Chapter 1

RESULTS OF BIOCHEMICAL BLOOD ANALYSIS AND MARKERS OF FIBRINOLYSIS IN PATIENTS WITH OSTEOARTHRITIS OF LARGE JOINTS REQUIRING ENDOPROSTHETICS

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INTRODUCTION

Today, endoprosthesis remains one of the most effective methods of treatment for patients in the late stages of osteoarthritis of large joints. However, it is known that operative interventions related to endoprosthesis of the hip and knee joints are associated with a number of complications: thrombosis and thromboembolism of the veins of the lower extremities, changes in biochemical and immunological indicators of homeostasis, the development of paraprosthetic infection[1].

Endoprosthesis of large joints is the most radical orthopedic method of treating osteoarthritis, which allows normalizing the function of the damaged joint in 90-96% of cases and eliminating pain syndrome, which significantly improves the quality of life of patients. It has been proven that total endoprosthesis is the predominant method of treatment for diseases of large joints. But the presence of uncompensated forms of concomitant pathology on the part of the cardiovascular and respiratory systems, pathologies of lipid, protein and carbohydrate metabolism can prevent surgical intervention[2].

No less important factor that affects the result of endoprosthesis is the implementation of the correct rehabilitation process. When determining the goal of rehabilitation, attention should be paid to the patient's age, the functional state of the cardiovascular system, liver, kidneys, and immunological disorders. It is known that the dynamics of indicators of the systemic immune response to endoprosthesis of large joints is caused directly

[1]Ahmed S.S., Begum F., Kayani B., Haddad F.S. Risk factors, diagnosis and management of prosthetic joint infection after total hip arthroplasty. *Expert. Rev. Med. Devices.* 2019. 16(12). P. 1063–1070. DOI: 10.1080/17434440.2019.1696673. Epub 2019

[2]Zhao J., Liang G., Hong K., Pan J., Luo M., Liu J., Huang B. Risk factors for postoperative delirium following total hip or knee arthroplasty: A meta-analysis. Front. Psychol. 2022 13:993136. DOI: 10.3389/fpsyg.2022.993136. eCollection 2022.

by surgical intervention and does not depend on the type of fixation of the implant. Therefore, the combination of the patient's changed immunological background before endoprosthesis and operative stress creates prerequisites for the development of immunodepression. At the same time, manifestations of complications at a later date after the operation, which may require repeated surgical intervention on other joints, are not excluded. After endoprosthesis implantation, the rehabilitation period in a hospital is up to 3 weeks. During this period, a number of clinical and metabolic disorders occur in the patient's body, which require pharmacological correction[3].

The issue of a comprehensive approach to the study of protein, lipid, carbohydrate and mineral metabolism, as well as the functional state of internal organs in patients after endoprosthesis of large joints with the use of modern biochemical markers, remains insufficiently studied today. The nature of changes in the processes of lipid peroxidation and the state of the antioxidant system in patients with total hip arthroplasty is of great importance. Some scientists consider osteoarthritis to be part of the metabolic syndrome, an integral pathogenetic link of which is obesity and arterial hypertension. The development of somatic complications in patients with osteoarthritis after endoprosthesis is often associated with cardiovascular disorders, anemic syndrome, and changes in the body's antioxidant defenses.[4]

During endoprosthesis, the issues of disorders of lipid metabolism and their peroxidation system, hemostasis, collagen, glycoprotein and proteoglycan exchange, activity of marker enzymes remain incompletely clarified. The expediency of these studies is dictated by the need to create well-founded schemes for medical correction of the condition of patients after endoprosthesis implantation in order to prevent negative treatment results, in particular, violations of the hemostasis system[5].

Thus, the relevance of our research is determined by the following. Patients with osteoarthritis of large joints requiring endoprosthesis often have concomitant diseases that complicate the course of the postoperative period and worsen the final result of treatment. In order to timely detect the possibility of concomitant pathology, it is necessary to use effective and informative laboratory tests that meet the requirements of evidence-based

[3]Konnyu K.J., Pinto D., Cao W., Aaron R.K., Panagiotou O.A., Bhuma M.R., Adam G.P., Balk E.M., Thoma L.M. Rehabilitation for Total Hip Arthroplasty: A Systematic Review. *Am. J. Phys. Med. Rehabil.* 2023. 102(1). P. 11–18. DOI: 10.1097/PHM.0000000000002007. Epub 2022 Mar 12.

[4]Ledford C.K., Elstad Z.M., Fruth K.M., Wilke B.K., Pagnano M.W., Berry D.J., Abdel M.P. The Impact of Metabolic Syndrome on Reoperations and Complications After Primary Total Hip Arthroplasty. *J. Arthroplasty.* 2022. 37(6). P. 1092–1097. DOI: 10.1016/j.arth.2022.01.091. Epub 2022 Feb 4.

[5]Yu X., Wu Y., Ning R. The deep vein thrombosis of the lower limb after total hip arthroplasty: what should we care. *BMC Musculoskeletal Disord.* 2021. 22(1). P. 547. DOI: 10.1186/s12891-021-04417-z.

medicine. This goal can be achieved by using an optimal set of biomarkers of inflammatory and destructive disorders, lipid metabolism, immune status and hemostasis. Of particular importance is the study of lipid metabolism disorders in patients with osteoarthritis of large joints after endoprosthetics. These disorders are not sufficiently studied, but they can significantly affect the general somatic condition of patients. The development of pharmacotherapy schemes for patients after endoprosthesis still does not take into account the results of laboratory studies, and does not fully correspond to the principles of personalized medicine.

1. Materials, methods and purpose of research

In the clinic of orthopedic arthrology and endoprosthetics of the State University "Institute of Spine and Joint Pathology named after prof. E. Sitenka of the National Academy of Medical Sciences of Ukraine" examined 175 patients (2013–2024) with stage I-IV osteoarthritis of the large joints, aged from 40 to 87 years. As a result, 65 patients with III and IV stages of osteoarthritis who needed endoprosthetics and 30 patients with III and IV stages of osteoarthritis who underwent endoprosthetics were selected for research. When taking an anamnesis and clinical examination, the following clinical symptoms were found in patients with gonarthrosis: pain from the inner or front surface of the joint during walking at rest, instability of the joint, in patients with coxarthrosis – lameness of the affected limb, pain in the inguinal region with radiation to the knee, restriction of hip rotation and abduction, flexion and extension, in severe cases – atrophy of the muscles of the hip and buttocks, shortening of the limb, severe lameness.

After the clinical examination, the patients underwent radiography of the affected joints. The stage of osteoarthritis was assessed according to the X-ray classification of Kellgren JH and Lawrence JS: I stage – questionable changes (doubtful narrowing of the joint space and possible marginal osteophytes); II stage – minimal manifestations (defined osteophytes and possible narrowing of the joint space); III stage – moderate manifestations (multiple osteophytes, pronounced narrowing of the joint space, signs of sclerosis, possible deformation of the bone edges); IV stage – pronounced manifestations (virtually absent joint gap, multiple osteophytes, osteosclerosis and deformation of the joint). Blood, serum and blood plasma were used as material for the study. Blood samples for research were taken from the ulnar vein on an empty stomach.

Biochemical research. During the examination of patients with osteoarthritis of the large joints at the III and IV stages, the following biochemical markers were determined in the blood serum: total protein – by the biuret method, protein fractions (albumin, α_1-, α_2-β– and γ-globulins) – by

the nephelometric method, glycoproteins – by the modified method of O. P. Shtenberg and Y. N. Dotsenko, chondroitin sulfates – according to the Nemeth–Csoka method in the modification of L. I. Slutsky, haptoglobin – by reaction with rivanol, C-reactive protein – by immunoenzymatic method, glucose – by enzymatic method, urea and uric acid – by urease method, creatinine – by Jaffe method, phosphorus – by Fiske-Subbarow method, magnesium – by color reaction with titanium in yellow, total and ionized calcium – on the AEK-01 electrolyte analyzer.

The content of total cholesterol was determined by the enzymatic colorimetric method using the Cholesterol PAP SL Mono kit, β-lipoproteins – by the turbidimetric method according to Burshtein and Samai, HDL cholesterol – was determined after precipitation from plasma by the action of heparin, manganese chloride or other precipitants, LDL, LDL, triglycerides, CA – calculated based on tests combined into a lipidogram, which includes triglycerides, total cholesterol and α-lipoprotein cholesterol. The content of LDL cholesterol was determined according to the formula: total cholesterol – (LDL cholesterol + LDL cholesterol). The cholesterol content of VLDL was calculated according to the formula: TG: 2.181; CA was determined as the ratio of the sum of LDL cholesterol and HDL cholesterol to HDL cholesterol.

The content of TBC products (malondialdehyde) was determined according to the instructions for the set of reagents. The activity of the enzymes AlAT, AsAT, alkaline phosphatase and GGTP was determined by kinetic methods, the activity of acid phosphatase – by the Bodanski method.

The content of fibrinogen in the blood plasma of patients with osteoarthritis and the fibrinolytic activity of the blood plasma were determined using ready-made reagent sets "XII-dependent fibrinolysis". The coefficient of hemostasiological adaptation was also calculated: KHA = FA (min.): fibrinogen (g/l).

Statistical data analysis was carried out using Microsoft Excel XP and Statsoft Statistica 6.0 software packages. Comparison of groups was carried out according to the Student's parametric test.

The aim of the study: to investigate laboratory markers of lipid, carbohydrate, protein metabolism and indicators of fibrinolysis in patients with osteoarthritis who require endoprosthetics, to assess the health status of patients.

2. Results of laboratory examination of patients with osteoarthritis of large joints who require endoprosthetics

Markers of lipid metabolism disorders. Lipid metabolism is one of the most complex metabolisms of the human body. The importance of lipids in the body is quite important: they form the basis of the central nervous system,

form the lipid matrix of cell membranes and organelles, and play a significant role in energy metabolism. To date, the existence of a relationship between disorders of lipid metabolism and the progression of osteoarthritis has been proven, however, in most cases, the leading mechanism of the development of inflammatory and destructive changes in the joints is associated with mechanical stress due to obesity. However, with obesity, there is not only a mechanical load on the joints, but also a metabolic syndrome and associated biochemical and systemic disturbances in lipid metabolism. Disorders of lipid metabolism are associated with such diseases as atherosclerosis, coronary heart disease, obesity, diabetes, etc. According to our previous studies, end-stage osteoarthritis requiring arthroplasty was often accompanied by an increase in serum total cholesterol and β-lipoproteins, especially in elderly patients.

In patients with osteoarthritis of the III and IV stages, there is a violation of lipid metabolism, which is manifested by changes in the lipid profile. When analyzing the results of laboratory tests, an increase in total cholesterol was found in 26.2% of patients (17 people) from the total number of patients. Such changes in total cholesterol content, in our opinion, can be explained by secondary hypercholesterolemia, which is often associated with concomitant liver diseases (for example, against the background of long-term treatment with nonsteroidal anti-inflammatory drugs), gout, arterial hypertension, endocrine pathology, coronary heart disease, and obesity. However, an elevated level of cholesterol does not provide specific information about a specific disease, but only reflects the pathology of lipid metabolism in general, which requires a study of lipidogram indicators. Violation of lipid metabolism in patients in the III and IV stages of osteoarthritis was manifested by corresponding changes in markers of lipid metabolism – HDL, LDL, VLDL, triglycerides, and β-lipoproteins. Blood lipoproteins are high-molecular water-soluble complexes of different classes of lipids (triglycerides, cholesterol) with proteins that form micellar structures for further transport of lipids in the blood.

In patients with stage III and IV osteoarthritis of large joints requiring endoprosthesis, there was a decrease in the content of HDL in 52.9% (27 people) of the total number of examined people, while the average indicator of HDL decreased by 27.9%. This class of lipoproteins is sometimes called anti-atherogenic, because their increased concentration significantly reduces the risk of developing and progressing atherosclerosis. They transport cholesterol from the tissues to the liver, thereby contributing to its transformation, removal from the body and reducing the risk of its deposition in blood vessels and the appearance of atherosclerotic lesions. A decrease in this fraction of lipoproteins (HDL) in the blood of patients with osteoarthritis of the III and IV stages was accompanied by an increase in the content of LDL

in the blood – an atherogenic fraction of lipoproteins that transports cholesterol to tissues. These compounds penetrate the vascular wall and can be a substrate for atherosclerotic arterial damage. The content of LDL was increased in 25.4% (13 people) of the examined patients, the average indicator was increased by 30.6%.

β-lipoproteins, which are part of LDL and often increase in the blood of patients with osteoarthritis in the terminal stages, can also be considered an important diagnostic marker of lipid metabolism disorders. According to our research, the content of β-lipoproteins in the blood of patients with III and IV stages of the disease was increased by 69.2% (45 patients), on average by 65.7% compared to the control group. Such dynamics of the increase in the content of β-lipoproteins in patients with osteoarthritis makes it possible to consider this biochemical marker more informative than the content of HDL, because in most patients with an increased content of total cholesterol, the CA value was higher than the indicator in the control group, which means that this test can be important for the initial assessment of patients' condition. In our opinion, in the case of an increase in the level of β-lipoproteins in the blood of patients with osteoarthritis, it is a prelude to a more in-depth examination of patients in the form of determining the fractional composition of lipoproteins and triglycerides, as well as KA.

An increase in the blood level of VLDL and triglycerides by 46.5% in 25.4% of patients with osteoarthritis who require endoprosthesis indicates the development of type II hyperlipoproteinemia, which is often manifested by coronary heart disease and atherosclerotic changes in blood vessels. At the same time, an increase in KA in 94.1% of patients (48 people) indicates the development of atherogenic dyslipidemia and, as a result, an increase in the risk of cardiovascular diseases in this category of patients.

According to our previous research, disturbances in the hemostasis system in the late stages of osteoarthritis of large joints are accompanied by disturbances in fibrinolysis, accumulation in the bloodstream of fibrin degradation products, as well as lipid peroxidation products – diene conjugates, which are also called TBC products. These compounds are classified as markers of body intoxication during the course of severe progressive diseases. Since in the late stages of osteoarthritis, a systemic inflammatory process with the activation of inflammatory and anti-inflammatory cytokines and proteins of the acute phase occurs in the body of patients, the increase in the content of TBC products in 66.7% of patients (34 individuals) can be considered completely natural and pathogenetically justified, while the average the indicator grew by 24.5%. Activation of lipid peroxide oxidation is worsened by progressive hypercholesterolemia, which occurs due to lipid peroxides disrupting the processes of its utilization to bile acids, which normally occurs in hepatocytes.

Thus, the increase in the blood of patients with stage III and IV osteoarthritis in the content of LDL, VLDL, and triglycerides against the background of a decrease in HDL concentration and an increase in CA indicate the important diagnostic value of these biochemical markers in the examination of this category of patients. The increased content of TBC products in the blood of patients with stage III and IV osteoarthritis indicates a violation of the body's oxidant status, which has important clinical and diagnostic significance and requires pharmacological correction.

Markers of disorders of protein and carbohydrate metabolism. Violation of protein metabolism in the body depends on its functional state, changes in the regulatory effects of the nervous and endocrine systems, as well as the nature of pathological processes. Violations of protein metabolism in osteoarthritis of large joints in patients who require endoprosthetics are, in most cases, of clinical and diagnostic significance precisely for assessing the degree of systemic inflammatory disorders. Significant changes in the protein spectrum of blood serum were found in patients with stage III and IV osteoarthritis of large joints. The albumin level was reduced in 64% of patients (16 people), on average – by 18.2% compared to the control group. Albumin synthesis occurs in hepatocytes, the functional state of which depends on many factors. These factors in patients with osteoarthritis can be associated, along with inflammatory and destructive processes in the joints with suppression of protein synthesis in the liver, taking NSAIDs as painkillers and other pharmacological drugs. It is possible that during the development of the pathological process in the tissues of the affected joints in the late stages of osteoarthritis, an inflammatory reaction develops in tissues where ischemia occurs due to impaired blood circulation. At the same time, albumin, which has transport functions, can be used to remove the products of degradation and necrobiosis of the tissues of the affected joints. At the same time, hypoalbuminemia is obviously compensated by an increase in the concentration of other proteins, as a result of which the concentration of total protein remains unchanged: the content of total protein was increased in the blood serum of only two patients, which did not affect the average index of total protein.

Marker proteins of globulin fractions are indicators of inflammation and can indicate the activity and severity of the pathological process both in the affected joints and in the body as a whole. In patients with osteoarthritis who require endoprosthetics, we found an increase in the concentration of α_1– and β-globulins. The content of the α1-fraction of globulins was increased in 84% of patients (21 people), on average – by 96.2% compared to the indicator of the control group. This fraction includes α1-antitrypsin, a glycoprotein that forms complexes with proteases, inhibiting the proteolytic activity of thrombin, plasmin, and proteases, which are released during the destruction

of leukocytes in the focus of inflammation. This fraction also includes the glycoprotein haptoglobin, which participates in detoxification processes and also protects tissues from proteolysis during the destruction of connective tissue structures of affected joints. The main proteins of the β-globulin fraction are LDLs, the increase of which in blood serum indicates atherogenic dyslipidemia and an increased risk of developing atherosclerosis.

The growth of individual fractions of globulins is accompanied by an increase in the content of total glycoproteins in blood serum: their concentration in patients with stage III and IV osteoarthritis who require endoprosthesis was increased in 100% of the examined patients by 54.5% compared to the control group. It is obvious that osteoarthritis of the III and IV stages was accompanied by an increase in the total content of glycoproteins in the blood serum against the background of a more pronounced increase in certain representatives of carbohydrate-protein complexes – haptoglobin and C-reactive protein.

The concentration of haptoglobin as a marker of acute inflammation was increased only in 9.2% of the total number of patients (5 people), while the average indicator of haptoglobin in the blood was increased by 40%. Such dynamics of this marker glycoprotein in the blood of patients with stage III and IV osteoarthritis can be explained by the simultaneous severe course of the acute systemic inflammatory process and the destructive process in the affected joints with a simultaneous violation of the functional state of hepatocytes, which is confirmed by an increase in the activity of liver marker enzymes. It is obvious that the increase in the concentration of haptoglobin in the blood of individual patients with osteoarthritis who require endoprosthesis should be considered as a cautious prognostic sign.

The content of C-reactive protein in the blood was increased by an average of 2.6 times in 41.8% of the total number of examined patients with osteoarthritis of the III and IV stages. An increase in this biochemical marker was not observed in the remaining 58.2% of patients. C-reactive protein is included in the fraction of γ-globulins, but it does not affect their total concentration, as it is a "minor" protein and is found in the blood in minimal amounts. Determination of the content of C-reactive protein in patients with severe stages of osteoarthritis is important for establishing the degree of systemic inflammation and determining pathological conditions comorbid with osteoarthritis.

It is obvious that C-reactive protein is formed as a result of partial or complete denaturation due to the breakdown of tissues during inflammatory and destructive processes, and the degree of its growth in blood serum is a marker of the activity of the course of latent inflammation, which is not accompanied by characteristic clinical or other manifestations. It is also known that C-reactive protein can be a prognostic marker of cardiovascular

disorders: it is able to bind and neutralize the mediator of the parasympathetic nervous system acetylcholine, influencing endothelium-dependent reactions of blood vessels, reducing its hypotensive effect.

The presence of destructive changes in joints with increased destruction of cartilage and bone tissue is confirmed by an increase in the content of chondroitin sulfates – components of proteoglycans of bone and cartilage tissue. An increase in the content of chondroitin sulfates was found in 100% of the examined patients with osteoarthritis requiring endoprosthetics, while the average indicator was increased 4 times compared to the control group. Such growth dynamics of chondroitin sulfate content is associated with severe inflammatory-dystrophic changes in the tissues of the affected joints in the III and IV stages of osteoarthritis, as well as, possibly, with a violation of the functional state of the liver, which is the site of destruction of these compounds. Thus, on the one hand, this biochemical marker indicates the destruction of connective tissue in the affected area (articular cartilage, subchondral bone), on the other hand, it indicates a decrease in the functional capacity of the liver to catabolize glycosaminoglycans.

Violations of the functional state of the liver are confirmed by changes in such biochemical markers as colloid-sediment tests – thymol test and Veltman's test. Changes in the colloidal properties of blood plasma proteins make it possible to assess the functional state of the liver in the early stages of its damage and during the development of liver fibrosis. Veltman's test in patients with stage III and IV osteoarthritis was characterized by an increase in the index in 14.7% of patients (5 people) and a decrease in 64.7% of patients (22 people). On average, the Veltman test score in patients with osteoarthritis was reduced by 20% compared to the control group. Thus, the growth of this biochemical marker in the blood serum of 14.7% of the examined patients confirmed an active systemic inflammatory process with tissue destruction, including, associated with the activation of the liver for the synthesis of proteins of the acute phase of inflammation, which have antiproteolytic properties and indicate exacerbation of osteoarthritis. A decrease in the Veltman test index in the remaining 64.7% of patients is the result of chronic inflammatory-destructive and proliferative processes with increased growth of connective tissue in the tissues of the affected joints, liver, and blood vessels.

Violation of the functional state of the liver is confirmed by an increase in the thymol test in 74.2% of patients with stage III and IV osteoarthritis (26 people), on average, the indicator increased by 2.4 times compared to the control group. The thymol test is an important test for detecting latent forms of the course of liver diseases, especially often it is increased in patients who have suffered viral hepatitis before, and also have chronic liver diseases of a non-infectious nature. According to our research, in patients with

osteoarthritis who require endoprosthesis, an increase in the thymol test can be an important laboratory sign of liver damage, for example, due to concomitant obesity, alcohol abuse, and also be a marker of previously transmitted infectious hepatitis.

It is known that the thymol test is a more informative laboratory marker of inflammatory liver damage than the activity of ALT, but it can also characterize other pathological conditions. There is a relationship between the thymol test indicator and blood lipoproteins: lipoproteins have a significant molecular weight and are prone to sedimentation, which can cause an increase in the thymol test. This allows us to assume that the increase in the thymol sample in the majority of examined patients in the III and IV stages of osteoarthritis is caused by lipid metabolism disorders.

The level of glycemia was elevated only in 23.5% of patients (8 people) from the total number of examined. The maximum glucose level in patients with osteoarthritis requiring arthroplasty was 8.6 mmol/L. The presence among examined patients with hyperglycemia may indicate the development of diabetes, and may also be the result of stress factors on the body. Hyperglycemia, as a rule, is caused by a violation of insulin synthesis (characteristic of type 1 diabetes – Insulin-dependent), insulin resistance (due to the development of type 2 diabetes – non-insulin-dependent), or the effect of counterregulatory hormones (glucagon, cortisol, catecholamines) and the influence of immune systems. The presence of hyperglycemia can be caused by a violation of glucose transport into muscle and adipose tissue, inhibition of glucose oxidation by phosphorylation with a decrease in the activity of hexokinase and glucokinase enzymes, a decrease in glycogen synthesis in the liver due to a decrease in the activity of glycogen synthetase, as well as an increase in gluconeogenesis. According to the data of modern laboratory endocrinology, glucose cannot serve as an early marker of diabetes, at the same time, during the examination of patients with osteoarthritis in the III and IV stages of the disease who require endoprosthetics, the detection of an elevated glucose level makes it possible to suspect diabetes and prescribe an additional examination to establish more severe metabolic disorders, or the exclusion of diabetes.

Thus, after analyzing markers of protein and carbohydrate metabolism in patients with osteoarthritis of large joints who require endoprosthetics, we found significant metabolic disorders. The presence of an inflammatory-destructive process in the joints in the terminal stages of osteoarthritis is accompanied by dyslipidemia, dysproteinemia, changes in colloid-sediment liver samples in the majority of patients.

Markers of fibrinolysis. Violation of the fibrinolysis system is accompanied by an increase in the blood content of fibrinogen, a protein of the acute phase of inflammation, which is part of the γ-globulin fraction. In

patients with osteoarthritis in stages III and IV who require endoprosthetics, it is mandatory to monitor the state of the fibrinolysis system to prevent hypercoagulation, which is a frequent cause of thromboembolic complications. When analyzing the results of the examination of patients, an increase in the concentration of fibrinogen was established in 87.7% of patients (57 people) from the total number, while the average index of fibrinogen content was increased by 96% compared to the control group (the control group –2.52±0.12 g/l, patients with osteoarthritis – 4.94±0.32 g/l ($p<0.001$). This was accompanied by an increase in the fibrinolytic activity (FA) of the blood in 63.1% of patients with osteoarthritis (41 people), which led to an increase in the average indicator of FA by 3.1 times compared to the control group (the control group –6.50±0.33 min., osteoarthritis patients – 20.02±1.39 min. ($p<0.001$).

In order to more objectively assess the state of the fibrinolysis system and predict hypercoagulable conditions in patients with stage III and IV osteoarthritis who require endoprosthetics, KHA was calculated – the coefficient of hemostasiological adaptation, which allows predicting thromboembolic complications during endoprosthetics in the early postoperative stages. It is believed that with KHA values from 7.2 to 8.4, starting from the 3rd day of surgery, the development of complications is almost absent, with a value of 8.5 and above, an unfavorable prognosis regarding the hypercoagulable state is observed. In our patients, before surgery, the KHA index ranged from 1.28 to 8.16, which indicates a low probability of developing thromboembolic complications during the course of osteoarthritis.

Markers of azotemia, uricemia and mineral metabolism. The study of markers of azotemia is important during the examination of patients with osteoarthritis before endoprosthesis, because the installation of a bone implant can cause severe immunological disorders and complications. Carrying out endoprosthetics requires a mandatory assessment of the functional state of the kidneys, since operative treatment for endoprosthetics includes, along with surgery, infusion therapy, as well as the use of painkillers and antibacterial agents. In the patients with osteoarthritis of the large joints in the III and IV stages of the disease who required endoprosthesis, no changes in the markers of the functional state of the kidneys – creatinine and urea – were observed. The level of uric acid in patients with stage III and IV osteoarthritis who require endoprosthesis was increased in 30.3% of the examined (10 people), while the average indicator increased by 40.4% compared to the control group (the control group – 270.0±12.45 mmol/l, patients with osteoarthritis – 379.0±18.31 mmol/l ($p<0.01$). Such dynamics of the content of uric acid indicates that 1/3 of patients have a violation of the metabolism of purine bases. According to American scientists, a high level of uric acid can

contribute to the progression of osteoarthritis, since the severity of osteoarthritis has a direct relationship with an increase in the level of uric acid in the blood, while patients may not suffer from gout. A high level of uric acid in the blood of patients with osteoarthritis, in our opinion, can be a consequence of concomitant diseases – arterial hypertension, chronic liver diseases, atherosclerosis, as well as excessive alcohol consumption, smoking, use of certain pharmacological drugs, consumption of food rich in purine bases.

During the study of indicators of mineral metabolism in patients with stage III and IV osteoarthritis who require endoprosthetics, no changes in calcium and phosphorus indicators were found. At the same time, the content of magnesium in blood serum was increased in 76.7% of patients (23 people), while the average indicator increased by 40.6% compared to the control group. The development of hypermagnesemia in patients in the terminal stages of osteoarthritis may indicate a decrease in the mineral density of bone tissue, since magnesium is one of the key markers of homeostasis, which is responsible for all links in the regulation of bone resorption in osteoarthritis – hormonal (parathormone, calcitonin, and vitamin D_3) and transport (subchondral bone, kidneys, intestines, intracellular fluid).

Also, based on the results of research by other authors, it is possible to assume a relationship between lipid metabolism disorders (increased blood levels of total cholesterol and LDL) and an increase in the level of hypermagnesemia as a biochemical marker of bone resorption during the destruction of subchondral bone in patients with osteoarthritis. In the examined patients, hypermagnesemia may also indicate the patients' intake of drugs containing magnesium, as well as due to the progression of atherosclerosis and arterial hypertension.

Activity of marker enzymes. According to their chemical structure, enzymes are specific proteins that perform the role of biological catalysts in the body and can act as laboratory markers of various metabolic disorders. In patients with osteoarthritis of the III and IV stages, enzyme activity was determined to assess metabolic processes in bone tissue, as well as establish the functional state of the liver. The activity of aminotransferases (AlAT and AsAT) was elevated only in 17.1% of patients (6 people) and 11.4% (4 people), respectively, which did not increase the average activity indicators of these enzymes in the group of patients with osteoarthritis, which indicates the absence of the vast majority of cytolytic syndrome patients.

GGTP activity was increased in 22.9% of examined patients with stage III and IV osteoarthritis (8 people), which increased the average activity of this enzyme by 54.2% compared to the control group (the control group 24.0±1.53 Units/l, patients with osteoarthritis – 37.00±5.61 Units/l ($p<0.05$). Such dynamics of GGTP activity, in our opinion, can be caused by

concomitant pathology of the hepatobiliary tract in patients with osteoarthritis (gallstone disease, chronic cholecystitis with intrahepatic cholestasis), alcohol abuse, as well as the toxic effect on the liver of the body's intoxication products due to severe inflammatory and destructive changes in the tissues of the affected joints and systemic inflammation. Activation of the GGTP enzyme can occur as a result of patients using sedative pharmacological drugs, be a marker of reparative processes in the liver during the recovery of patients, since this enzyme ensures the transport of amino acids through cell membranes.

The activity of alkaline phosphatase in patients with stages III and IV of osteoarthritis was increased in 23.1% of the examined (15 people), while the average indicator increased by 54% compared to the control group (control group – 166.0±12.50 Units/l, patients with osteoarthritis – 256.0±10.11 Units/l ($p<0.001$). Alkaline phosphatase is a rather non-specific enzyme, it contains four main isozymes: liver, bone, kidney and intestinal. An increase in the activity of alkaline phosphatase in parallel with an increase in the activity of GGTP was established only in 3 patients, which may indicate the presence of cholestasis due to liver damage. In the remaining 12 patients, the activity of alkaline phosphatase was increased, but the activity of GGTP did not go beyond the limits of permissible fluctuations of individuals of the control group. This suggests that the increase in the activity of alkaline phosphatase in these patients is due to the activation of its bone isoenzyme in connection with the destruction of subchondral bone tissue of the affected joints and an increase in the metabolic activity of osteoblasts – cells that are responsible for reparative processes in bone tissue. In parallel with the increase in the activity of alkaline phosphatase, 29.2% of patients (19 people) had an increase in the activity of acid phosphatase, while the average indicator of the activity of this enzyme increased by 25% compared to the control group. It should be noted that increased acid phosphatase activity in 12 out of 19 patients was accompanied by normal values of alkaline phosphatase activity, and only 7 patients had elevated levels of both enzymes. In our opinion, this is a natural process, because in the III and IV stages of osteoarthritis of large joints, the increase in the activity of acid phosphatase indicates the activation of osteoclasts – cells that ensure bone resorption during destructive processes in bone tissue. It is also known that the highest activity of the acid phosphatase enzyme is observed in severe long-term and recurrent pathological processes, which include osteoarthritis. It should be noted that the increase in the activity of alkaline and acid phosphatases occurs during the destruction of bone tissue due to osteoporosis, which often accompanies severe forms of osteoarthritis, especially in elderly patients. Direct confirmation of osteoporosis, unfortunately, can only be obtained with the help of a bone biopsy.

CONCLUSIONS

1. When analyzing the results of the clinical examination of patients with stage III and IV osteoarthritis who require endoprosthesis, the determination of biochemical markers of lipid, protein, carbohydrate, mineral metabolism, and markers of fibrinolysis, the health status of patients was evaluated taking into account comorbidity.

2. In patients with osteoarthritis of the III and IV stages, a violation of lipid metabolism was established, which was manifested by an increase in the blood serum of total cholesterol, β-lipoproteins, HDL, LDL-C, triglycerides, as well as KA, which indicates atherogenic dyslipidemia and increased cardiovascular risk in this patient categories of patients.

3. An increase in the concentration of TBC products in the blood serum of patients with stage III and IV osteoarthritis is a marker of the activation of lipid peroxidation, which indicates severe violations of the body's antioxidant status and requires pharmacological correction.

4. During the study of protein and carbohydrate metabolism in patients with stage III and IV osteoarthritis who require endoprosthesis, hypoalbuminemia, an increase in the concentration of proteins in the blood serum of the acute phase of inflammation (total glycoproteins, α_1– and β-globulins, C-reactive protein, haptoglobin) and markers of proteoglycan destruction (chondroitin sulfates), changes in colloid-sediment samples (thymol test, Veltman test), in some cases – hypoglycemia, which indicates the presence of a severe systemic inflammatory process and disorders of the functional state of the liver in this category of patients.

5. An increase in the concentration of fibrinogen, FA and an increase in KHA in patients with stage III and IV osteoarthritis compared to clinically healthy individuals indicates the possibility of further use of this coefficient to assess the risks of thromboembolic complications in patients after endoprosthetics.

6. A high level of uric acid in the blood of patients with III and IV stages of osteoarthritis indicates a violation of purine metabolism in this category of patients, which requires monitoring and pharmacological correction.

7. An increase in the activity of GGTP in the blood serum of some patients with osteoarthritis of the III and IV stages indicates a violation of the functional state of the hepatobiliary system in the form of cholestasis, which can be caused by the severity of the course of systemic inflammation, uncontrolled use of painkillers and alcohol.

SUMMARY

Today, endoprosthesis remains one of the most effective methods of treatment for patients in the late stages of osteoarthritis of large joints. However, it is known that operative interventions for endoprosthetics of hip

and knee joints are associated with a number of complications: thrombosis and thromboembolism of veins of the lower extremities, changes in biochemical and immunological indicators of homeostasis, development of paraprosthetic infection. When analyzing the results of the clinical examination of patients with stage III and IV osteoarthritis who require endoprosthesis, the determination of biochemical markers of lipid, protein, carbohydrate, mineral metabolism, and markers of fibrinolysis, the health status of patients was assessed taking into account comorbidity. In patients with osteoarthritis of the III and IV stages, a violation of lipid metabolism was established, which indicates atherogenic dyslipidemia and an increased cardiovascular risk in this category of patients. An increase in the concentration of TBC products in the blood serum of patients with stage III and IV osteoarthritis is a marker of the activation of lipid peroxidation. Hypoalbuminemia, an increase in the blood concentration of proteins of the acute phase of inflammation and markers of proteoglycan destruction, changes in colloid-sediment samples, and in some cases – hypoglycemia were also found in the patients, which indicates the presence of a severe systemic inflammatory process and disorders of the functional state of the liver in this category of patients. An increase in the concentration of fibrinogen, FA and an increase in KHA in patients indicates the possibility of further use of this coefficient to assess the risks of thromboembolic complications in patients after endoprosthetics. A high level of uric acid in the blood of patients with stage III and IV of osteoarthritis indicates a violation of purine metabolism. An increase in the activity of GHTP in the blood serum of some patients with osteoarthritis of the III and IV stages indicates a violation of the functional state of the hepatobiliary system in the form of cholestasis.

Bibliography

1. Ahmed S.S., Begum F., Kayani B., Haddad F.S. Risk factors, diagnosis and management of prosthetic joint infection after total hip arthroplasty. *Expert. Rev. Med. Devices.* 2019. 16(12). P. 1063–1070. DOI: 10.1080/17434440.2019.1696673. Epub 2019
2. Zhao J., Liang G., Hong K., Pan J., Luo M., Liu J., Huang B. Risk factors for postoperative delirium following total hip or knee arthroplasty: A meta-analysis. *Front. Psychol.* 2022 13:993136. DOI: 10.3389/fpsyg.2022.993136. eCollection 2022.
3. Konnyu K.J., Pinto D., Cao W., Aaron R.K., Panagiotou O.A., Bhuma M.R., Adam G.P., Balk E.M., Thoma L.M. Rehabilitation for Total Hip Arthroplasty: A Systematic Review. *Am. J. Phys. Med. Rehabil.* 2023. 102(1). P. 11 – 18. doi: 10.1097/PHM.0000000000002007. Epub 2022 Mar 12.

4. Ledford C.K., Elstad Z.M., Fruth K.M., Wilke B.K., Pagnano M.W., Berry D.J., Abdel M.P. The Impact of Metabolic Syndrome on Reoperations and Complications After Primary Total Hip Arthroplasty. *J. Arthroplasty*. 2022. 37(6). P. 1092–1097. doi: 10.1016/j.arth.2022.01.091. Epub 2022 Feb 4.

5. Yu X., Wu Y., Ning R. The deep vein thrombosis of lower limb after total hip arthroplasty: what should we care. *BMC Musculoskelet Disord.* 2021. 22(1). P. 547. doi: 10.1186/s12891-021-04417-z.

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