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ORIGINAL ARTICLE

FEATURES OF THE CLINICAL COURSE OF OSTEOARTHRITIS IN COMBINATION WITH DIABETES MELLITUS

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ABSTRACT

The aim: To examine the features of the clinical course of osteoarthritis in combination with type 2 diabetes on the background of obesity and hypertension.
Materials and methods: 116 patients who were in the inpatient stage of treatment in the rheumatology department of the Chernivtsi Regional Clinical Hospital during 2015-2017 were examined. The epidemiological and clinical features of osteoarthritis in patients with type 2 diabetes mellitus were also analyzed.
Results: It was found that the course of osteoarthritis is extremely severe with limited range of motion in the joints, their deformation and significant deterioration of functional capacity, duration of pain, periodic prolonged exacerbations, the predominance of knee and hip injuries (64.8%) and 14.8 persons - small joints. This showed the progression and generalization of processes in various joints, aggravation of the course and prognosis of osteoarthritis, especially in women. Their prevalence was registered at II radiological stage (59.27% and 74.0%, respectively).
Conclusions: The authors emphasize that such a clinical course indicates the worst prognosis. This multimorbidity of diseases requires treatment, observation and consultation with a traumatologist, rheumatologist and endocrinologist, due to the multisystem approach to the treatment and rehabilitation of such patients with an emphasis on individual clinical features (including gender) and the course of comorbidities or syndromes.

KEY WORDS: metabolic syndrome, osteoarthritis, type 2 diabetes mellitus, multimorbidity, gender features

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INTRODUCTION

Osteoarthritis (OA) is a serious medical and social problem due to the high risk of developing limitations of the musculoskeletal system, which lead to impaired performance, reduced quality of life of patients [1,2]. About half of patients with OA have an additional five or more comorbidities. Some significant factors in the development and progression of OA are diabetes and obesity, which are a cluster of four cardiometabolic risk factors, obesity, along with aging and injury. Chronic low-grade inflammation plays a role in the development and progression of both OA and type 2 diabetes, which makes it possible to consider it a common feature of both diseases [3]. The pathogenesis of OA is associated with a combination of genetic, epigenetic, biomechanical, and metabolic factors that lead to the development of persistent inflammation of all joint structures, involvement in the pathological process of immune system cells, adipose tissue, their mediators, and the formation of various clinical variants [4].

Thus, the study of clinical and pathogenetic features of the combined course of OA and diabetes mellitus 2 is relevant because it contributes to a personalized approach to the tactics of treatment and rehabilitation of such patients.

THE AIM

The aim of the study was to investigate the features of the clinical course of osteoarthritis (OA) in combination with type 2 diabetes mellitus on the background of obesity and hypertension (AH).

MATERIALS AND METHODS

116 patients, who were in the rheumatology department of the Chernivtsi Regional Clinical Hospital during

2015-2017, were examined. In carrying out our work, we were guided by generally accepted world and domestic legal directives: the basic principles of the Helsinki Declaration on Biometric Research (1974), the basic standards of GCP, as well as the "Ethical Principles of Medical Research with the Involvement of People". The Assembly of the World Medical Association (2000), Orders of the Ministry of Health of Ukraine № 281 from 01.11.2000, № 66 from 13.02.2006 and № 690 from 23.09.2009. The design of the study and the informed patient consent form were approved by the Commission on Biomedical Ethics of the Bukovynian State Medical University.

Inclusion criteria were the presence of OA, type 2 diabetes, obesity, hypertension (AH), obtaining informed consent to participate in the study.

The exclusion criteria were patients who had suffered an acute myocardial infarction or had recently been hospitalized for heart failure; have treatment-resistant hypertension with CAT ≥200 mm Hg or DBP ≥100 mm Hg); persons with signs of pulmonary heart decompensation, cancer; patients with tuberculosis, bronchiectasis; persons who have undergone surgery during the last 4 weeks; refusal of the patient to participate in the study.

The average age of patients was 58.60 ± 8.25 years, the duration of the disease - from 5 to 23 years (15.52 ± 6.25 years). Among the surveyed sick women there were 91 (78.45%) and 25 (21.55%) men, the ratio of "women: men" was 3.6: 1, which did not differ from the average population. When dividing patients into age groups, qualitative age periods recommended by the World Health Organization (WHO) Committee of Experts were adopted: young age (25-44 years), middle age (44-60 years), elderly age (60-75 years), senile (75-90 years) [5]. Among the surveyed middle-aged women there were 54 females and 18 males. In the group of elderly people there were 5 men and 28 women. The rest of the subjects were elderly (5). The age and sex of the comparison group did not differ significantly.

Taking into account the complaints, anamnesis, objective status, data of general clinical and instrumental methods of examination, the following clinical groups of dynamic observation were identified:

Group I - 37 patients with OA;

Group II - 21 patients with OA in combination with hypertension;

Group III - 41 patients with OA with concomitant hypertension and obesity;

Group IV - 17 patients with OA in combination with abdominal obesity and type 2 diabetes with hypertension and obesity;

Group V - 25 practically healthy persons (PHP). By age and sex patients were comparable with patients of other groups.

The diagnosis of OA was established on the basis of complaints, anamnesis, results of clinical-laboratory and instrumental researches according to the criteria specified in the Order of the Ministry of Health of Ukraine from 12.10.2006 № 676 and the American College of Rheumatology (ACR, 2012).

The intensity of the pain syndrome was expressed by the pain index. The intensity of crunch in the joints was described by the tribal system. Joint deformity was assessed by three types of changes: limitation of range of motion; axial deformation; violation of contact of articular surfaces.

The Lequesne Algo functional Index was used to assess the pain syndrome and the general condition of the patient. According to the questionnaire, 3 indicators were determined: pain or discomfort, the maximum distance when walking without pain and functional activity. The maximum distance when walking without pain was estimated in points. Functional activity was determined in points according to patients' answers to questions.

We also evaluated the WOMAC index (Western Ontario and McMaster University). The assessment was performed on a visual scale in millimeters. The indicator "0" was regarded as the absence of pain, stiffness or difficulty, at 100 mm the intensity of pain, stiffness or difficulty was considered maximum.

These clinical and functional tests were determined on admission to the hospital. All patients underwent X-ray examination of the affected joints to determine the radiological stage of OA.

Body mass index (BMI) was calculated by the ratio of body weight (kg) / height (m2), also determined the waist-to-hip ratio. According to the Kettle index, the diagnosis of "obesity" was established at a BMI> 30 kg / m2. It was believed that abdominal obesity in men showed waist circumference > 94 cm, and in women> 80 cm Insulin resistance was assessed using the method of homeostatic model - HOMA (homeostasismodelassessment). The HOMA index was determined by the formula: IR = concentration of GL (mmol / ml x Ins (μOD / l / 22.5) (GL - fasting glucose index (mmol / ml; Ins - fasting insulin index (μOd / l), 22.5 - coefficient by which the indicators in the numerator are divided). The norm was considered to be the index 2.27-2.77.

The diagnosis of type 2 diabetes was made by an endocrinologist with appropriate research in an endocrinology clinic.

Statistical processing was performed using MS® Excel TM 2010, Primer of Biostatistics® 6.05 and Statistica ™ 7.0 (Statsoft® Inc). A computer register (database) of the obtained indicators was created in the Microsoft Excel system. The normality of the distribution of parameters in the samples was determined by the Kolmogorov-Smirn-

Table I. Frequency of arthralgia symptoms in patients with OA in combination with type 2 diabetes mellitus, hypertension and obesity

Arthralgia symptoms	All patients n = 116		I group OA, n=37		II group, OA+ hypertension, n=21		III group OA+ hypertension+ abdominal obesity, n=41		IV group OA+ hypertension+ abdominal obesity + diabetes, n=17	
	Quantity	%	Quantity	%	Quantity	%	Quantity	%	Quantity	%
Pain without load	19	16,38	4	10,81	4	19,05	8	19,51	3	17,65
Pain during active movements	62	53,45	25	67,57	9	42,86	18	43,90	10	58,82
Pain during passive movements	30	25,86	9	24,32	7	33,33	10	24,39	4	23,53
Pain during palpation	16	13,79	0	0,00	1	4,76	7	17,07	8	47,06
Feeling of tightness	44	37,93	2	5,41	5	23,81	20	48,78	17	100,00
Restriction of movements in joints	116	100,00	37	100,00	21	100,00	41	100,00	17	100,00
Intra-articular crepitation	81	69,83	2	5,41	21	100,00	41	100,00	17	100,00
Swelling	38	32,76	0	0,00	5	23,81	20	48,78	13	76,47
Deformations	116	100,00	37	100,00	21	100,00	41	100,00	17	100,00

Table II. The results of the assessment of the functional state of the joints according to the WOMAC index in patients with OA, combined with type 2 diabetes, obesity and hypertension

Indexes, units of measurement, mm	Groups of examined patients			
	I group OA, n=37	II group, OA+ hypertension, n=21	III group OA+ hypertension+ abdominal obesity, n=41	IV group OA+ hypertension+ abdominal obesity + diabetes, n=17
WOMAC, pain, mm	205,1±18,1	226,5±19,9	249,5±26,3	283,5±11,3p1
WOMAC , stiffness, mm	50,5±5,3	59,8±3,67	87,7±4,2 p1/p2	107,4±5,9 p1/p2
WOMAC, functional insufficiency, mm	754,2±26,8	814,4±25,9	906,9±22,7 p1/p2	1091,6±12,3p1/ p2/p3

Notes: p1 - significant in relation to the indicators of group I ($p < 0,05$); p2 - significant in relation to the indicators of group II ($p < 0,05$); p3 - significant in relation to the indicators of group III ($p < 0,05$).

ov test. Data reliability was calculated using a two-sample (for independent samples) or a pair (for dependent) Student's t-test with a distribution close to normal; Data are given as M ± m. Nominal data are presented in the form of quantitative and percentage values.

Correlation was calculated using Pearson's linear parametric correlation coefficient and Spearman's nonparametric rank correlation coefficient.

RESULTS

Analysis of the causes and social risk factors for OA showed that from the point of view of patients, humidity and cold were most often important (as cleaners, janitors, caretakers, builders). 37 patients indicated a systematically extended working day or the need to work night shifts for several years. Seasonal dependence of exacerbations of the disease (spring and autumn periods) was detected in 79 (68.1%) people. Genetic predisposition to OA (according to anamnestic data) was found in 21 patients. Half of the patients associated OA with menopause. One third of the involved patients indicated an association of disease progression with an increase in body weight. 39 patients indicated that type 2 diabetes and obesity contributed to the worsening of the clinical picture of OA.

Table III. Distribution of patients with osteoarthritis combined with type 2 diabetes, obesity and hypertension depending on the group of affected joints and the degree of functional disorders of the joints

Groups of patients	DFDJ, n=116			Groups of affected joints				
	I degree, n=76 (%)	II degree, n=37 (%)	III degree, n=3 (%)	Gonarthrosis, n=76 (%)	Coxarthrosis, n=3 (%)	Gonarthrosis + coxarthrosis n=18 (%)	Gonarthrosis + small joints, n=12 (%)	Small joints, n=7 (%)
I group OA, n=37	35 (94,6%)	2 (5,4%)	0 (0%)	33 (89%)	0(0%)	0(0%)	0(0%)	4 (11%)
II group, OA+ hypertension, n=21	16 (76,2%)	5 (23,8%)	0 (0%)	16 (76,2%)	0(0%)	0(0%)	4 (19%)	1 (4,8%)
III group OA+ hypertension+ abdominal obesity, n=41	21 (51,2%)	20 (48,8%)	0(0%)	26 (63,4%)	1 (2,4%	7 (17,2)	6 (14,6%)	1 (2,4%)
IV group OA+ hypertension+ abdominal obesity + diabetes, n=17	4 (23,5%)	10 (58,8%)	3 (17,7%)	1(5,9%)	2 (11,7)	11 (64,8%)	2(11,7)	1 (5,9%)

Note: OA - osteoarthritis, DFDJ - the degree of functional disorders of the joints

Table IV. Distribution of patients according to the Leken's index

Leken's index in points	Groups of examined patients			
	I group OA, n=37	II group, OA+ hypertension, n=21	III group OA+ hypertension+ abdominal obesity, n=41	IV group OA+ hypertension+ abdominal obesity + diabetes, n=17
Mild OA (1-4)	-	-	-	-
Moderate OA (5-7)	25 (67,6%)	10 (47,6%)	5 (12,2%)	-
Severe OA (8-10)	9 (24,3%)	7 (33,3%)	18 (43,9%)	4 (23,5%)
Very severe OA (11-13)	4 (7,8%)	4 (19,1%)	10 (24.4%)	3 (17,6%)
Extremely severe OA (14 i >)	-	-	8 (19,5%)	10 (58,9%)

Analyzing the clinical symptoms, it was found that the main complaints in patients of group I were pain in the affected joints, which bothered when descending or ascending the stairs, when moving from a sitting position to vertical, sometimes at rest (by nature they were aching, patients noted their intensity as moderate). The frequency of arthralgia symptoms is showed in Table I.

It was noted that in patients of group III joint pain during active and passive movements occurred in a larger number of patients than in patients of group IU (in 18 against 10 patients and in 10 against 4, respectively). This feature was also observed when comparing the following symptoms: a feeling of tightness (in 20 vs. 17), restricted movement, intra-articular crepitation and joint deformity (in 41 vs. 17).

Analysis of the results of the assessment of the functional state of the joints according to the WOMAC index showed that all examined patients complained of pain associated with exercise (116 people), impaired mobility and daily activities, which significantly increased with increasing OA (61 patients) and accession of comorbid pathology (in 79 patients). In patients of the IV group (17 people) the intensity of pain increased, and this group was also characterized by morning pain, impaired mobility with a significant deterioration in daily activities (Table II).

There was a significant increase in negative feelings in patients of groups III and IV (1.02 times in patients of group III, and in group IV 1.30 times compared with isolated OA). Deterioration of functional capacity was registered in patients of group III 1.2 times, and in group IV - 1.4 times more often compared with the isolated course of OA. Therefore, in patients with comorbidity with type 2 diabetes, these indicators were significantly increased compared with those examined in all groups ($p < 0.05$).

According to X-ray data, some features of the course of comorbid pathology (including gender) were identified. Among them, 37 (67.27%) women with the degree

Table V. Distribution of patients with osteoarthritis in accordance to body weight, type 2 diabetes mellitus, hypertension

Groups of patients	Body weight, n=116				Degrees of blood pressure increase, n=116			Type 2 diabetes, n=17 (%)
	Normal body weight, n=37 (%)	Overweight, n=27 (%)	I degree obesity, n=24 (%)	II and III degrees obesity, n=28 (%)	Normal BP, n=37 (%)	Hypertension of 1 degree, n=34 (%)	Hypertension of 2 degree, n=45 (%)	
I group OA, n=37	37 (100%)	0	0	0	37 (100%)	0	0	0
II group, OA+ hypertension, n=21	0	21 (100%)	0	0	0	18 (85,7%)	3 (14,3%)	
III group OA+ hypertension+ abdominal obesity, n=41	0	6 (14,6%)	21 (51,2%)	14 (34,2%)	0	16 (39%)	25 (61 %)	0
IV group OA+ hypertension+ abdominal obesity + diabetes, n=17	0	0	3 (17,6%)	14 (82,4)	0	0	17 (100%)	17 (100%)

Table VI. Indicators of carbohydrate metabolism in patients with osteoarthritis, M ± m

Indicators	Control	Groups of examined patients			
		I group OA, n=37	II group, OA+ hypertension, n=21	III group OA+ hypertension+ abdominal obesity, n=41	IV group OA+ hypertension+ abdominal obesity + diabetes, n=17
Insulin, μu / ml	8,51±0,74	9,31±0,37	11,23±1,12 p=0,047	13,05±1,44 p=0,007 p_1<0,05	21,25±2,75 p<0,001 p_1<0,001 p_2=0,002 $p_{3=}$0,01
C-peptide, ng / ml	2,05±0,16	2,56±0,53	2,68±0,27 p<0,05	3,08±0,17 p<0,05	3,27±0,34 p=0,002
Glucose, mmol / l	3,94±0,29	4,54±0,21 p=0,099	4,95±0,24 p=0,01	5,23±0,28 p=0,002 p_1=0,05	8,77±0,25 p<0,001 p_1<0,001 p_2<0,001 p_3<0,001
НвA_1C, %	5,36±0,42	5,42±0,26	5,65±0,37	6,21±0,48	8,11±0,23 p<0,001 p_1<0,001 p_2=0,002 p_3<0,001
HOMA-IR	1,48±0,07	1,82±0,14 p=0,03	2,39±0,87	3,12±0,82 p=0,05	9,95±0,34 p<0,001 p_1<0,001 p_2<0,001 p_3<0,001

Notes: p - the probability of differences in indicators with the control group; p_1 – the probability of differences in indicators with group I; p_2 – the probability of differences with the II group; p_3 – the probability of differences with the III group.

of functional disorder I (DFD I) and 15 (32.73%) men were identified, with DFD II two women and one man were found, which amounted to 3.63% of the number patients with I radiological stage. Regarding the second radiological stage, the prevalence of patients with DFD II (34 persons (58.62%) of the total number of persons with radiological stage II) among them were 31 persons (91.17%) and 3 men (8.82%). Thus DFD I was observed at 24 persons from them at 18 women and 6 men).

Since the localization of joint lesions and the severity of osteoarthritis are important for determining the ability to work, the quality of life of patients, the dependence of the degree of functional disorders on the groups of affected joints was studied (Table III).

In 33 (89.0%) persons of the I group of patients (with isolated OA) the lesions of the knee joints with the predominance of the I degree of functional disorders were established. Defeat of knee joints was found in 16 (76.2%) persons and hip - in 4 (19%) patients of group II, with the prevailing degree of functional disorders. In group III (OA + hypertension + abdominal obesity) along with lesions of the knee joints in 26 (63.4%) patients there were lesions of the hip in 7 (17.2%) persons and hip and small joints - in 6 (14.6%) , functional disorders of I and II degree were registered almost equally. Lesions of the knee and hip joints with functional disorders of the II degree prevailed in 58.8% of the examined IV group.

Determination of the severity of OA in patients of group IV according to the Leken's index showed that mild OA did not occur among the examined groups of patients. It was moderate in most patients of group I (25 (67.6%) people). Among the groups of patients with comorbidity, the highest percentage were patients of group III, where OA was combined with abdominal obesity and hypertension, severe course was characteristic of 18 (43.9%) patients. Extremely severe course was observed in patients of groups III and IV (Table IV). This required consultation with a traumatologist rheumatologist to decide on the appropriateness of conservative treatment or surgery.

Whereas body weight is an integrative indicator of carbohydrate and fat metabolism disorders, atherogenic dyslipidemia, hyperuricemia, insulin resistance, microalbuminuria, risk of hypertension, obesity, and type 2 diabetes, increases the risk of coronary heart disease and mortality, its indicators were studied in all patients (Table V). Patients in group I body weight did not exceed the norm. All patients of group II were overweight. In patients of group III obesity of the II degree prevailed (it was established in 21 (51.2%) patients), and in group IV (in the presence of type 2 diabetes) obesity of the II-III degree prevailed in all subjects.

Depending on body weight, pain in patients with OA and severe joint deformity was more common during active and passive movements (70.69%). Deterioration of the clinical course in patients of III and IV groups was established. Pain increased in patients of group III by 1.02 times, in group IV by 1.30 times, and the deterioration of the degree of SFN was registered 1.2 times in patients of group III and 1.4 times in group IV compared with isolated OA. Therefore, in patients with comorbidity with type 2 diabetes, these values were significantly higher than in other subjects ($p < 0.05$).

Since the presence of concomitant insulin resistance in patients with OA contributes to the growth of biomarkers of destruction of cartilage, cartilage matrix and persistence of inflammation of articular cartilage, synovial tissue, we studied the state of carbohydrate metabolism by the content of immunoreactive insulin, C-peptide, glycosylated hemoglobin (HвA1C), and glucose in the blood of patients (Table VI).

It was found that fasting glucose levels were significantly increased in patients of groups III and IV compared with the group of patients with isolated osteoarthritis (group I) ($p1 < 0.05$, $p1 < 0.001$, respectively). As for the indicators of glycated hemoglobin, they showed a similar relationship. The HOMA index was significantly elevated in patients with comorbid course, the highest rate was in group IV patients ($p3 < 0,001$). That is, with type 2 diabetes, insulin resistance increases, which can be reflected in the clinical course of OA. Such conditions can form both symptoms of OA and cardiovascular events in type 2 diabetes, obesity, hypertension, worsening the course of the disease. Confirmation of this can be found in patients of III and II groups increase in blood glucose levels by 1.34 ($p < 0.05$) and 2.23 times ($p < 0.05$) compared with group I ($p < 0.001$) and, even, compared with patients in group III ($p3 < 0.001$).

DISCUSSION

One of the most significant problems of modern rheumatology is OA, which is associated with a steady increase in the incidence of this disease and insufficient effectiveness of treatment, especially in comorbidity with other diseases. The total direct and indirect costs of treating degenerative lesions of the musculoskeletal system account for about 6% of the gross national product, even in the United States, and if the trend of increasing life expectancy continues, they will only increase [6,7].

Our analysis of risk factors for OA showed that the formation of the disease is influenced by working conditions, social factors, seasonality (found in 79 (68.1%) people), genetic predisposition was found in 21 patients. Genetic mutations lead to enzymopathy, and are the cause of chronic recurrent inflammation in the tissues of the joints, especially in cartilage.

Literature data show that patients with OA often have abdominal obesity, which exacerbates the chronic inflammatory process in the joints, aggravates the course of comorbid diseases and worsens the results of treatment [8]. One third of the patients we included in the study also pointed to the association of disease progression with an increase in body weight, contributing to the deterioration of the clinical picture of OA in 39 patients. Pain increased in patients with OA, hypertension and obesity 1.02 times, and in polymorbidity with type 2 diabetes - 1.30 times. Deterioration of the degree of DFD (compared with isolated OA) was registered 1.2 times and 1.4 times, respectively. This can be explained by a violation of microcirculation, which contributes to venous

stasis and hypertension, the occurrence of focal ischemic necrosis of bone. Angiogenesis at the junction of articular hyaline cartilage and adjacent subchondral bone reduces the thickness of subchondral bone, which contributes to the development of abnormal biomechanical stress and enhances degenerative-inflammatory changes in cartilage. The dependence of the intensity of pain during active and passive movements, joint deformities with limited range of motion in the joints, body weight and deterioration of clinical course in patients of these groups can be explained in the atherosclerotic hypothesis. There are reports that high plasma cholesterol and triglycerides are positively associated with joint pain [9-12]. Since the location of joint lesions and the severity of osteoarthritis are important for determining the ability to work and quality of life of patients, the dependence of the degree of functional disorders on the groups of affected joints was studied. Analysis of the results of the assessment of the functional state of the joints according to the WOMAC index showed that patients with polymorbidity OA with type 2 diabetes increased pain intensity, morning pain, mobility impairment with significant deterioration of daily activities, which significantly increased with increasing OA and, especially in polymorbidity with type 2 diabetes ($p < 0.05$). We consider this to be such that comorbidity and polymorbidity aggravate the course of osteoarthritis. Thus, according to our data, the presence of type 2 diabetes and obesity in OA changes the clinical picture, the intensity of the joint syndrome, contributes to greater destruction of cartilage and bone, as evidenced by radiological stages and degrees of joint dysfunction. It can be assumed that this is due to the degree of proliferative sclerotic morphological changes in the joints to a greater extent than inflammatory ones that occur in patients with obesity and hypertension (possibly in type 2 diabetes due to the prevalence of sclerotic and fibrotic processes in the joints clinical symptoms of inflammation, which are typical for obesity without type 2 diabetes, do not dominate). This corresponded to the results obtained in the works of other researchers [13,14].

It is known that OA is often pathogenetically associated with components of MS: insulin resistance, type 2 diabetes, coronary heart disease, hyperlipidemia, hypertension and coronary heart disease [15]. Symptoms such as osteophytosis, osteocystosis, osteosuration, osteoporosis, subchondral sclerosis, meniscus lesions, development of Baker's cysts and enthesopathy due to insulin resistance (IR), as indicated by indicators of adsorption-glycemic activity changes in static surface tension and phase angle of tensiograms.

The combination of OA with MS, obesity is associated by a number of authors with significant disorders of lipid metabolism, which further contributes to the development of atherosclerotic processes and type 2 diabetes [15-17]. In addition, parallels were found between obesity, cardiovascular pathology and the presence of OA, in particular, with lesions of the joints of the hands and lower extremities. According to various sources, the frequency of diagnosing a combination of hypertension and OA in obese patients ranges from 53% to 78%. Our results confirm that polymorbidity of OA with type 2 diabetes, obesity and hypertension in the clinical course of OA increases the degree of obesity, degree and stage of hypertension, which negatively affects the prognosis of such multimorbidity of diseases (with emphasis on the development of negative cardiovascular events) [18]. It is known that the increase in blood pressure in patients with type 2 diabetes can be accompanied by hypoalgesia due to the correlation between high blood pressure values and a decrease in the perception of joint pain due to differences in the level of β-endorphins [19,20]. At the same time, patients have increased anxiety, high levels of psycho-emotional stress, which contributes to the lack of effectiveness of treatment [21].

According to the results obtained, insulin resistance in type 2 diabetes is reflected in the clinical course of OA, worsening the course of the disease, and cardiovascular events. The increase in blood glucose levels in such patients by 1.34 ($p < 0.05$) and 2.23 times, respectively ($p < 0.05$) compared with those in the group with isolated OA ($p < 0.001$) coincide with the results of 19 European cohorts can be caused by oxidative stress, activation of inducible NO synthase in the vascular endothelium, hypoxia, obesity, disorders of carbohydrate metabolism [22,23]. It is known that the energy substrate for chondrocytes is anaerobically metabolized glucose. The presence of hyperglycemia (as the main symptom of MS) leads to the activation of the polyol pathway of glucose metabolism and non-enzymatic glucosylation of proteins, which causes damage to muscles and periatricular tissues. Hyperglycemia and OA interact at both the local and systemic levels. Local effects of oxidative stress and glucosylation of end products exacerbate cartilage damage, and the accumulation of toxic glycolysis products may contribute to the progression of OA (wrist joints in people aged 55-62 years, with a higher incidence in overweight patients, diabetes and hypertension) [24]. The presence of concomitant IR in patients with OA promotes the growth of biomarkers of cartilage tissue destruction: aggrecan - a product of degradation of cartilage matrix, antibodies to collagen II. The cascade of catabolic processes with the participation of aggrecinases, collagenases, metalloproteinases, nitric oxide synthetase, cyclooxygenase-2 and the destruction of cartilage matrix due to the action of IL1β, TNF-α, Progression leads to activation of humoral and persistence of inflammation of articular cartilage and synovial tissue.

Thus, this combination requires careful monitoring of body weight, hyperglycemia, which may be exacerbated by dyslipidemia, disorders of the system "proteolysis-fibrinolysis", which affects the condition of cartilage and synovial membrane of the joint.

CONCLUSIONS

1. The polymorbid course of osteoarthritis with type 2 diabetes, obesity and hypertension is characterized by a higher frequency (by 20.9% - during passive movements, by 13.2% - without load) and intensity (1.4 times) of joint pain, severe damage to hip joints and their combination with damage to knee joints in 64.8% of patients, deterioration of functional capacity (by 1.45 times) with a predominance in a larger proportion (76.5%) of patients of II and III degrees of functional insufficiency of joints in comparison with isolated osteoarthritis.
2. According to the WOMAC index, it was established that patients with osteoarthritis, including in combination with type 2 diabetes, against the background of obesity and hypertension, complain of pain associated with physical exertion, impaired mobility and daily activities, which significantly increased with increasing stage and the addition of comorbid pathology, especially for patients with OA, type 2 diabetes, obesity and hypertension.
3. It was established that the fasting glucose levels are significantly increased in the groups of patients with the combined course of osteoarthritis against the background of arterial hypertension, abdominal obesity, as well as against the background of polymorbidity compared to the group of patients with isolated osteoarthritis ($p1<0.05$, $p1<0.001$, respectively, which confirmed by a similar dependence of glycated hemoglobin indicators

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