424-425.

4.Shishkin A. N. Modern ideas about the etiology and pathogenesis of intra-dialysis hypotension (literature review) / A. N. Shishkin, Yu. Yu. Fedorova // Bulletin of St. Petersburg University. - 2012. - No. 3. - pp. 23-33.

5.Booth J, Pinney J, Davenport A. The effect of vascular access modality on changes in fluid content in the arms as determined by multifrequency bioimpedance. Nephrol Dial Transplant 2011; 26(1): pp.227-231

6.Chang TI, Paik J, Greene T et al. Intradialytic hypotension and vascular access thrombosis. J Am Soc Nephrol 2011; 22(8): pp.1526-1533

7.Chesterton LJ, Selby NM, Burton OJ et al. Cool dialysate reduces asymptomatic intradialytic hypotension and increases baroreflex variability. HemodialInt 2009; 13(2): pp.189-196

8.Gabrielli D, Kristal B, Katzarski K et al. Improved intradialytic stability during haemodialysis with blood volume-controlled ultrafiltration. J Nephrol 2009; 22(2): pp.232-240

9.Korkor AB, Bretzmann CM, Eastwood DE. Effect of dialysate temperature on intradialytic hypotension. Dial Transplant 2010; 39(9): pp.377-385

10.Pakfetrat M, Roozbeh Shahroodi J, Malekmakan L et al. Is there an association between intradialytic hypotension and serum magnesium changes? Hemodial Int 2010; 14(4): 492-497

11.Phillipps LM, Harris DC. Review: modeling the dialysate. Nephrology (Carlton) 2010; 15(4): pp.393-398

12.van der Sande FM, Wystrychowski G, Kooman JP et al. Control of core temperature and blood pressure stability during hemodialysis. Clin Am Soc Nephrol 2009; 4(1): pp.93-98

13.Venkat A, Kaufmann K, Venkat KK. Care of end-stage renal disease patient on dialysis in the ED. Am J Emerg Med 2006; 24(7): pp.847-858

PLACE OF ENDOTHELIAL DYSFUNCTION IN THE FORMATION OF OBSTRUCTIVE PULMONARY DISEASE IN ARTERIAL HYPERTENSION

Nafisa Shamukhamedova
Botir Daminov
Gulchekhra Kadirova
E-mail: nafis.shamuk@bk.ru
Tashkent Pediatric Medical Institute Republic of Uzbekistan

Abstacrt.Chronic obstructive pulmonary disease and arterial hypertension are common diseases with the formation of cardiorespiratory comorbidity, which mutually aggravates the condition of patients, forming certain features of the course of the disease due to the commonality of some links of pathogenesis. The article presents literature data on the role of endothelial dysfunction in the progression of chronic obstructive pulmonary disease in arterial hypertension.

Keywords: chronic obstructive pulmonary disease, arterial hypertension, endothelial dysfunction.

Introduction. Chronic obstructive pulmonary disease (COPD) is a common pathology, leading to death, disability of millions of people. The prevalence of COPD in the world is growing and among people over 40 varies from 7 to 18.2% [14.42]. In the structure of total mortality from respiratory diseases, COPD is the first among the causes of mortality. Each year, COPD is the cause of death of about 3 million people, according to forecasts by World Health Organization experts, by 2030, COPD will take 4th place among other causes of mortality due to the spreading epidemic of smoking and a decrease in mortality from other causes [29].

The combination of COPD and cardiovascular disease, in particular arterial hypertension (AH), is one of the most common aggravating comorbid conditions in the clinic. The prevalence of arterial hypertension (AH) among patients with COPD varies widely and amounts to 76.3% of cases, averaging 34.3% [1.24.33].

In the studies of V. S. Zadiochenko [3], the concept of comorbidity is put forward on the agenda, which implies the formation of interconnections and mutual influences between coexisting diseases, as well as the presence of common pathogenetic mechanisms, such as chronic inflammation of low gradation, oxidative stress and endothelial dysfunction.

COPD is considered as a systemic disease with various extrapulmonary manifestations, which in most cases determines the prognosis and outcome of the disease. Moreover, violations of vascular changes are of no small importance, in particular, cardiovascular complications are among the main systemic manifestations of COPD [44]. Thus, cardiovascular diseases (CVD) are more common in patients with COPD than in the general population.

The development of cardiorespiratory comorbidity, accompanied by a mutual aggravation syndrome, due to the commonality of some links of pathogenesis, forms a special clinical picture that leads to a worsening prognosis of the disease and dictates the consideration of this condition in a special framework and requires new diagnostic approaches to improve therapeutic tactics [7].

Cardiorespiratory comorbidity of COPD and AH is a combination of complex multi-stage pathogenetic processes, among which the leading factor is difficult to identify. The main pathogenetic mechanisms leading to the development and progression of hypertension

in COPD are systemic inflammation and oxidative stress, which causes dysfunction and / or damage to the endothelium [55], which serves as an independent predictor of poor prognosis for most cardiovascular diseases and makes vascular endothelium a vulnerable target.

According to literature, to date, not all mechanisms of the pathogenesis of hypertension in COPD and their relationships have been sufficiently studied. In recent decades, in the pathogenesis of hypertension, as well as in atherogenesis, great importance has been attached to studying the role of endothelium and the development of endothelial dysfunction [23].

In case of vascular disturbances in the combined course of arterial hypertension and COPD, endothelial dysfunction, early disturbances in the ratio of prooxidant and antioxidant systems, high lipoperoxidation syndrome, tissue hypoxia, systemic disorders of vascular-platelet and fibrinolytic hemostasis with depletion of anticoagulant reserve are important [6].

Some common mechanisms in the pathogenesis of COPD and hypertension can be distinguished - this is the development of a systemic inflammatory response, oxidative stress and endothelial dysfunction, which are considered to be a key link in the development of cardiorespiratory comorbidity [20,49].

In this case, the formation of secondary pulmonary arterial hypertension (PAH) with an increase in the load on the right heart and left atrium leads to a deterioration of the coronary reserve, which enhances myocardial ischemia in both ventricles and leads to the progression of both coronary and pulmonary insufficiency.

There is also an inverse relationship, i.e. CVD impact on the development of exacerbations of COPD. So, not only the frequency of exacerbations affects the quality of life, but in most cases determines the prognosis of the disease in these patients. According to the results of the study, the cause of acute exacerbation of COPD requiring hospitalization in more than 40% of cases was the destabilization of CVD [8].

Among patients with bronchial obstructive diseases, not only local inflammation of the bronchi, but also persistent systemic inflammation, which is characteristic of patients with COPD, makes a significant contribution to the pathogenesis of atherosclerosis and other cardiovascular diseases, contributing to the development and progression of endothelial dysfunction. This explains the ongoing interest in the study of this pathology [43].

In recent years, more and more information has been accumulating that assessing the state of the endothelium can be of great clinical importance to expand understanding of the pathogenesis of many diseases and predict the development of complications. All this indicates that the development of ED is currently one of the main components in the pathogenesis of hypertension and COPD.

Endothelial dysfunction is understood to mean a violation of parity between the production of vasodilating, angioprotective, antiproliferative factors, on the one hand, and vasoconstrictor, prothrombotic, proliferative endothelial producers, on the other.

Endothelial dysfunction (ED) and chronic persistent inflammation are interrelated processes that play a key role in the development and progression of both COPD and hypertension. These mechanisms constantly potentiate each other, creating a vicious cycle, and contribute to the formation and progression of hypertension in COPD.

Research data from recent decades indicate the important role of ED in the study of the pathogenesis of diseases with combined pathology, which is an important mechanism for their formation and progression [21,22,25,45].

Endothelial dysfunction affects the severity of the clinical picture. Of direct clinical importance is the assessment of the degree of these disorders, which will reveal the subtle mechanisms of the onset and development of diseases. At present, various markers of ED have been identified, which can act as an indicator of both the severity of the disease and the effectiveness of the drug therapy, as well as methods for their assessment [21,22,25,45].

Vascular endothelium is a hormonally active tissue that regulates vascular tone by releasing vasodilating and vasoconstrictor factors and models the contractile activity of smooth muscle cells. Endothelial cells are the first to experience the effects of free oxygen radicals, oxidized low density lipoproteins, high cholesterol concentrations and hydrostatic pressure inside the vessels lined with them. With various vascular diseases and metabolic disorders, the ability of endothelial cells to release relaxing factors decreases, while the formation of vasoconstrictor factors persists or increases, which leads to ED [13].

ED is a complex process, based on, firstly, an imbalance between processes such as vasoconstriction and vasodilation, secondly, impaired production of factors of inflammation and vascular proliferation, and thirdly, damage to the thrombosis system. All this ultimately leads to remodeling of the vascular wall [17].

ED is considered as a systemic disorder characterized primarily by a decrease in the production of nitric oxide (NO). ED is a pathological condition that worsens vascular homeostasis and leads to the loss of protective properties of endothelial cells [19,31,39,40,60].

The leading role in the pathogenesis of ED is assigned to NO [17,19,60]. NO is synthesized in endothelial cells from L-arginine under the influence of the enzyme endothelial NO synthase (eNOS). Under the influence of various mediators, an increase in the concentration of intracellular calcium (Ca2 +) occurs, where it, by binding, forms the Ca2 + -calmodulin complex, which, acting as a cofactor, activates eNOS. The synthesis of NO proceeds with the participation of a number of other cofactors [39,40]. NO penetrates smooth muscle cells and causes relaxation by activating guanylate cyclase, thereby increasing the concentration of cyclic guanosine monophosphate, which, in turn, mediates the effects of NO. NO is a mediator of endothelium-dependent vasodilation (EDVD) due to the inhibitory effect on vasoconstrictors such as AT II and endothelin (ET). In addition, NO inhibits platelet aggregation, leukocyte adhesion, infiltration and proliferation of vascular smooth muscle cells. NO inhibits oxidative modification of LDL [31].

Specific inactivation of the eNOS gene is accompanied by an increase in mean blood pressure by approximately 15-20 mm Hg. Art. It is proved that patients with hypertension have a less vasodilating response to intraarterial administration of acetylcholine compared with the control normotensive group. There is also an inducible form of NO synthase (iNOS), which is produced in the vascular wall during inflammatory processes. iNOS produces an excess amount of NO, which leads to vasoconstriction and a decrease in endothelium-dependent vasodilation [19,39,40]. It is clear that the more iNOS is produced, the more severe the clinical manifestations.

In contrast to NO, as a vasodilator, the body produces a powerful vasoconstrictor - ET-1 or, in a number of literary sources, simply ET [21,25,54]. ET-1 belongs to the number of biologically active bicyclic polypeptides of a wide spectrum of action, consisting of a combination of 21 amino acids. Today it is one of the most significant regulators of the functional state of vascular endothelium.

It is known that endothelin-1 has a powerful vasoconstrictor effect, inhibits the formation of NO in the vessels, mediates the mitogenic effect, enhances the proliferation of cardiomyocytes and smooth muscle cells of the vascular wall, and stimulates the production of a number of cytokines and growth factors. In response to hypoxia, an increase in endothelial production of vasoconstrictor substances was noted along with a decrease in the formation of vasodilating substances. Endothelin-1 is considered as a marker of many vascular pathologies: coronary heart disease [55], myocardial infarction, atherosclerotic vascular damage, hypertension, preeclampsia and eclampsia, renal vascular pathology, ischemic brain damage, non-infectious pulmonary diseases. In patients with COPD with hypoxemia, the level of endothelin-1 in arterial blood is higher than in patients with COPD without hypoxemia [55].

The production of ET-1 in the body is promoted by hypoxia, ischemia, hemodynamic overload, changes in acid-base balance, hyperglycemia, hypercholesterolemia, oxidative stress [25,30,40]. Inducers of ET synthesis are vasoconstrictors, growth factors, cytokines, thrombin, and adhesion molecules. In contrast, ET synthesis inhibitors are prostacyclin, estrogens, atrial natriuretic peptide, as well as the previously mentioned NO.

From the above it follows that endothelial dysfunction is considered as the main mechanism for the formation of increased pressure and its complications, and also serves as a quantitative marker of its progression [38].

Studies by S.I.Ovcharenko and co-authors on the determination of markers of systemic inflammation and endothelial dysfunction and their relationship with various parameters in patients with COPD in combination with hypertension revealed high levels of markers of inflammation and ED (highly sensitive C-reactive protein - hsCPB, a soluble form of the cell-cell adhesion molecule Type 1 - sICAM-1, endothelin-1 and sP-selectin). The study noted that as systolic blood pressure increases and bronchial obstruction worsens, the degree of violation of markers of inflammatory status and ED increases [10].

According to some authors, it was found that endothelium is involved in the pathological process at the earliest stages of increased pressure [48].

A number of clinical studies indicate that not only with increasing pressure, but also with other pathological conditions, an increase in ET-1 level is noted [38,40,57].

The concentration of ET-1 in blood plasma was highest in patients with hypertension, combined with atherosclerotic lesions of the arteries [60].

Particular importance should be given to the contribution of ED to the pathogenesis of chronic obstructive pulmonary disease (COPD). The systemic inflammation observed in COPD appears to be a key determinant of pulmonary and systemic ED [15.51.59]. However, a meta-analysis of an Italian group of scientists did not reveal a correlation between ED risk factors for COPD, but established a clear relationship between COPD and ED [16]. A number of studies have identified the relationship between airflow obstruction and endothelial status, assessed by determining the levels of C-reactive protein, interleukin-6, and malondialdehyde, as well as testing with endothelial-independent vasodilation [17].

The presence of high levels of ET-1 among patients with COPD contributes to a more malignant course of both pulmonary and cardiac pathology, leading to cardiovascular remodeling, which is manifested by dilatation of all heart chambers and the formation of chronic pulmonary heart [15,26,34,35,37,52] .

There are also two other ET isoforms - ET-2 and ET-3. Between themselves ET differ in the sequence of amino acids. The synthesis of all three ETs is encoded by

different genes [25,30]. ETs are identified in various organs and tissues. ET-1 is defined in endothelial cells, but unlike other ETs, it can also be synthesized in smooth muscle cells of blood vessels, neurons, hepatocytes, endometrium, mesagangliocytes, mammary endotheliocytes, and tissue basophils. Under pathophysiological conditions, a large number of nonendothelial cells in the heart, including cardiomyocytes, can also synthesize ET-1 in response to stretching of the myocardium, AT II, and norepinephrine [53].

Studies to determine the level of markers of inflammation, ED and their relationship with various parameters in patients with COPD in combination with hypertension revealed that the levels of ET-1 and s-Selectin exceeded normal values. An increased level of biochemical markers of ED can be a consequence of endothelial damage. The results showed an increase in the level of the studied markers (hsCRP, sICAM1, ET-1, sRselectin), which indicates the presence of active systemic inflammation and ED in patients with COPD + AH. It has been established that vascular wall lesions in patients with COPD + AH are characterized by a high level of soluble form of sICAM1, which confirms the presence of endothelial damaging factors [10].

The revealed statistically significant linear correlation between the level of hsCRP, ET-1 with FEV1 and SBP confirm the role of bronchial obstruction in the formation and progression of cardiovascular pathology, which indicates the presence of common pathogenetic processes in patients with COPD with hypertension. In the process of examining patients with COPD with hypertension, it was revealed that as the SBP increased and bronchial obstruction worsened, the degree of violation of the markers of inflammatory status and ED increased [10].

A prospective study [55] showed the relationship between endothelial dysfunction and the development of adverse cardiovascular complications in patients with coronary heart disease, hypertension, and peripheral atherosclerosis.That is why the concept of endothelium as a target organ in the prevention and treatment of CVD is currently formulated.

This position was also confirmed in the studies of S.I.Ovcharenko, Z.N. Nersenyan, in which, in order to determine prognostic significant markers of inflammatory status and endothelial dysfunction in patients with COPD in combination with hypertension. Thus, it was shown in the work that, as bronchial obstruction worsens, the intensity of markers of inflammation and endothelial dysfunction increases [10].

A local inflammatory response in the lungs is accompanied by activation of systemic inflammation, increased oxidative stress, which also leads to impaired vascular endothelial function [27]. These processes are caused by the action of various acute-phase parameters (C-reactive protein - CRP) and pro-inflammatory cytokines (interferon?, interleukins-IL, tumor necrosis factor ?-TNF?), the level and activity of which increase significantly in many chronic diseases of internal organs, including with COPD [9]. The literature data indicate that the development of ED is currently one of the main factors in the pathogenesis of PAH in COPD.

Recently, the role of NO has been actively studied in the pathogenesis of lung diseases. It has been shown that ED in COPD is manifested by a decrease in vasodilation, which may be due to both a decrease in the release of the endothelial relaxing factor and a decrease in the susceptibility of vascular smooth muscles to this substance [11]. With prolonged hypoxia, endothelial relaxation functions decrease, which causes a narrowing of the vessels of the lungs and the occurrence of PAH. NO in COPD determines a particularly high oxidative activity in the lower respiratory tract, as inducible NO synthase is expressed mainly during their inflammation. E.G. Zarubina et al. [4] a study

was conducted of endothelial regulation of vascular tone using ultrasound in patients with COPD in the acute stage and coronary heart disease. It was established that the increase in NO in patients with combined pathology was less in comparison with the group with only COPD and the group with coronary heart disease.

Some studies presented data on an increase in selectin levels in patients with COPD and PAH, indicating the development of ED [58].

As mentioned above, endothelin-1, a polypeptide that is synthesized in bronchial epithelium, endothelium, and macrophages, plays an important role in the pathogenesis of ED. An increase in its concentration is recorded in patients with COPD and PAH, provoking the development of vasoconstriction and the progression of ED [28]. So, when examining patients with COPD in combination with coronary heart disease and hypertension (GB), ED was revealed, manifested by overproduction of endothelin-1 and natriuretic peptide C [2]. At the same time, it is indicated that CNP is a more sensitive indirect marker of ED. This indicates an exacerbation of NO deficiency in the combination of COPD with AH compared with mononosology. Similar results were obtained in the work of S. A. Pribylov [12], where patients with COPD and chronic heart failure (CHF) of ischemic origin showed a higher plasma content of endothelin-1 in combination with ED and an increase in pulmonary pressure, accompanied by diastolic myocardial dysfunction.

According to the research of A.Kh. Akhmineva [2], the study of markers of endothelial dysfunction in chronic obstructive pulmonary disease in a combined pathology in patients with COPD in combination with hypertension and coronary heart disease revealed endothelial dysfunction, manifested by hyper-production of ET-1 and NPS. There was a statistically significant increase in the level of NSAIDs in the group of patients with COPD + AH compared with those in the groups AH and COPD, while the level of ET-1 with a combination of COPD + AH remained comparable to the levels in the groups of patients with COPD and AH. This indicates that CNP is a more sensitive indirect indicator of endothelial dysfunction and indicates an aggravation of nitric oxide deficiency in the combination of COPD + AH compared with mononosology.

It is believed that circulating endothelial progenitor cells (CEPCs) play an important role in maintaining the integrity of the endothelium [32]. There is evidence that a decrease in the level of CEPCs disrupts the systemic function of the vascular wall, which in turn increases the cardiovascular risk.

In the work of S. Pizarro et al. [47] in patients with COPD, a decrease in the number of CEPCs that perform a reparative function in response to damage to the vascular wall and / or tissue ischemia was found, which in turn led to the progression of atherosclerosis and the development of CVD. A study in patients with COPD [36] combined with PAH showed a decrease in CEPCs. Moreover, the number and functional abilities of CEPCs had a negative correlation with the level of pressure in the pulmonary artery. It is suggested that a violation of epigenetic regulation plays a role in the dysfunction of CEPCs, which may contribute to the development of cardiovascular events in patients with COPD [46].

There is evidence of the involvement of Rhokinase in vascular endothelial damage. To date, 2 of its isoforms are known: Rho-kinase1 and Rho-kinase2. The latter is expressed in vascular smooth muscle cells and endothelial cells. Activation of Rho kinase 2 of active GTP-bound Rho-A leads to sensitization of calcium in smooth muscle cells through phosphorylation-mediated inhibition of myosin light chain phosphatase activity and thereby enhances the activity of the regulatory myosin light

chain. It is known that Rho-kinase is involved in many pathophysiological processes, among which the following can be distinguished: narrowing of blood vessels, including the development of myogenic tone and excessive contractile ability of smooth muscles, reduction of smooth muscles of the bronchi in COPD, PAH, ED. These data are confirmed by a number of studies. So, in the work of Y.Bei et al. [18] showed that activation of RhoA / Rhokinase plays an important role in the development of ED in patients with COPD. A significant decrease in endothelium-dependent relaxation and NO levels was found, while the activity of RhoA / Rhokinase was increased in the pulmonary arteries of patients with COPD compared with the control group. Thus, the researchers associated the development of ED in patients with COPD with a suppression of the activity of endothelial NO synthase and activation of RhoA / Rhokinase.

According to N.A. Caroli, A.P. Rebrova during exacerbation in patients with COPD with hypertension, the rates of EDVD were significantly lower than in patients without hypertension [5]. A decrease in EDVD of less than 10% in patients with COPD in the presence of hypertension is detected 2 times more often than without it (59.1% versus 25%) and almost 6 times more often than in healthy individuals (59.1% versus 10%). The data obtained indicate a more pronounced violation of the endothelium-dependent function of the vascular wall in patients with COPD in the presence of hypertension. An increase in the number of circulating endothelial cells (CEC) and their conglomerates in patients with COPD during an exacerbation of the disease, regardless of the presence of hypertension, was also found. Thus, this work has demonstrated that patients with COPD without hypertension already have damage to the vascular wall and impaired antithrombogenic and vasoregulatory function of the endothelium. Moreover, these disorders exist both in the period of exacerbation and in the period of a stable state of patients, and are more pronounced in patients with severe COPD. The identified violations are based on a whole range of pathogenetic factors. The data obtained confirm that the presence of hypertension in patients with COPD leads to more pronounced damage to the vascular wall and a violation of its vasoregulatory function than in patients without hypertension. These differences are most pronounced during an exacerbation of COPD, which may be due to the depletion of compensatory mechanisms in patients with hypertension. Moreover, in the period of stable course of COPD in patients with hypertension, damage to the vascular wall is more pronounced, and in the period of exacerbation, a violation of EDVD is more pronounced than in patients with COPD without hypertension.

Conclusion. Thus, the combination of hypertension and COPD has a negative effect on the state of the vascular wall. In comorbid conditions, endothelial damage and endothelial dysfunction are more pronounced than in the presence of a single disease.

Endothelial dysfunction and chronic persistent inflammation are interrelated processes that play a key role in the development and progression of both COPD and hypertension. These mechanisms constantly potentiate each other, creating a vicious cycle, and contribute to the formation and progression of hypertension in COPD. The appearance of cardiorespiratory comorbidity, accompanied by a syndrome of mutual burdening, forms the features of the clinical picture and diagnosis, which causes certain difficulties in the management of such patients.

It is important to note that the task of modern researchers is to find ways of early detection and correction of changes in the functioning of the endothelium. Only a comprehensive assessment of endothelial function can act as the severity of the prognosis of ED in patients with COPD, as well as an indicator of the effectiveness of drug

therapy. To improve the duration and quality of life of patients, reduce the risk, the frequency of complications and mortality rates, it is necessary to study the function of the endothelium in more detail and look for ways of drug correction taking into account the pathogenetic mechanisms of its formation.

References:

1.Arterial hypertension and COPD - a rational choice of therapy // T.V. Adasheva, V.S. Zadionchenko, M.V. Matsievich [et al.] // Rus. honey. journal -2006. -T. 14, No. 10. - pp.795-800.

2.Akhmineeva A.Kh. Biochemical markers of endothelial dysfunction in chronic obstructive pulmonary disease in combination with hypertension, coronary heart disease Therapeutic archive, 2014, Volume: 4s. 2014.-N 3.-pp.20-23.

3.Zadionchenko V.S. Arterial hypertension and chronic obstructive pulmonary disease are clinical and pathogenetic parallels and treatment options. Grew up. cardiol. journal 2009; 6: 62-9./ Zadionchenko V.S.Arterial'naiagi pertoniiai khronicheskaiaobstruktivnaia bolezn 'legkikh - kliniko-patogeneticheskie paralleli i vozmozhnosti terapii. Ros. kardiol. zhurn. 2009; 6: 62-9. [in Russian].

4.Zarubina E.G., Mishina E.A., Osadchuk M.A. The role of endothelial dysfunction in the pathogenesis of combined cardiopulmonary diseases. Clinical medicine. 2006; 5: 31-34.

5.Karoli N.A., Rebrov A.P. Chronic obstructive pulmonary disease and arterial hypertension: the vascular wall as a target organ in comorbid patients. Rational Pharmacotherapy in Cardiology 2017; 13 (4) / Rational Pharmacotherapy in Cardiology 2017; 13 (4), 513-518.

6.Clinical Dopplerography of occlusive lesions of the arteries of the brain and limbs: textbook. Method. leadership / E.B. Cooperberg, A.E. Gaidashev, A.V. Lavrentyev [et al.] .- M.: Publishing House of the SCSSH RAMS them. Bakuleva, 2007. - 256 p.

7.Kubazhi Khalil. Peculiarities of the course and prognosis in patients with chronic obstructive pulmonary disease in combination with coronary heart disease and arterial hypertension: Diss. ... cand. honey. sciences. Ryazan; 2013.

8.Kutsenko M.A., Chuchalin A.G. The paradigm of comorbidity: syntropy of COPD and IHD. Russian medical journal. 2014; 5: 389-393.

9.Mamaeva M.G., Demko I.V., Verigo Y.I. et al. Markers of systemic inflammation and endothelial dysfunction in patients with chronic obstructive pulmonary disease. Siberian Medical Review. 2014; 1 (85): 12-19.

10.Ovcharenko S.I., Nersesyan Z.N., Morozova T.E. Chronic obstructive pulmonary disease in combination with arterial hypertension: an assessment of systemic inflammation and endothelial dysfunction. Pulmonology. 2015; 25 (5): 561-565.

11.Poplavskaya E.E., Lis M.A. The state of endothelial function and phagocytosis activity in chronic obstructive pulmonary disease and coronary heart disease. Journal of Grodno State Medical University. 2010; 1 (29): 29-31.

12.Pribylov S.A. Pulmonary hypertension, endothelial dysfunction and their correction with lisinopril in patients with heart failure with a combination of coronary heart disease and chronic obstructive pulmonary disease. Cardiology. 2006; 46 (9): 36-40.

13.Yarmysh N.V., Terrible L.N. Endothelial dysfunction and its regulatory factors. Bulletin of problems of biology and medicine. 2014; 2 (111): 37-43.

14.Agusti A., Calverley P.M., Celli B. Characterisation of COPD heterogeneity in the ECLIPSE cohort. Respir. Res.2010; 11: 122.

15.Almagro P, Cabrera FJ, Diez J, Boixeda R, Alonso Ortiz MB, Murio C et al. Comorbidities and Short-term Prognosis in Patients Hospitalized for Acute Exacerbation of COPD. Chest. 2012;142(5):1126-33. DOI: 10.1378/chest.11-2413.

16.Ambrosino P, Lupoli R, Iervolino S, De Felice A, Pappone N, Storino A et al. Clinical assessment of endothelial function in patients with chronic obstructive pulmonary disease: a systematic review with meta-analysis. Internal and Emergency Medicine.2017;12(6):877-85.DOI: 10.1007/s11739-017-1690-0.

17.Babushkina I. V., Sergeeva A. S., Pivovarov Yu. I., Kurilskaya T. E., Koryakina L. B. Structural and Functional Properties of Vascular Endothelium. Kardiologiia. 2015;55(2):82-6

18.Bei Y., DuongQuy S., HuaHuy T. Et al. Activation of RhoA/Rhokinase pathway accounts for pulmonary endothelial dysfunction in patients withchronic obstructive pulmonary disease. Physiol. Rep. 2013; 1 (5): e00105.

19.Bulaeva N. A., Golukhova E. Z. Endothelial dysfunction and oxidative stress: role in the development of cardiovascular disease. Creative cardiology. 2013;1:14-22.

20.Campo G., Pavasini R., Malag?M. et al. Chronic obstructive pulmonary disease and ischemic heart disease como bidity: overview of mechanisms and clinical management. Cardiovasc. Drugs Ther. 2015;29 (2): 147-157.

21.Capone C, Faraco G, Coleman C, Young CN, Pickel VM, Anrather J et al. Endothelin1-Dependent Neurovascular Dysfunction in Chronic Intermittent Hypoxia. Hypertension. 2012;60 (1):106-13. DOI: 10.1161/ HYPERTENSIONAHA.112.193672.

22.Cavailles A, Brinchault-Rabin G, Dixmier A, Goupil F, GutGo bert C, Marchand-Adam S et al. Comorbidities of COPD. Euro pean Respiratory Review. 2013;22(130):454-75. DOI: 10.1183/ 09059180.00008612.

23.Chandra D., Gupta A., Strollo P.J. Jr, et al. Airflow Limitation and Endothelial Dysfunction. Unrelated and Independent Predictors of Atherosclerosis. Am J Respir Crit Care Med. 2016;194(1):38-47.

24.Chandy D., Aronow W.S., Banach M. Current perspectives on treatment of hypertensive patients with chronic obstructive pulmonary disease. Integr Blood Press Control. 2013; 6:101-9.

25.Davenport AP, Hyndman KA, Dhaun N, Southan C, Kohan DE, Pollock JS et al. Endothelin. Pharmacological Reviews. 2016; 68(2):357-418. DOI: 10.1124/ pr.115.011833.

26.Ives SJ, Harris RA, Witman MAH, Fjeldstad AS, Garten RS, McDaniel Jet al. Vascular Dysfunction and Chronic Obstructive Pulmonary Disease: The Role of Redox Balance.Hypertension.2014;63(3):459-67.DOI:10.1161/ HYPERTENSIONAHA.113.02255.

27.Fabbri L.M., Rabe K.F., Ukena C. et al. From COPD to chronic systemic inflammatory syndrome? Lancet. 2007; 370: 797-799.

28.Feng E.Z., Yang S.Y., Huang N.X. et al. Plasma endothelin-1 and nitric oxide correlate with ligustrazine alleviation of pulmonary artery hypertension in patients of chronic cor pulmonale from high altitude plateau during acute exacerbation.Zhongguo Ying Yong Sheng Li Xue Za Zhi. 2014; 30 (6): 532-537.

29.Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. (Global Initiative for Chronic Obstructive lung Disease (GOLD). The updated 2015 report is available on 3. www.goldcopd.com).

30.Golukhova E. Z., Aliyeva A. M., Kakuchaya T. T., Arakelyan G. G., Bulae va N. I.

Endothelin - modern biomarker of cardiovascular diseases. Creative cardiology. 2011;2:97-103.

31.Gungor ZB, Sipahioglu N, Sonmez H, Ekmekci H, Toprak S, Ayaz G et al. Endothelial Dysfunction Markers in Low Cardiovascular Risk Individuals: Comparison of Males and Females. Journal of Medical Biochemistry. 2017;36(1):62-72. DOI: 10.1515/jomb-2016-0030.

32.Janssen W.J., Yunt Z.X., Muldrow A. et al. Circulating hematopoietic progenitor cells are decreased in COPD. COPD. 2014; 11 (3): 277-289.

33.Karoli N.A., Rebrov A.P. Arterial hypertension in patients with bronchial asthma and chronic obstructive pulmonary disease. Klinitsist. 2011;2:20-30.

34.Kirkham PA, Barnes PJ. Oxidative Stress in COPD. Chest. 2013;144(1):266-73. DOI: 10.1378/chest.12-2664.

35.Kushnarenko N. N., Govorin A. V. Clinical significance of endothelial dysfunction and insulin resistance syndrome in patients with gout with hypertension. Rational Pharmacotherapy in Cardiology. 2013;9(5):482-7.9 ISSN 0022-9040.

36.Liu P., Zhang H., Liu J. et al. Changes of number and function of late endothelial progenitor cells in peripheral blood of COPD patients combined with pulmonary hypertension. Thorac. Cardiovasc. Surg. 2014 Sep. 16. [Epub ahead of print].

37.Mannino DM, Sanderson WT. Using Big Data to Reveal Chronic Respiratory Disease Mortality Patterns and Identify Potential Public Health Interventions. JAMA. 2017;318(12):1112-4. DOI: 10.1001/jama.2017.11746.

38.Mel'nikova Yu.S., Makarova T.P. Endothelial dysfunction as a central link chronic diseases pathogenesis. Kazan medical journal. 2015;96(4):659-65.

39.Mordi I, Mordi N, Delles C, Tzemos N. Endothelial dysfunction in human essential hypertension: Journal of Hypertension.2016;34(8):1464-72.

40.Mnzel T, Camici GG, Maack C, Bonetti NR, Fuster V, Kovacic JC. Impact of Oxidative Stress on the Heart and Vasculature. Journal of the American College of Cardiology.2017;70(2):212-29.DOI: 10.1016/j.jacc.2017. 05.035.

41.Mnzel T, Gori T, Keaney JF, Maack C, Daiber A. Pathophysiological role of oxidative stress in systolic and diastolic heart failure and its the rapeutic implications. European Heart Journal. 2015;36(38):2555-64. DOI: 10.1093/eurheartj/ehv305.

42.Murray C.J., Lopez A.D. Measuring the global burden of disease. N. Engl. J. Med. 2013; 369: 448-457.

43.Nosratola D., Bernardo R. Mechanisms of disease: oxidative stress and inflammation in the pathogenesis of hypertension. Nat. Clin. Pract. Nephrol. 2006; 2 (10): 582-593.

44.Pan J., Xu L. Cai S.X. et al. The association of pulmonary function with carotid atherosclerosis in older Chinese: Guangzhou Biobank Cohort StudyCVD Subcohort. Atherosclerosis. 2015; 243 (2): 469-476.

45.Park KH, Park WJ. Endothelial Dysfunction: Clinical Implications in Cardiovascular Disease and Therapeutic Approaches. Journal of Kore an Medical Science. 2015;30(9):1213-25. DOI: 10.3346/jkms.2015.30.9.1213.

46.Paschalaki K.E., Starke R.D., Hu Y. et al. Dysfunction of endothelial progenitor cells from smokers and chronic obstructive pulmonary disease patients due to increased DNA damage and senescence. Stem. Cells.2013; 31 (12): 2813-2826.

47.Pizarro S., GarcaLucio J., Peinado V.I. et al. Circulating progenitor cells and vascular dysfunction in chronic obstructive pulmonary disease. PLoS One.2014; 9 (8): e106163.

48.Popova M. A., Terentyeva N. N., Dolgopolova D. A., Marenina T. V. Endothelial dysfunction with stable angina and myocardial infarction in combination with chronic obstructive pulmonary disease. Bulletin of Siberian medicine. 2015;14(6):68-74.

49.RodriguezMiguelez P., Seigler N., Bass L. et al. Assessments of endothelial function and arterial stiffness are reproducible in patients with COPD. Int. J. Chron. Obstruct. Pulm. Dis.2015; 10: 1977-1986.; 11. Campo G., Pavasini R., Malag?M. et al. Chronic obstructive pulmonary disease and ischemic heart disease como bidity: overview of mechanisms and clinical management. Cardiovasc. Drugs Ther. 2015;29 (2): 147-157.

50.Schneider K.M., O'Donnell B.E., Dean D. Prevalence of multiple chronic conditions in the United States' Medicare population. Health Qual. Life Outcomes.2009; 7: 82.

51.Selikhova M. A., Kuvaev V. S. Up-to-date state of the problem concerning endothelial dysfunction correction in COPD. Aspirantskiy Vestnik Povolzhiya. 2012;5-6:66-8

52.Shpagin I. S., Kotova O. S., Pospelova T. I., Gerasimenko O. N., Shpagina L. A., Ermakova M. A. Chronic obstructive pulmonary disease in combination with essential arterial hypertension: clinical, functional and molecular genetic features. Bulletin of mo dern clinical medicine. 2016;9(4):56-65..

53.Smiljic S. The clinical significance of endocardial endothelial dysfunction. Medicina. 2017;53(5):295-302. DOI: 10.1016/j.medici.2017.08.003.

54.Strisciuglio T, De Luca S, Capuano E, Luciano R, Niglio T, Trimarco B et al. Endothelial Dysfunction: Its Clinical Value and Methods of Assessment. Current Atherosclerosis Reports. 2014;16(6). DOI: 10.1007/s11883-014-0417-1.

55.Suylen R.I., Smits J.F., Daemen M.J. Pulmonary artery remodeling difference in hypoxia and monocrotaline induced pulmonary hypertension. Am. J. Respir. Erit. Care Med. 2008; 157: 1423-1428.

56.Takahashi T., Kubo H. The role of microparticles in chronic obstructive pulmonary disease. Int. J. Chron. Obstruct.Pulm. Dis. 2014; 9: 303-314.

57.Talavera-Adame D. Endothelium-derived essential signals involved in pancreas organogenesis. World Journal of Experimental Medicine. 2015;5(2):40. DOI: 10.5493/ wjem.v5.i2.40.

58.Tanaseanu C., Tudor S., Tamsulea I. et al. Vascular endothelial growth factor, lipoporotein-associated phopholipase A2, sPselectin and antiphospholipid antibodies, biological markers with prognostic value in pulmonary hypertension associated with chronic obstructive pulmonary disease and systemic lupus erithematosus. Eur. J. Med. Res. 2007; 12 (4): 145-151.

59.Vignon-Zellweger N, Heiden S, Miyauchi T, Emoto N. Endothelin and endothelin receptors in the renal and cardiovascular systems. Life Sciences. 2012;91(13-14):490-500. DOI: 10.1016/j.lfs.2012.03.026.

60.Vorobeva E. N., Vorobyev R. I., Sharlaeva E. A., Fomicheva M. L., Sokolova G. G., Kazyzaeva A. S. et al. Endothelial dysfunction in cardiovascular diseases: risk factors, methods of diagnosis and correction. Acta Biologica Sibirica. 2016;2(1):21-40.

MORPHOLOGICAL FEATURES OF ISCHEMIC AND HEMORRHAGIC BRAIN STROKES

Kamalova M.I., Islamov SH.E.
Samarkand State Medical Institute, Republic of Uzbekistan

Abstract. The article is devoted to pathomorphological features of ischemic and hemorrhagic brain strokes. The aim of the research was to establish morphological peculiarities of brain stroke development in the basins of carotid, vertebral-basilar and both arterial systems. The analysis of 50 cases of tanatological study in which acute cerebral blood circulation disorder was diagnosed was carried out.

It has been established that changes in the microcirculatory channel vessels during a hemorrhagic stroke are caused by hypoxia and ischemia of the brain, its swelling, and a sharp violation of vascular permeability. Such changes are local and widespread, can be divided into acute, which occurred during a stroke, and chronic, which developed before the stroke. Pathomorphological changes cover all structural and functional levels of the arterial system of the brain, the most important of which are the vessels of the microcirculatory channel.

Keywords: acute cerebral circulation disorder, brain, ischemic stroke, hemorrhagic stroke, pathomorphological features.

Introduction. At present, high frequency of strokes can be caused by the lack of an effective primary and secondary prevention system for stroke, as well as their over diagnosis. Clarification of this issue is associated with a detailed study of risk factors, the course and prevention of stroke in our country. Comparatively little studied remains the question of the implementation of secondary prevention of ischemic stroke in our country, especially with its different subtypes, which makes relevant further research in this direction [10]. There are three main types of stroke: ischemic stroke, cerebral stroke and subarachnoid hemorrhage. Intracerebral hemorrhage and (not in all classifications) non-traumatic subraumatic hemorrhage are classified as hemorrhagic insult. According to international multicenter studies, the ratio of ischemic to hemorrhagic strokes is 4:1-5:1 on average (80-85% and 15-20%) [6,11,18]. According to practical medicine, the most common ischemic type of stroke, which is of high medical and social significance due to its leading position in the structure of morbidity, disability and mortality in many countries. According to pathological and anatomical studies, heart attacks with clinical manifestations were characterized by a great variety of magnitude and localization [5]. Stroke incidence in the Russian Federation is one of the highest in the world, reaching almost 5 cases per 1000 people per year, with the share of ischemic strokes accounting for up to 87% of all strokes (20). Only 8-10% of strokes end in complete restoration of impaired function, while most surviving patients have a marked neurological deficit, often resulting in severe disability (14). Stroke fatality in different countries is 1.3-1.8 per 1000 people per year, increasing 1.5 times with repeated stroke. In recent decades, the idea of pathogenetic subtypes of strokes and criteria for their diagnosis has been formed, and certain difficulties arise in tanatological practice [16]. Usually, ischemic strokes of the cerebral hemispheres in case of cerebral circulation disorders in the pool of the internal carotid artery are 2-5 times more frequent than in the pool of the vertebrobasilar system, especially in the cortical subcortical branches of the middle cerebral artery. The problem of determining the age of cerebral stroke is

particularly relevant in forensic practice, where sudden death occurs on the scene in the absence of anamnesis, investigation and other data on the circumstances of the case. Therefore, the identification of characteristic morphological changes in brain stroke, as well as the creation of a classification of stroke on the basis of this representation are extremely important tools for the choice of tactics for their treatment and secondary prevention, the definition of short- and long-term prognosis, standardization in clinical and epidemiological studies.

Research materials and methods. As a material, a retrospective analysis of 20 reports of forensic examinations conducted at the Tanatological Department of the Samarkand Regional Branch of the Republican Scientific and Practical Center for Forensic Medical Examination and 28 protocols of pathological and anatomical examination of the subdivisions of the Republican Pathological Anatomical Center in the period 2019-2020 was carried out. Generally accepted research methods were applied, i.e. macro- and microscopic study of the brain and its arterial system was conducted at all structural and functional levels, including the main arteries of the head - internal carotid and vertebral arteries, intracranial arteries - vessels of the williesian circle and their branches, as well as intra cerebral arteries and vessels of the microcirculatory channel (ICR). The study of the brain determined the size and localization of intracerebral hematomas, the presence of a blood rupture into the ventricular system, the severity of cerebral edema, dislocation and compression of its trunk.

. Visible brain changes (small hemorrhages, perivascular edema, white spongiform state) were taken into account. Microscopic examination of the brain was carried out in the histological preparations encased in paraffin. Which were stained with hematoxylin and eosin, according to the methods of Van Gijson (determination of collagen fibers and myocytes in vessels), Weigert (determination of elastic fibers in vessels). Particular attention was paid to the microcirculatory vessels within the hematoma, in the perifocal zone, as well as at a distance from the hematoma.

The results of the research and their discussion. All were diagnosed with acute cerebral blood circulation disorder (ACBD) by ischemic and hemorrhagic types. Among them 36 men (75.0%) aged 20 to 72 years, 12 women (25.0%) aged 33 to 65 years. In all cases, massive intracerebral haemorrhages were detected, located in 64% of cases in the hemispheres of the brain: lateral - 53%, medial - 15%, mixed - 32%. The volume of hemorrhagic foci exceeded 40 cm?. In 16% of observations quite large hemorrhages were found in the brainstem and cerebellar hemispheres. In most cases, blood has spread to the ventricular system, accompanied by swelling, dislocation and compression of the brain stem, often causing death. Many observations revealed previously transferred NMK in the form of posthemorrhagic cysts of various sizes (67%), localized mainly in brain regions, symmetrical fresh hematoma, significant longevity single lacunar infarcts (LI), as well as organized and organized multiple LI (lacunar state of the brain), which in more than a third of cases were combined with organized foci of hemorrhage [4]. Organized ischemia and lacunar foci were most often located in the basal nuclei and white matter of both brain hemispheres, sometimes in the thalamus, brain bridge, and cerebellar hemispheres. The microscopic examination of all sectioned cases revealed changes in the intracerebral arteries, which are typical for hypertensive angiopathy and cause major brain haemorrhages: plasma impregnation of arterial walls and hemorrhage in them with stenosis and lumen lining, focal or total fibrinoid necrosis with formation of miliary aneurysm, as well as primary (isolated) necrosis of middle arterial muscle

cells with vascular rupture.

The hemorrhages were found to have occurred against the background of small-focus and diffuse changes in brain matter characteristic of hypertensive encephalopathy and caused by severe arterial and CDM pathology of the brain - small-focus perivascular hemorrhages, foci of perivascular edema, brain tissue necrosis in the perivascular region, periventricular white matter edema [19]. In chronic changes, fibrosis and thickening of the walls of capillaries and other microvessels with narrowing, emptying and obliteration of their lumen were revealed. Active proliferation of cell wall elements of many microvessels with the formation of convolutions - microvascular formations with multiple lumen, which are a sign of adaptive changes of the ICR, which developed in the ischemically hypoxic state of the brain due to the reduction of blood flow through the arteries, which underwent severe destructive changes with concomitant stenosis and obliteration, was also revealed.

The above chronic changes of the ICR were found in the cortex and white matter of hemispheres and cerebellum, basal nuclei, thalamus, various parts of the brain stem, including nuclei of cranial nerves and reticular formation. Leukostasis was detected in small vessels and leukodiasis. The walls of a number of microvessels located near the hemorrhage were necrotized. On the first day, at a considerable distance from the hematoma, a sharply pronounced edema of the brain substance was detected, giving it a spongiform structure, full-blooded PCR, arteries and veins, stasis and thrombosis in capillaries, perivascular hemorrhages with erythrocyte proliferation along white matter fibers. Blood that penetrated the perivascular spaces from the hematoma was found in them at quite large distances from the hematoma up to the subarachnoid space.

Acute changes of the ICR, which were observed in a number of cases of particularly severe hemorrhagic stroke with the development of extensive hematomas and blood rupture into the ventricles, also included the phenomena characteristic of the syndrome of disseminated intravascular blood clotting: widespread microvascular thrombosis with clot fragmentation, pre-thrombotic state in vestigial clusters of fibrin threads in veins, thromboemboles in the lumen of the latter, as well as pericapillary, periarterial and perivenular hemorrhages [2]At the same time it has been established that ICR takes an active part at different stages of hematoma organization: from edema and organization of necrosis of the surrounding brain tissue in the initial stage, to reabsorption of red blood cells in the second stage and formation of gliomezodermal scar around the pseudocyst in the final stage. Ischemic strokes were also divided into acute (up to 3 days) and subacute (4-6 days) strokes. Fresh strokes were macroscopically characterized by the following: respectively, the focus of colliquation necrosis revealed a well-defined hemorrhagic component in the form of a dark red hemorrhage under the soft cerebral membranes and into the cerebral cortex, the demarcation line (perifocal zone) is not determined. In microscopic examination - signs of cerebral substance edema with the appearance of multiple honeycomb (hole) cavities along the perimeter of strokes, further signs of ischemic strokes in the form of migration of blood cells (neutrophils, monocytes, etc.) through the wall of vessels [3, 8, 9]. During the day, when examined in the focus of ischemic strokes and the adjacent soft envelopes, stagnation of blood vessels, cyanosis, swelling and other signs of aseptic inflammation are observed. At the same time, the consistency of the brain, as well as the structure of the furrows and curves have not been changed. Brain tissue in the section has a clearly distinguishable boundary between layers (cortex and white matter) [21]. Over time, the focus was clearer and pale. There is no demarcation line. The stroke area has a slightly bluish hue,

usual consistency, or is slightly soft to the touch, without sharp borders, and passes into the surrounding brain tissue. After a day of macroscopic aseptic inflammation has indistinct outlines with blurred borders. The cortex is pale grey with a pink or red hue (due to the hemorrhagic component). The white substance in the pathological focus is lighter than the surrounding undamaged tissue (due to ischemic emptying of microcirculatory channel vessels and swelling of the stroke zone). On the 2nd-3rd day, the swelling in the soft membranes and brain matter is significantly pronounced (especially in the border zone) and reaches its maximum. The line of demarcation in the stroke zone was not visually detected or indistinctly expressed. Only at palpation the borders of the pathological focus can be determined by the difference in consistency between the flabby area of the heart attack and the unchanged elastic (springing) surrounding tissues. Sometimes on the 3rd day the edge of the necrosis zone on the periphery of the stroke may swell up visually above the surface of the slice (edematous border zone). Slight softening of the brain substance and visual absence of a demarcation line are important macroscopic criteria for stroke in the acute stage of development, with a limitation period of up to 3 days [1].In amicroscopic examination on the periphery of the focal point of ischemic stroke, cerebral edema in the form of enlarged perivascular spaces was detected in the first 24 hours; in the border zone there is a distinct increase in the vascular network due to hyperemia of the reserve capillaries. The marginal position of segmental leukocytes, plasma diapaedesis, neutrophils and erythrocytes in the stroke zone through the dilated vascular wall was noted. There is a gradual increase in the number of drainage forms of oligodendroglyocytes, i.e., macroglia cells with a large volume of cytoplasm and eccentrically located nuclei [7]. The characteristic irreversible ischemic changes of neurons (tigerolysis, reduction of volume and eosinophilia of cytoplasm, as well as its vacuumization, blurring of nuclear membrane, turbidity of nucleoplasm, etc.) were detected. A day later, ring-shaped perivascular hemorrhages (microscopic equivalents of the hemorrhagic component) were detected around the vessels of the soft membranes and in grey matter. Some red blood cells are poorly coloured by leaching. With increasing hemolysis of erythrocytes, a blood pigment appears, which looks like small grains of dark brown color. In the border zone, swelling of brain tissue is quickly detected, which reaches its maximum by the 3rd day. Characteristically, the oedema with the accumulation of drainage forms of glia becomes so intense that gray and white brain matter during microscopic examination becomes honeycomb (holey, porous), reminiscent of bee honeycomb. Hole (honeycomb) character of the brain substance (visible only in histological examination) is an important differential-diagnostic criterion for ischemic stroke [13]. In later terms (duration about 4-6 days) the organization of stroke is noted, and it is typical that simultaneously with collictional necrosis and resorption of ischemic stroke zone there is a gradual increase of proliferation processes. The formation of a stale hemorrhagic component was observed (i.e. various combinations of shades of green, yellow and brown appear in the stroke area due to neutrophilic autolysis of the blood pigment).The examination reveals moist necrosis and tissue resorption,

so the brain becomes flabby. Characteristic of the presence of signs of stale hemorrhagic component (change in blood pigment color) in the brain membranes, cortex and white matter of the brain. In this case, the soft membranes are mainly in the course of blood vessels intensively impregnated with products of hemoglobin decomposition (hemosiderin). First, they have a slightly greenish or greenish-yellow color, and then a rusty hue with coloring of the affected tissues of varying intensity from dark brown to light yellow [15]. Necrotized bark has a rusty appearance with a variety of shades of colors and their

combinations (green, brown, yellow). In a number of observations, the stale hemorrhagic component spread from the cortex to the subject white matter. In such cases, in the white matter adjoining the cortex, the width of the zone of imbination by the decaying blood pigments is usually about 0.3-0.5 cm. This is due to the lesions of the short cortical medullary arteries and arterioles, which supply blood to the bark and the adjoining arched (associative) fibres of white matter. With the progression of the pathological process (with major strokes) stroke zone extends to the pool of cortical and medullary arteries of medium length. At that time, the stale hemorrhagic component also captured the middle parts of the white matter, which was rarely observed. Sometimes there were cases of isolated damage to the white matter of the brain only, then the so-called white (gray) heart attacks are formed, ie without the hemorrhagic component. In exceptional cases, white (grey) heart attacks may also occur in the cerebral cortex [16].

In microscopic examination - the organization of stroke in the early stage (4-6 days) is manifested by increasing the number of drainage forms of oligodendrogliocytes and reactive changes in astrocytes along the edge of the boundary zone. The perforated (honeycomb) character of the affected tissue is preserved and small vascular gaps begin to form. In general, the phenomena of cerebral edema decrease and make up an area no wider than 0.2-0.4 cm in the border zone on the periphery of stroke.Cotoval nature of brain substance and the degree of oedema in the perifocal zone are important microscopic differential-diagnostic signs of heart attacks with the limitation period of 4-6 days [12]. Vascular proliferation with mitosis in endothelial cells and sclerosis sites has been noted. In the demarcation zone, except for reserve capillaries, proliferation of newly formed capillaries is observed. Single macrophages are detected along the vessels in the boundary zone. In the focus of stroke, the vascular pattern is generally preserved. Only in some places a peculiar "amputation" of microvessels is observed, in which case fresh small-point or focal hemorrhages may appear, visible histologically [17].

Conclusion. As a result of the morphological studies carried out, differential diagnostic features of hemodynamic strokes have been established and, at the same time, some features of their implementation have been noted. In particular, changes in the vessels of the ICR during hemorrhagic stroke are caused by hypoxia and ischemia of the brain, its swelling, sharp disturbance of the blood vessels permeability. These changes are local and widespread, can be divided into acute, which occurred during a stroke, and chronic, which developed before the stroke. In the initial period of stroke development (2-3 days) the picture of the expressed fresh hemorrhagic component in the form of dark red is characteristic.

hemorrhages (subarachnoidal and foci in the brain tissue adjacent to the soft cerebral membranes). In typical cases, in the acute stage of stroke, the hemorrhage is located only in the cerebral cortex (especially in its surface layers adjacent to the soft membranes), less often the hemorrhagic component captures not only the cortex but also the white matter of the brain.

Conclusions. In the later stages of stroke (the period of the organising stroke) a heart attack lasting about 4-6 days) there is a stale hemorrhagic component with spreading from the cortex to the white matter of the brain (in the area of stroke there are different combinations of shades of green, yellow and brown colors due to neutrophilic autolysis of the pigment of blood). The revealed feature of color scale of not fresh hemorrhagic component as a differential-diagnostic criterion to distinguish the stages of strokes, it is necessary to apply in conjunction with other macroscopic criteria (flabby brain consistency and the emergence of demarcation lines). Also to clarify the stage of brain stroke

development it is necessary to perform histological examination (presence of signs of neutrophil and macrophage autolysis development). Thus change of hemorrhagic component character with occurrence of fine point or focal fresh hemorrhages in a stroke focus should be considered at interpretation of results on determination of duration of strokes formation. Pathomorphological changes cover all structural and functional levels of the arterial system of the brain, the most important of which is the ICR vessels.

References

1.Anttila J.E., Whitaker K.W., Wires E.S., Harvey B.K., Airavaara M. Role of microglia in ischemic focal stroke and recovery: focus on toll-like receptors. //Prog. Neuropsychopharmacol. Biol. Psychiatry. - 2016. - №79(Pt A), - P.3-14.

2.Brites D., Vaz, A.R. Microglia centered pathogenesis in ALS: insights in cell interconnectivity. // Front. Cell. Neurosci. - 2014. №8. - P.117.

3.Colonna M., Butovsky O. Microglia function in the central nervous system during health and neurodegeneration. // Annu. Rev. Immunol. - 2017. - №35 - P. 441-468.

4.Cooke R.A., Stewart B. Colour Atlas of Anatomical Pathology. - Churchill Livingstone. - 2004. - 300 p.

5.Donnan G. A., Fisher M., Macleod M., Davis S. M. Stroke (англ.) // The Lancet. - Elsevier, 2008. - May (vol. 371, no. 9624). - P. 1612-1623.

6.European Stroke Initiative recommendations for stroke management: update 2003 // Cerebrovasc. Dis. - 2003. - Vol. 16, - P.311-337.

7.Faustino J., Wang X., Johnson C.E., Klibanov A., Derugin N., Wendland M.F., et al. Microglial cells contribute to endogenous brain defenses after acute neonatal focal stroke. // J. Neurosci. - 2011. - №31. - P.12992-13001.

8.Fumagalli S., Perego C., Ortolano F., De Simoni M.G. CX3CR1 deficiency induces an early protective inflammatory environment in ischemic mice. // Glia. - 2013. - №61. P. 827-842.

9.Gelderblom M., Leypoldt F., Steinbach K., Behrens D.C., Choe U., Siler D.A., et al. Temporal and spatial dynamics of cerebral immune cell accumulation in stroke. / / Stroke. - 2009. №40. - P. 1849-1857.

10.Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980-2015: a systematic analysis for the Global Burden of Disease Study 2015 (англ.) // The Lancet. - London, England: Elsevier, 2016-10-08. - Vol. 388, iss. 10053. - P. 1459-1544.

11.Goldstein L.B., Bushnell Ch.D., Adams R.J. et al. Guidelines for the Primary Prevention of Stroke: A Guideline for Healthcare Professionals From the American Heart Association // Stroke. - 2011. - Vol. 42. - P. 517-584.

12.Jack C.A., Ruffini F., Bar-Or A., Antel J.P. Microglia and multiple sclerosis. // J. Neurosci. Res. - 2005. - №81. - P.363-373.

13.Kriz J. Inflammation in ischemic brain injury: timing is important. // Crit. Rev. Neurobiol. - 2006. - №18. - P. 145-157.

14.Lloyd-Jones D., Adams R.J., Brown T.M. et al. Heart disease and stroke statistics - 2010 update: a report from the AHA // Circulation. - 2010. - Vol. 121. - P. 215-246.

15.Morrison H.W., Filosa J.A. A quantitative spatiotemporal analysis of microglia morphology during ischemic stroke and reperfusion. // J. Neuroinflammation. - 2013. №10. - P.4.

16.Oehmichen M., Roland N.Auer, Hans G?nter K?nig, Kurt A. Jellinger. Forensic

Neuropathology and Neurology . - Springer, 2005. - 660 p.

17.Streit W.J., Mrak R.E., Griffin W.S. Microglia and neuroinflammation: a pathological perspective. // J. Neuroinflammation. - 2004. - №1. P.14.

18.Towfighi A., Saver J. L. Stroke declines from third to fourth leading cause of death in the United States: historical perspective and challenges ahead (англ.) // Stroke journal.- Lippincott Williams & Wilkins., 2011.- August (vol.42, no.8).- P.2351-2355.

19.van Gijn J., Kerr R.S., Rinkel G.J. Subarachnoid haemorrhage (англ.) // The Lancet. - Elsevier, 2007. - Vol. 369, №9558. - P. 306-318.

20.WHO Disease and injury country estimates. World Health Organization (2009).

21.Wolf S.A., Boddeke H.W., Kettenmann H. Microglia in physiology and disease. / / Annu. Rev. Physiol. - 2017. - №79. - P. 619-643.

IS THE MEGAURETER THE PROBLEM OF YESTERDAY, TODAY OR TOMORROW?

Yu.M. Akhmedov
I.Yu., Akhmedov
G.S. Karimova
Samarkand State Medical Institute, Republic of Uzbekistan

Abstract.Congenital malformations of the ureters, in particular the megaureter, are a frequent and fairly common pathology of the urinary system. According to different authors, it makes up from 22% to 40% of all malformations. The increase in the number of early diagnosis of this disease, the lack of a unified view of the factors of their development, the use of various diagnostic methods, the presence of a large number of surgical treatment methods, the high percentage of unsatisfactory results and the prospect of developing new treatment algorithms make this disease an urgent issue of pediatric surgery.

Keywords: Megaureter, reflux, obstruction, ureters, anomaly, dysfunction, ureterovesical segment.

Introduction.

Congenital malformations of the ureters, in particular the megaureter, are a frequent and fairly common pathology of the urinary system. According to different authors, it makes up from 22% to 40% of all malformations [2].

Every year in a scientific children's surgical publication there are a fairly large number of works relating to the problem of obstruction of the ureters in children. This is due to the high frequency of development and the increase in the number of early diagnosis of this disease, the lack of a single look at the factors of their development and, as a result, the use of a large number of surgical treatment methods as well as methods of preoperative algorithms for preparing the patient for treatment, as well as the appointment of postoperative care and drug treatment [4].

Among pediatric patients with certain diseases, congenital anomalies of the urinary tract occur in up to 40% of cases. Most often, congenital anomalies of the ureters are diagnosed at the age of several months to 10 years, there are cases of accidental diagnosis in the study for other complaints. Also of great importance is the level of development of diagnostic methods and the general state of medicine in each region [1.19].

The manifestation of congenital anomalies of the ureters in children depends in most cases not on the stage, but on the period of the onset of the disease and the appearance and increase in the number of secondary complications in each patient [12,20].

Despite the annual development of medicine, according to several authors, the megaureter has a tendency to increase the incidence rate, the violation of the urodynamics caused by this pathology creates favorable conditions for the development of an ascending infection (pyelonephritis) and scarring of kidney tissue with a further loss of their function. Even with modern diagnostic systems and already established methods of treating this disease with late diagnosis and inappropriate treatment tactics, 23-27% of children develop one of the most formidable complications of chronic renal failure (CRF) [3,6,13].

In the early diagnosis and an attempt to quickly solve the problems of this disease, unsatisfactory results of surgical treatment are observed in 10-30% of patients, which

gives rise to further research and implementation of the latest achievements of medicine and pharmacology in solving the problem [20].

Incidence. Megaureter is a common diagnosis in children visiting a pediatric urologist, accounting for 28% of children with urinary tract obstruction. The diagnosis is more common in boys than in girls, and in most cases is on the left side. It can be bilateral in 25% of cases, and the contralateral kidney is absent or present as dysplastic in 10-15% of cases [11,12,13].

Embryology and pathophysiology. Many scientific studies have been carried out describing the histological origin of the megaureter, and although they often differ from each other, all studies often show an abundance of connective tissue in the abnormal ureter [17,18,19]. Lee et al. demonstrated that the ratio of collagen to smooth muscle in normal ureters is 0.52, while in obstructive and reflux megaureters it is 0.78 and 1.99, respectively [21]. Other studies have shown the presence of smooth muscle cells in these ureters that produce abnormally increased amounts of collagen. It has also been proven that the muscles in these segments of the ureter react abnormally to neurotransmitters, emphasizing the abnormal behavior of these cells [17,18,19,20].

Primary obstructive megaureter is considered functional obstruction. It is believed that in the ureter there is an aperistical articular (adynamic) segment, which leads to insufficient peristalsis of the ureter and, consequently, to the outflow of urine. This distal segment was examined histologically, and it was found that it contains elevated levels of collagen type I and III (mainly type I). It is this enhanced fibrosis that is associated with a violation of intercellular connections and leads to arrhythmias and ureter obstruction [7,8,9,11]. However, there are many other theories regarding the development of obstructive megaureters. Some scientists have proved atrophy of the internal longitudinal muscles in these segments of the ureter (the longitudinal muscles transmit peristalsis) and hypertrophy of the external, compressive circular muscle, which leads to obstruction [12,13].

Other histological findings that claim to reflect the causal aspect of the obstructive megaureter include distal ureter segments without muscle tissue, but simply a fibrous, static end. At the same time, distal segments of the ureter with a non-urethral, non-destructive muscle, which reacts excessively to the adrenergic stimulus, leading to an almost tonic contraction, have been documented in others [1,14,15,16]. It was found that the proximal enlarged segment of the ureter was also found in the composition of the altered connective tissue, and this fibrosis and the expansion itself can lead to ureter arrhythmias and poor transmission of peristaltic waves. It is important to note that the expansion of the upper parts of the tract (although in itself it represents a significant pathology) plays an important role in the reaction of the urinary tract to the presence of obstruction. The urinary system in children is more flexible than in adult patients, and this expansion allows you to reduce pressure, allowing the kidneys to produce urine in the urinary tract [1,2,3]. In addition to the above-described adynamic segment on the terminal ureter in the obstructive megaureter, other anatomical causes may lead to a similar clinical scenario. Both congenital distal ureteral strictures and distal ureter valves can be almost indistinguishable from the classic obstructive omegaureter [17,18,19]. Secondary obstructive megaureter is an obstructive process secondary to increased intravesical pressure of any other cause. Common causes are spinal dystraphism and a neurogenic bladder, which can raise detrusor pressure to more than 40 cm mm of water. Art., causing physiological obstruction and hydronephrosis. Neurogenic urinary dysfunction, if it is severe enough to raise the pressure in the bladder above a safe range, can also be

the cause. Posterior urethral valves or other causes of infravesical obstruction can also lead to similar results [1,18,19]. Other anatomical causes of secondary, distal obstruction of the ureter include ureterocele, ectopic ureter, diverticulum of the bladder, periurethral fibrosis, and external compression of the retroperitoneal tumor, masses, or aberrant vessels [1,18,19].

The primary and secondary reflux megaureter are simply a reflux ureter that is dilated. Pathology mimics the pathology of any reflux ureter with a short intravesical ureter and submucosal tunnel. They may be associated with abnormalities of the ureterovesical segment, which makes reflux more likely, such as periurethral diverticula. In some children, in addition to the ureters, megacystomegaureter syndrome is observed, in which the bladder is noticeably widened and has a thin wall [18]. The distal segment of reflux megaureters also shows a histological disorder with increased fibrosis (very similar to obstructive megaureters); however, in these cases, type III collagen is predominant [11].

Primary non-obstructive non-reflux megaureter - most cases of the megaureter end up being non-obstructive, non-reflux species. This is very encouraging, as it confirms that a simple observation will serve as therapy for most children. However, as already mentioned, the absence of obstruction can be difficult to prove [1,18]. When evaluating a megaureter, some important points should be taken into account that can help prevent unnecessary interference. First of all, the fact that the baby was born with a functioning kidney indicates that any degree of ureteral obstruction is not complete, since the kidney would not form normally under conditions of an early or very high degree of obstruction. The fetus produces large volumes of urine compared to an infant, and if this diuresis precedes the natural canalization of the distal ureter, a megaureter may develop (hypothesis of delayed maturation). Since the ureter in the fetus is very obedient, a slight increase in the flow of urine can cause the ureter to expand even in the absence of obstruction and reflux. It is this compatible urinary system that allows the baby's kidney to continue to function in conditions of varying degrees of obstruction or reflux without suffering injuries under pressure, so expansion may not cause harm to the child [1,2,3,18].

Secondary non-obstructive non-reflux megaureter. Cases of non-obstructive and non-reflux megaurether for a reason not related to the anatomy of the ureter are called secondary. It is in this category that dilatation is possible due to a high yield of fetal urine, increased elasticity of the ureter of the fetus (due to the composition of the extracellular matrix, including increased type II collagen and elastin concentration), or transient obstruction during development (for example, ureteral folds) or delay in the development of normal peristalsis) [18]. There are many other relatively benign causes of the secondary megaureter. For example, urinary tract infections can lead to a temporary expansion of the ureter due to the presence of bacterial endotoxins that can inhibit peristalsis. As already mentioned, any increase in urine output can lead to an expansion of the fetal / baby collection system. Some possible causes of diuresis include lithium toxicity, diabetes insipidus or diabetes mellitus, sickle cell nephropathy, or psychogenic polydipsia [18].

Diagnostics. Currently, the use of prenatal ultrasound has increased the diagnosis of megaureter. Cases detected later in life are often accompanied by urinary tract infections, hematuria and / or pain [21,22]. After diagnosis (in utero or after childbirth), the first and most affordable method is an ultrasound of the kidneys and bladder. Ultrasonography is a simple, safe and painless study that can provide important information about kidney

size, parenchyma thickness, echogenicity and architecture, as well as the expansion of the renal pelvis and ureter, the thickness of the bladder wall and, in some cases, the urethra. Although an experienced pediatric surgeon can conclude some functional diagnoses from ultrasound examinations, it is important to remember that an ultrasound exam is only descriptive and does not provide detailed information about renal function [19,21].

Further, an integral part of the diagnosis of a megaureter is the conduct of radionuclide imaging and excretory urography, which make it possible to assess the structure of the kidneys and ureters, as well as their functional state.

A radionuclide study reveals a decrease in the accumulation and elimination of the radiopharmaceutical by the parenchyma and the collective kidney system. In this case, it is necessary to take into account the dependence on age for removing the radiopharmaceutical in children of the first weeks of life.

Excretory urogram visualize the delay in the discharge of contrast medium by the kidneys, the violation of the collector system, the expansion and tortuosity of the ureters. To conduct this study, a radiopaque substance is administered at a rate of 1-2 mg / kg body weight, but not more than 60 ml per study. Pictures are taken after 1.5.15.30 minutes from the time of administration and after urination. Also, if necessary, you can take delayed pictures after 1, 2 and 3 hours.

For a more accurate diagnosis, a specialist can perform cystoureterography myciation to determine the degree of reflux; a warm solution of an iodine-containing radiopaque compound is introduced into the urinary bladder through an installed catheter until an imperative urge. Pictures are taken with a full bladder during urination and on an empty bladder.

Also, patients can undergo cystoscopy in which it is possible to visualize the signs of chronic cystitis (bullous or granular formations on the mucous membrane), narrowing or vice versa, gaping of the mouths of the ureters, deformation and possible displacement.

Along with the above visualization methods, the most important part of examining children suffering from various forms of megaureter is the histological examination of surgical material, which allows morphologically verifying the diagnosis and studying structural changes in the ureter tissue to further improve treatment tactics.

Treatment. Primary reflux megaureter. All pediatric surgeons are familiar with the standard treatment for reflux, and the treatment of primary reflux megaurether is no different. Initially, even with severe dilatation and severe reflux, medical treatment (antibiotic prophylaxis) and observation are all that is needed. Surgical intervention is considered only for persistent high reflux in older children (especially with recurrent pyelonephritis) and in children who could not receive medical treatment. Since the frequency of complications of ureteroneocystostomy is high when performed in children under the age of one year, cutaneous ureterostomy or vesicostomy can be used as a temporary measure in children requiring surgical intervention [18].

Secondary reflux or obstructive megaureter. Obviously, secondary reflux must be treated, eliminating the cause of increased intravesical pressure leading to reflux. For example, in children with posterior urethral valves and reflux, valve ablation and proper treatment of the bladder often lead to a rapid resolution of reflux. Neurogenic bladders with elevated detrusor leakage point pressure (> 40 cm mm.wat.) should be treated with a combination of drug therapy (i.e. anticholinergic treatment), clean intermittent catheterization, and surgery if necessary. Often, cases of prune stomach and diabetes insipidus can be controlled by observation, suggesting that appropriate drug therapy is starting [18].

Non obstructive or obstructive megaureter. In cases where a megaureter may possibly be difficult, the decision to have surgery is difficult. Even in cases of obvious obstruction, early surgical intervention is fraught with ahigher complication rate.The basic principle that should be observed is that no surgery should be performed unless renal function is significantly affected and urinary tract infections are not a serious problem. Instead, suppression of antibiotics under close observation is all that is required. As a rule, surgical recovery is required at the age of 1 to 2 years, if the condition worsens [1,3,18].

In some rare cases, early intervention is required. To prevent complications associated with non-reflux therapy, re-implant surgery in children, other surgical options should be considered, such as loop ureterostomy, reflux reimplantation, and even the installation of an ureteric stent. From the point of view of the formation of algorithms that make it possible to decide which of the children will need surgical intervention, no good parameters determine the children who will decide and those that will deteriorate. In general, more than 70% of cases are resolved within 2 years of observation. Although there is no correlation with any definable factors (such as the degree of hydronephrosis) for which children will need surgical intervention and which are not, there is a correlation between the age of resolution and the degree of dilatation in infants [24].

Surgical methods. Surgical methods used for the final treatment of reflux and obstructive megaureters include re-implantation of the ureter of the enlarged ureter. The same parameters that are used to ensure a successful operation, like the traditional re-implantation operation, are also applicable to megaureters (i.e., the ratio of the length of the tunnel 5: 1 to the diameter of the ureter). In the case of obstructive megaureters, the distal adynamic segment must be completely amputated from the ureter, and often after removal of the obstruction, the diameter of the ureter is reduced to a size that allows standard reimplantation without narrowing. However, most reflux and obstructive megaureters require narrowing in order to provide a submucosal tunnel size suitable for a child's bladder [2,3,18].

To date, surgeons have proposed more than 200 methods of surgical correction of the ureter. The choice of the method and method of surgical intervention is determined by the nature and degree of the clinical manifestation of the disease, the presence of complications, the general condition of the patient, and also the experience of treating the corresponding patients with a medical institution [12.17].

An analysis of recent literature has shown that conservative treatment of malformation does not give the desired results, it can be used in the preoperative period, since with the most competent selection of medicines it is possible to achieve remission of pyelonephritis for several weeks and very rarely for several months. However, when ascertaining normal kidney function, it is advisable to temporarily abandon surgical treatment, since it is extremely difficult to conduct a differential diagnosis between neuromuscular dysplasia of the ureter, functional obstruction of the ureter, and disproportion of its growth in young children [7,11].

Taking into account the attending physician's technical diversity and features of various techniques, their choice should be based primarily on the anatomical and functional state of the vesicoureteral anastomosis. The right choice of surgical intervention is the key to successful treatment of a child's disease caused by damage to the vesicoureteral segment. In addition, the inclusion of the method of surgical correction of the vesicoureteral segment in the algorithm of diagnostic treatment in the treatment of children with MTCT and various forms of supravesical obstruction allows predicting the outcome of the disease in the postoperative period [17].

The most etiopathogenetically substantiated approaches for surgical treatment of lesions of the vesicoureteral segment in children are methods aimed at increasing the length of the intramural ureter by laying a submucosal tunnel. The most popular of these proposed treatment methods was the antireflux operation Politano & Leadbetter, which was introduced in 1958 [10].The main principle of the surgical operation was to create a submucosal tunnel for implantation of the ureter, cut off from the original location of its mouth. A high percentage of positive results of this operation, reaching 95%, determined the widespread use of this technique. E.Ya. Huseynov points out that along with the length of the submucosal tunnel, the so-called "support" function of the Lieto triangle plays a significant role in the reliability of the antireflux protection of the vesicoureteral segment.

If we consider the causes of the imperfection of one or another surgical technique for correction of the vesicoureteral segment, the author relies on the following anatomical and functional criteria: the length of the intravesical part of the ureter, the lateral ectopia of the ureteral mouth, the "support" function of the Lieto triangle, the degree of the angle of entry of the ureter into the bladder.

Conclusion

Thus, an analysis of the literature made it possible to determine and reveal that issues of early diagnosis and properly balanced treatment of this disease of the urinary system in children today remain among the urgent problems of pediatric surgery and urology.

References.

1.Smirnov I.E., Shamov B.K., Sharkov S.M., Kucherenko A.G., Yatsyk S.P. Biomarkers in the early diagnosis of megaureter in children. Russian Pediatric Journal 2011; 3; 31-36

3.Hvorostov I.N., Zorkin S.N., Smirnov I.E. Obstructive uropathy. Urology. 2005; 4 (1): 73-76

4.AkhmedovYu.M., Akhmedzhanov IA, MavlyanovF.ShIntravesical surgical correction of the distal ureter in children. // West. about pr. 2006 st 205

5.SharkovS.M., YatsykS.P., FominD.K., AkhmedovYu.M. Obstruction of the upper urinarytract in children. Monograph. Union of Pediatricians of Russia, Moscow 2012 st 6-9

6.Yu.M. Akhmedov, I.A. Akhmedzhanov, Sh. Kh. Mavlyanov, F.Sh. Mavlyanov, K.N. Ibragimov, J.Zh. Kurbanov. X-ray planimetric methods for the diagnosis of obstructive uropathy in children. Saratov Journal of Medical Scientific Research, 2007

7.Pavlov A.Yu. Obstructive uropathies and severe forms of urolithiasis in children Moscow 1997

8.AyvazyanA.V., Voyno-YasenetskyA.M. Malformationsofthekidneysandureters. - M .: Nauka, 1988 .-- 488 p

9.Atlasofpediatricoperativesurgery. Author: PuriP. Publisher: MEDpress-inform, 2009

10.Combined violation of the urodynamics of the upper urinary tract in children. CM. Sharkov, Yu.M. Akhmedov - Pediatric Surgery, 1999

11.Shokeir, A.A. and Nijman, R.J. Primary megaureter: current trends in diagnosis and treatment. BJU Int. 86, (2000) 861-868.

12.Manzoni, C. Megaureter. Rays 27, 83-85. (2002)

13.Wilcox, D. and Mouriquand, P. Management of megaureter in children. Eur. Urol. 34, 73-78.(1998)

14.Report of working party to establish an international nomenclature for the large

ureter. Birth Defects Orig. Artic. Ser. 13, 3-8.(1977)

15.Belman, A.B. Megaureter. Classification, etiology, and management. Urol. Clin. North Am. 1, 497-513. (1974)

16.Koff, S.A. and Campbell, K. Nonoperative management of unilateral neonatal hydronephrosis. J. Urol. 148, 525-531. (1992)

17.Friedrich, U., Schreiber, D., Gottschalk, E., and Dietz, W [Ultrastructure of the distal ureter in congenital malformations in childhood]. Z. Kinderchir. 42, 94-102. (1987)

18.Hanna, M.K., Jeffs, R.D., Sturgess, J.M., and Barkin, M. Ureteral structure and ultrastructure. Part III. The congenitally dilated ureter (megaureter). J. Urol. 117, 24-27(1977).

19.Vlad, M., Ionescu, N., Ispas, A.T., Ungureanu, E., and Stoica, C. Morphological study of congenital megaureter. Rom. J. Morphol. Embryol. 48, 381-390. (2007)

20.Lee, B.R., Silver, R.I., Partin, A.W., Epstein, J.I., and Gearhart, J.P. A quantitative histologic analysis of collagen subtypes: the primary obstructed and refluxing megaureter of childhood. Urology 51, 820-823. (1998)

21.MacKinnon, K.J. Primary megaureter. Birth Defects Orig. Artic. Ser. 13, 15-16. (1977)

22.Mackinnon, K.J., Foote, J.W., Wiglesworth, F.W., and Blennerhassett, J.B. The pathology of the adynamic distal ureteral segment. J. Urol. 103, 134-137. (1970).

23.Dixon, J.S., Jen, P.Y., Yeung, C.K., and Gosling, J.A. The vesico-ureteric junction in three cases of primary obstructive megaureter associated with ectopic ureteric insertion. Br. J. Urol. 81, 580-584. (1998)

24.Gosling, J.A. and Dixon, J.S. Functional obstruction of the ureter and renal pelvis. A histological and electron microscopic study. Br. J. Urol. 50, 145-152. (1978).

25.Hofmann, J., Friedrich, U., Hofmann, B., and Grabner, R. Acetylcholinesterase activities in association with congenital malformation of the terminal ureter in infants and children. Z. Kinderchir. 41, 32-34. (1986)

26.Summaria, V., Minordi, L.M., Canade, A., and Speca, S. Megaureter and ureteral valves. Rays 27,89-91.(2002)

27.Khoury, A. and Bagli, D. Reflux and megaureter. In Campbell-Walsh Urology. 9th ed. Wein, A.J. et al., Eds. WB Saunders, Philadelphia. (2007)

28.Berrocal, T., Lopez-Pereira, P., Arjonilla, A., and Gutierrez, J. Anomalies of the distal ureter, bladder, and urethra in children: embryologic, radiologic, and pathologic features. Radiographics 22, 1139-1164. (2002)

29.Nadira Farmanova, Shahruz Hikmatov And Lola Pulatova Studying the mineral composition of the urological composition Journal of Biomedicine and Practice2019-2-68-76 http://dx.doi.org/10.26739/2181-9297-2019-2-9

PREOPERATIVE MISTAKES IN THE SURGICAL TREATMENT OF UPPER RETRO MICROGNATIA

Jasur Rizaev
Samarkand state medical institute, Uzbekistan, e-mail: rector@sammi.uz
Aziz Kubaev
Samarkand state medical institute, Uzbekistan

Abstract.The analysis of scientific literature devoted to preoperative mistakes of surgical treatment of patients with upper retro- micrognathia was carried out. Long-term experience of surgical treatment has shown that the main mistakes of the preoperative period are neglect of motivation and assessment of mental health of patients, insufficient development of a complex training scheme with interdisciplinary participation and methods of forecasting aesthetic and functional results that can lead to various complications in the subsequent stages of treatment of patients with upper micrognatia. A special role in making mistakes is given to the inconsistency of opinions of orthognatic surgeons to the clinical and radiological essence, to the use of various classifications and terms to denote this form of facial skeleton disharmony, which often leads to an erroneous choice of treatment method. The necessity of multidisciplinary approach in surgical treatment of patients with upper retro-micrognathia has been emphasized.

Keywords: upper retro- micrognathia, surgical treatment, mistakes in diagnostics and treatment.

Upper retro-micrognathia is the most common disharmony of the development of the maxilla and its occurrence is from 1.6 to 12% of the total number of facial skeleton disharmonies (12.13). The complex topographic and anatomical relief of the face, its social significance, proximity to the brain and other vital organs, the location of large blood vessels, nerves are a difficult task for orthognathic operations on the maxilla. According to many authors, surgical treatment of upper micrognathia from 6.1 to 9% of cases is accompanied by various complications that adversely affect the aesthetic and functional results of treatment. Currently, various types of Le-Fort osteotomy and its multisegmental variants are mainly used for surgical correction of upper micrognathia. With combined deformations of the jaws, these operations are performed in combination with reconstructive operations of the zygomatic bones and mandible. An analysis of the scientific literature of the last several decades has shown the use of various criteria to classify the complications of orthognathic operations. Most often, specialists use a chronological criterion for this purpose, which includes preoperative errors, intraoperative and postoperative complications (5,16,18,20,23,25).

The analysis of the scientific literature of the last thirty years devoted to preoperative errors and the various complications of surgical treatment of patients with upper retro-micrognathia associated with it has been carried out.

According to some authors, preoperative disadvantages include motivational and diagnostic mistakes. The results of studies by some clinicians showed that in 62% of patients, the main motivation for visiting an orthognathic surgeon was an improvement in the aesthetic parameters of the face. 18% have functional and another 18% have aesthetic and functional problems (21). However, after orthognathic operations, they may experience functional problems that adversely affect the normal physiological activity of the maxillofacial region. Therefore, before performing an orthognathic operation,

the surgeon must plan the jaw osteotomy with a prediction of the optimal balance of functional and aesthetic changes in the maxillofacial region. Also, the patient must be given the opportunity to choose which is more important - aesthetic or functional problems (29).

An important role in the preparation of patients with skeletal forms of mandible deformations is played by the rational outpatient rehabilitation of the maxillofacial region with the participation of an oral surgeon and other specialists. In 4 - 8% of patients after surgery, inflammatory complications most often develop, such as exacerbation of chronic periodontitis, suppuration of a wound near a diseased tooth, osteomyelitis fragment, oroanthral fistula, and exacerbation of sinusitis that was not eliminated before surgery (3.18). Errors of the preoperative preparatory period include the lack of a rational preoperative orthodontic treatment with interdisciplinary participation. According to the literature, orthodontic appliances do not always have an effective effect on skeletal forms of jaw deformation (8.9).

However, orthodontic treatment with the elimination of obstructive diseases of the upper respiratory tract in children and adolescents with the participation of an otorhinolaryngologist leads to normalization of nasal breathing, correction of the dental arches of the jaws and proper growth of the facial skeleton (15).

Preoperative errors also arise as a result of the inconsistency of clinicians' approaches to the clinical and radiological nature, the failure to use unified terminology and classification of jaw deformities and complex examination methods (4). As a result of such errors, the same jaw deformations are described under various terms, and an inadequate treatment protocol is accordingly selected. Often the combination of upper micrognathia with lower macrognathia is diagnosed as lower macrognathia and osteotomy is performed on only one mandible. Moving one of the mandible posteriorly leads to a narrowing of the oral cavity, pharynx and disruption of the usual neuromuscular balance of the maxillofacial region. In this case, after removal of the intermaxillary traction, the tongue, pharyngeal muscles, and chewing muscles tend to occupy their original position, which leads to the displacement of the fragments to the initial position. Observations of a number of authors established the occurrence of relapses of jaw deformities from 4 to 75% of those operated on one mandible (2.12).

Currently, to eliminate such errors, a comprehensive examination is being performed before the operation, and based on modeling the optimal balance of the face and bite using diagnostic models, photographs, TRG or 3D images, adequate methods of jaw osteotomy are selected. Over the past several decades, the standard for the correction of upper micrognathia has been selected various options for osteotomy of the maxilla according to Le For-1. With a combination of deformation of the maxilla with lower macrognatia, combined osteotomies of the jaws are planned. Surgery on the maxilla is combined with a sagittal splitting or vertical osteotomy of the branches of the mandible. The use of combined variants of jaw osteotomy, in the opinion of V.I. Gunko, (6) leaves the volume of the oral cavity unchanged or slightly expands it, which neutralizes the expelling effect of the tongue on the mandible moved backward.

The most common mistake in the preoperative period is the prediction of aesthetic results of the face and the choice of method of operation. When eliminating upper retro-micrognathia, it is often impossible to predict the aesthetic results of a face in patients with unexpressed zygomatic, infraorbital and paranasal regions. As a choice, we used various options for osteotomy of the maxilla at the level of Le Fort 2, and 3. The choice of methods of osteotomy at the level of Le Fort 2 and 3 allows you to achieve good

aesthetic results. But according to V. M. Bezrukov, these operations are too long, accompanied by a large number of blood loss and relapses, which caused their rare use in clinical practice. To eliminate the above drawbacks, he proposed the use of an osteotomy of the middle zone of the face with osteotomy lines closer to the infraorbital margin with the inclusion of the lower parts of the zygomatic bones (4). Other authors in this case propose combining an osteotomy of the maxilla with an osteotomy of the zygomatic bones (10). The results of the analysis of our experience in the treatment of patients with upper micrognathia showed that the choice of these methods allows achieving good aesthetic results in patients without pathology of the nasal cavity and does not take into account its aesthetics.

Until today, with orthognathic treatment of upper micrognathia, the problem of preoperative prediction of aesthetic changes in the shape of the nose and the choice of method for their correction remains unresolved. Moving the maxilla forward and upward often leads to deformation of the tip and wings of the nose, which does not always meet the increased aesthetic needs of patients. To prevent deformation of the external nose after moving the maxillary complex anteriorly, various rhinoplasty methods have been proposed. In 1981, V.M. Bezrukov proposed a method for sickle-shaped resection of the cartilaginous part of the nasal septum with a base directed to the bottom of the nose, which is most shown for patients with a forward-looking nose shape as a result of an increase in septum cartilage. To improve the results, the method was improved by removing the anterior nasal spine of the maxilla. For patients with short and wide forms of the nose with a nose bridge, various rhinoplasty options using auto-allografts or implants are proposed, which lead to an improvement in its external contours. To eliminate the excessive expansion of the bases of the wings of the nose, it is proposed to use various options for septum plasty and fixation of the wings with sutures that hold them in position. However, in the postoperative period, part of the patients noted expansion of the wings, curvature of the septum and difficulty in nasal breathing, which indicates the debatability of their use and insufficiently developed indications for them (7,22,26,27,28).

All the above facts prove that the choice of the method of osteotomy of the maxilla without taking into account the type of face and nose shape and the morphofunctional state of the maxillary complex of patients does not always lead to optimal aesthetic and functional results, which requires the development of new methods of surgical treatment that exclude these complications.

As it can be seen from the analysis of the available scientific literature, upper micrognathia is a fairly common disharmony among deformations of the facial skeleton, and its surgical correction from 6, 1-9% of cases is accompanied with various complications. These complications can be observed during various periods after surgery. However, their occurrence in most cases is associated with preoperative errors in the diagnosis, planning and prediction of treatment results.

An analysis of literature data and clinical experience has shown that the most common mistakes in the preoperative period are to ignore treatment motivation and treatment planning without assessing the mental health of patients, which can lead to patient dissatisfaction with the aesthetic results of treatment. The inclusion in the scheme of a comprehensive examination of a psychologist, psychiatrist and method for determining mental health on the Josef scale leads to a correct assessment of the patient's motivation and mental health and the planning of the treatment process, taking into account these features.

In our opinion, the most common mistakes in the preoperative period include the lack of a preoperative scheme for the comprehensive preparation of patients with interdisciplinary participation. Sanitation of the pharyngeal cavity and treatment of obstructive diseases of the upper respiratory tract with the participation of an ENT specialist and orthodontic correction can eliminate all chronic foci of infection and lead to the correct growth of the maxillary complex. Such a joint approach reduces the volume of surgical intervention and is the prevention of inflammatory complications and relapses of deformation.

Important for optimal orthognathic surgery is the joint work of an oral surgeon and an orthodontist. Planned tooth extraction, oral segmental osteotomy within two to three teeth, and compactosteotomy with rational orthodontic treatment corrects dentoalveolar deformities of the jaw and creates optimal conditions for reconstructive surgery. The most common errors of the preoperative period are the contradictory opinions of clinicians on the clinical and radiological nature of jaw deformities, the use of various classifications and terminology in the diagnosis of upper micrognathia. As a result of such errors, upper micrognathia is often diagnosed as lower macrognathia. Erroneous surgery on the mandible does not lead to the achievement of optimal aesthetic and functional results. In patients operated in this way, in most cases, relapses of deformities and other functional disorders of the maxillofacial region are observed. The use of unified terminology, classification, complex examination methods leads to improved diagnostic accuracy and an adequate choice of the surgical method.

Another serious problem of the preoperative period is the lack of accuracy in predicting the aesthetic results of the middle zone of the face and the choice of correction method. An inadequate choice of the method of operations for the middle zone of the face can lead to dissatisfaction of patients with upper micrognathia with the aesthetic and functional results of treatment, which are manifested in the form of indistinct contours of the zygomatic, infraorbital regions and deformation of the external nose and difficulty in nasal breathing. In our opinion, accurate prediction and selection of an appropriate method depending on the type of face and nose shape allows you to fix the aesthetic contours of the middle zone of the face and minimally violates the aesthetics of the nose in patients without difficulty in nasal breathing. In cases of difficulty in nasal breathing in patients with an elongated-concave type of face, our use of the developed method for osteotomy of the middle zone of the face with the expansion of the bone cavity of the nose is the most shown. The method allows to correct the bite, restores nasal breathing and preserves its aesthetic contours. The aesthetic contours of the infraorbital and zygomatic areas are also improved.

Conclusion

Thus, the results of the analysis of the scientific literature showed that the cause of preoperative errors in the orthognathic treatment of upper micrognathia is the inconsistency of opinions of clinicians about its clinical and radiological essence, failure to use the same terminology and classification, ignoring the motivation and mental status of patients, insufficient development of preoperative outpatient preparation for orthognathic operations involving related specialists, lack of clear indications for various options m osteotomies of the maxilla with the aesthetic and performance morphofunctionalmidface.

Referenes.

1.Abdukadyrov, A. (2007). Improvement of reconstructive operations in adult patients with combined deformities of the jaw. Abstract. diss. for a job. scientist step. Doct. honey.

sciences. 2 p.m. 21 / A. Abdukadyrov, Tashkent: 2007.-25 p.

2.Abdukadyrov A., MukhamedievaF.Sh.,Kurbanov F.R. (2019). Outpatient preparation algorithm for adult patients for orthognathic surgery. Stomatologiya, (1-2), 46-51.

3.Andreishchev, A. R., Karpishchenko, S. A., Baindurashvili, A. A., &Shakhnazarov, A. E. (2010). Endoscopic assessment of the condition of the nasal cavity after reconstructive operations on the upper jaw. Russianotorhinolaryngology, (2), 12-16.

4.Bezrukov, V. M. (1981). Clinic, diagnosis and treatment of congenital deformations of the middle zone of the facial skeleton. Moscow.

5.Belova, O.M., &Gunko, V.I. (2010). Analysis of errors and complications in the surgical treatment of patients with jaw deformities.Bulletin of the Peoples' Friendship University of Russia. Series: Medicine, (1).

6.Gunko, V.I. (1986). Clinic, diagnosis and treatment of patients with combined deformities of the jaw. Diss. Doct. honey. sciences. M, 525.

7.Gunko, V. I., Zandelov, V. L., &Kalmykov, A. V. (2000). Prevention of postoperative deformities of the nose after bone-reconstructive surgery on the maxillary complex. Dentistry, (2), 25-28.

8.Kalamkarov, H.A., Rabukhina, N.A., &Bezrukov, V.M. (1981). Deformations of the facial skull. M .: Medicine, 240, 2.

9.Makhsudov S.N. (2002). Clinical, radiological and biometric indicators of rhinopharyngeal tooth abnormalities, their complex orthodontic treatment. Abstract. diss. for a job. scientist step. Doct. honey. sciences. 2 p.m. 21 / A. Abdukadyrov, Tashkent: B. and., 2002.-25 p.

10.Mitroshenkov, P.N. (2005). Plastic surgery of total and subtotal defects of the upper and middle zones of the facial skeleton. NewinDentistry, (6), 89-96.

11.Ruzin, G.P. (2006). A short course of lectures on surgical dentistry and maxillofacial surgery: a manual for international students. Kiev: Bookplus.

12.Sukachev, V. A. (1984). Atlas of reconstructive operations on the jaw.

13.Sukachev V.A., Gunko V.I., Abdukadyrov A. A new method for vertical osteotomy of the branches of the lower jaw.-M., 1989.- S. 138-139.

14.Tairov, W.T., &Dzhumaev, Sh. M. (2016). Reconstructive surgery for defects and deformities of the lower jaw. Science, NewTechnologiesandInnovations, (7), 88-94.

15.Khasanov S.A., Babakhanov G.K., Makhsudov S.N. (2019). Integration tactics of specialists in the complex treatment of children with curvature of the nasal septum, combined with anomalies in the development of the upper jaw. Tashkent. Guidelines, 20.

16.Hrle, F.(1980).Le Fort I ostectomy (using miniplates) for correction of the long face. Internationaljournaloforalsurgery, 9(6), 427-432.

17.Kim, Y. K. (2017). Complications associated with orthognathic surgery. Journal of the Korean Association of Oral and Maxillofacial Surgeons, 43(1), 3-15.

18.Jdrzejewski, M., Smekta?a, T., Sporniak-Tutak, K., &Olszewski, R. (2015). Preoperative, intraoperative, and postoperative complications in orthognathic surgery: a systematic review. Clinicaloralinvestigations, 19(5), 969-977.

19.Kim, J. H., Kim, S. G., & Oh, J. S. (2010). Complications related to orthognathic surgery. MaxillofacialPlasticandReconstructiveSurgery, 32(5), 416-421.

20.Kramer, F. J., Baethge, C., Swennen, G., Teltzrow, T., Schulze, A., Berten, J., &Brachvogel, P. (2004). Intra-and perioperative complications of the LeFort I osteotomy: a prospective evaluation of 1000 patients. JournalofCraniofacialSurgery, 15(6), 971-977.

21.Lee, K. H., & Lee, S. H. (1999). A clinical study of orthognathic surgery patients'satisfaction and psychologic change. Journal of the Korean Association of Oral and Maxillofacial Surgeons, 25(2), 151-164.

22.Monnazzi, M. S., Mannarino, F. S., &Gabrielli, M. F. R. (2014). Extraoral alar base cinch. A modification for the technique. Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology, 26(2), 142-144.

23.De molvan Otterloo, J. J., Tuinizing, D., Greebe, R. B., & Van der Kwast, W. M. (1991). Intra-and early postoperative complications of the Le Fort I osteotomy: a retrospective study on 410 cases. Journalofcranio-maxillo-facialsurgery, 19(5), 217-222.

24.Obwegeser, H. L. (1969). Surgical correction of small or retrodisplaced maxillae the "dish-face" deformity. PlasticandreconstructiveSurgery, 43(4), 351-365.

25.Proffit, W. R., Phillips, C., &Turvey, T. A. (1991). Stability after surgical-orthodontic corrective of skeletal Class III malocclusion. 3. Combined maxillary and mandibular procedures. The International journal of adult orthodontics and orthognathic surgery, 6(4), 211-225.

26.Shams, M. G., &Motamedi, M. H. K. (2002). A more effective alar cinch technique. Journaloforalandmaxillofacialsurgery, 60(6), 712-715.

27.Politis, C., Lambrichts, I., &Agbaje, J. O. (2014). Neuropathic pain after orthognathic surgery. Oral surgery, oral medicine, oral pathology and oral radiology, 117(2), e102-e107.

28.Shin, Y. M., Lee, S. T., & Kwon, T. G. (2016). Surgical correction of septal deviation after Le Fort I osteotomy. Maxillofacialplasticandreconstructivesurgery, 38(1), 21.

29.Yen, C. Y., Kuo, C. L., Liu, I. H., Su, W. C., Jiang, H. R., Huang, I. G., ... & Lee, S. Y. (2016). Modified alar base cinch suture fixation at the bilateral lower border of the piriform rim after a maxillary Le Fort I osteotomy. Internationaljournaloforalandmaxillofacialsurgery, 45(11), 1459-1463.

30.Kahramon Shomurodov, Improvement of surgical treatment of fractures of the lower wall of orbit RanoMirhusanova Journal of Biomedicine and Practice 2016-1- 15-19 http://dx.doi.org/10.26739/2181-9300-2016-1-3

31.Kahramon Shomurodov Aspects of the development of surgical treatment of congenital cleft palate Journal of Biomedicine and Practice 2016-1- 24-30 http:// dx.doi.org/10.26739/2181-9300-2016-1-5

Internet address: http://ejournals.id/index.php/EJMM/issue/archive
E-mail: info@ejournals.id
Published by ejournals PVT LTD
Issued Bimonthly
DOI prefix: 10.52325
Potsdamer Straße 170, 10784 Berlin, Germany