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Studying The Role Of Cartilago Oligomer Matrix Protein (Comp) In Joint Structure Changes In Osteoarthritis

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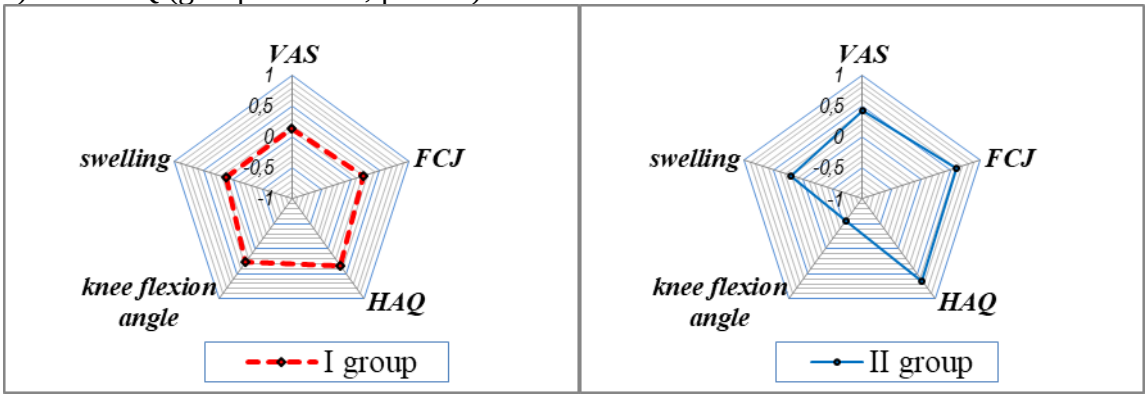
ANNOTATION
Objective: To study the role of cartilage oligomeric matrix protein in structural changes in joints in patients with osteoarthritis (OA). **Material and methods:** We observed 50 patients diagnosed with osteoarthritis aged 54.5±4.4 years, of whom 43.8% had radiographic stage 0, 40% had stage I, and 16.2% had stage II. Patients in the main group received treatment aimed at reducing the amount of cartilage oligomeric matrix protein, while patients in the control group received traditional treatment. **Results:** In addition to clinical improvement and a decrease in the intensity of pain in the knee joint, patients in the main group also had lower levels of SOMP, CRP, and ESR in the blood serum compared to patients in the control group. **Conclusions:** The treatment method aimed at the dynamics of COMP differs from the traditional one in that it is aimed at suppressing the reactions of cartilage destruction in OA.
Key words: osteoarthritis, cartilage oligomeric matrix protein (COMP), radiographic changes, knee, destruction

In the world, a number of scientific researches are being carried out on the characteristics of accurate diagnosis of osteoartrit (OA) in the early stages. In this regard, assessing the amount of cartilage oligomeric matrix protein (COMP) in relation to the clinical characteristics of the form, duration and changes in joint structures of OA, and, in addition, determining the location of this protein in the early stages of cartilage destruction is the key to preventing the progression of early cartilage destruction is of particular importance in the development of treatment methods [1,4]. Changes in articular structures observed due to OA are accompanied by a specific clinical manifestation – articular syndrome. In patients with osteoarthritis, serum COMP levels increase with increasing severity of articular cartilage destruction. In turn, the analysis of clinical features based on changes in the articular structures of the COMP, allowed us to draw certain conclusions [4,10]. It is known that in response to degenerative changes in cartilage, a local inflammatory process is observed. However, this situation leads to a mutual exacerbation of degenerative and inflammatory processes. Therefore, it is reasonable to estimate the magnitude of changes in COMP based on these processes [3,6]. Therefore, at the next stage of the study, changes in the structure of the joints and the clinical course of OA were studied in connection with changes in the amount of COMP [2]. According to the results of correlation analysis, an increase in the amount of COMP in the blood serum of patients with OA, that is, an acceleration of the process of destruction of joint bones, has a negative effect on changes in the angle of joint flexion of knee-joint. Indeed, as shown in Figure 1, the knee flexion angle depended on the shift in the amount of COMP. Moreover, in group I, the correlation between the angle of flexion of the knee joint and COMP was correct (r=0.27), but against the background of worsening radiological changes, this relationship turned into a negative inverse relationship, i.e. in group II r=-0.55, in group III r=-0.61, in group IV r=-0.72 ($p<0.05$). However, this leads to a significant change in the indicators of functional capacity of joints (FCJ) and HAQ (group I r=0.71; $p<0.05$).



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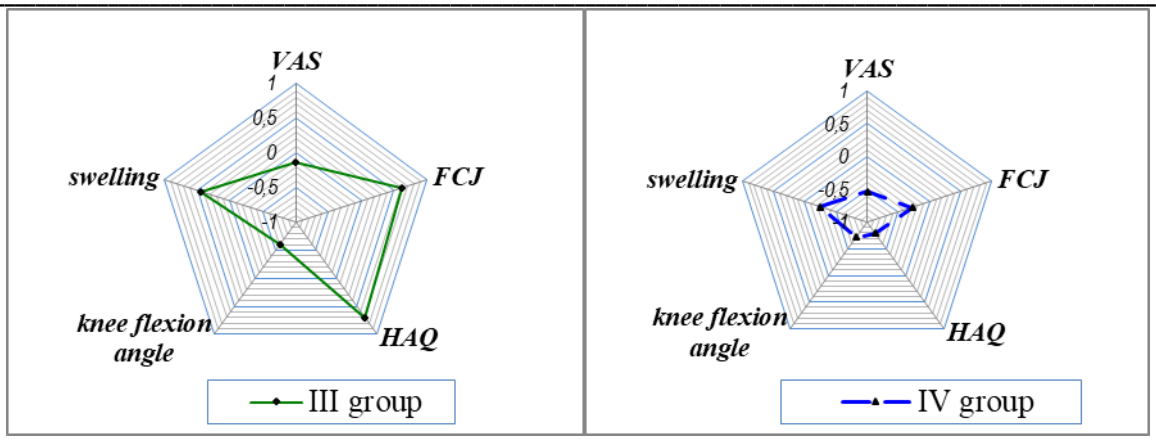

Fig. 1. Cross-correlation with joint syndrome and activity based on changes in the amount of COMP. VAS - visual analogue scale. FCJ – functional capacity of joints.

As can be seen from Figure 1, the correlation between the HAQ index and COMP in group I was positive r=0.35, but at stages III-IV of OA it turned into a strong negative correlation r=-0.79 ($p<0.01$). A similar situation was observed with FCJ.

In turn, the correlations between COMP and VAS and the degree of joint swelling also changed depending on disorders in the structure of the joint. In addition, in OA, improved remodeling due to destruction of the knee joint caused increased pain in the joint, that is, the correlation between the VAS score and the number of COMP in group I was not significant (r = 0.13).), and in group IV the correlation was, on the contrary, moderately negative. (r=-0.53; $p<0.05$) turned.

1 table

Correlation between COMP amount and joint syndrome (r)

Indicators	I group, n=46	II group, n=28	III group, n=26	IV group, n=25
Synovitis	0,15	0,12	0,19	-0,22
Morning sickness	0,04	-0,08	0,17	0,11
The thickness of the cartilage	0,61	0,24	-0,12	-0,45
Leken index	-0,12	0,19	0,33	0,43
WOMAC-index	0,61	0,21	-0,19	-0,39
Assessment by Lysholm	-0,67	-0,11	0,28	0,82

In addition, in group I, joint swelling was insignificant (r = 0.11), and in group IV the correlation turned into an inverse negative relationship (r = -0.22).

It is well known that the appearance of reactive synovitis in OA indicates the predominance of the inflammatory process, and often it is based on joint blockage [5]. As can be seen from Table 1, COMP in patients did not have a pronounced correlation ($p>0.05$) with synovitis observed at different radiological stages of OA, however, in group IV this relationship acquired a weak negative relationship r = -0.22. This indicates obvious changes in the thickness of the joints and an increase in the frequency of synovitis due to osteophytosis. Moreover, there was no significant correlation between the duration of morning sickness and the increase in COMP levels. On the other hand, it should be shown that the amount of COMP increased based on the change in cartilage thickness as determined by ultrasound examination (UE). In fact, as shown in Table 1, the correlation between them is a positive correlation found in groups I and II (r=0.61 and r=0.24, respectively), with a moderate inverse correlation in group IV (r=-0. 45; $p<0.05$) turned. Consequently, the amount of COMP increases due to the decrease in cartilage thickness.

In patients with knee OA, the amount of COMP was changed along with the limitation of joint function. Table 1 shows that the Lequesne index does not have a significant correlation ($p>0.05$) with the number of COMP in groups I and II. In groups III and IV, on the contrary, the connection between them turned into a moderate positive correlation (r=0.33 and r=0.43, respectively; $p<0.05$). The correlation between the

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WOMAC index and COMP, positive in groups I and II, was replaced by an inverse relationship in group IV (r=-0.39; p<0.05). The inverse relationship between Lysholm scale indicators and COMP in groups I and II developed into a strong direct relationship (r=0.82; p<0.05) in group IV.

Thus, the progressive changes in joint structure due to the destruction of articular cartilage observed in OA result in a wide range of COMP levels. Moreover, an increase in the amount of COMP is accompanied by a change in the articular syndrome, that is, pain and an exacerbation of the angle of flexion of the joints, and the function of the joints in patients is limited [8].

It is known that with OA, the joint tendon is initially involved in the pathological process and its rupture is observed [7,9]. However, the clinical picture of this disease in the early period is associated with the nonspecificity of the articular syndrome and the difficulties of diagnosis during X-ray examination. Consequently, this creates the possibility of diagnostic errors. However, visualization of the joint structure using MRI makes it possible to identify the smallest anatomical defects of the cartilage. However, it is of practical importance to determine changes in the number of COMP in the early stages of early MRI defects of the knee joint [10].

At the initial stage of this disease, the traditionally used standard x-ray method does not give satisfactory results in diagnosing OA in the early stages and leads to indirect conclusions. Thus, in patients with OA, digital representative MRI of the knee joint can detect minute changes in OA cartilage. Although, with their help, assessing the sensitivity to the dynamics of the amount of COMP can indicate its place in diagnosis.

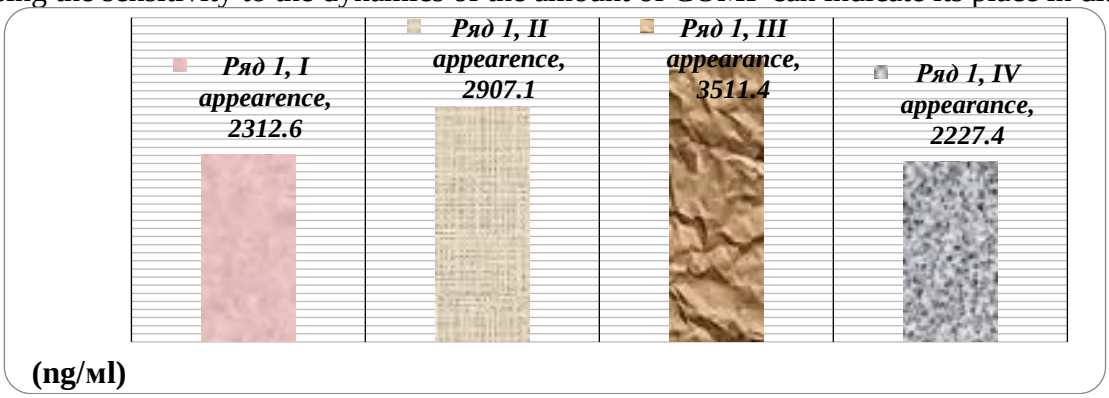

Fig. 2. Changes in COMP levels in relation to radiographic appearances of the knee joint in patients with OA.

Comparison of changes in the number of COMP from four radiographs of OA patients showed that there were differences between them. As can be seen from Figure 2, radiological changes in the knee joint, i.e. the amount of COMP in the first projection increased significantly (p<0.05) to 2312.4±202.3 ng/ml compared to the control group. The amount of COMP in form II of the radiological change was 2907.1±202.3 ng/ml, but did not differ statistically significantly from form I. It should be said that the largest amount of COMP in the blood serum of patients was detected in form III and was significantly (p <0.05) different from other forms. In the IV form of radiological changes in OA, i.e. due to osteophytosis, the concentration of COMP in the blood serum is reduced compared to other forms (p<0.02).

2 table

Comparison of indicators according to the BLOX/MOAKS system, n=125

Cartilage map	Comparison of indicators according to the BLOX/MOAKS system, abs (%)		Percentage of increased COMP, %	The presence of R signs, %
	Dislocation relative to the bone: - no - Defects no	-	-	-

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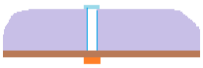
	Dislocation relative to the bone: - no - Defects <5%	24 (19,2)	95,8	-
	Bone loss <5%	11 (8,8)	100	27,3
	Defects <10%	10 (8)	100	30
	Dislocation relative to the bone: - no - Defects 5-15%	13 (10,4)	100	69,2
	Bone loss <5%	9 (7,2)	100	88,9
	Defects 10-50%	13 (10,4)	100	100
	Bone loss <10% Defects 10-75%	16 (12,8)	100	100
	Dislocation relative to the bone: -no	11 (8,8)	100	100
	Defects >75%	18 (14,4)	100	100

Note. Symbols on the map: figure in ink - cartilage; red color line – the size of completely lost areas in the cartilage; air colored line – the size of the defect in the cartilage.

Evaluation of the diagnostic sensitivity of COMP in OA was performed by imaging the knee joint on MRI and mapping it to a mapping system, as mentioned above. In this case, the calculation method according to the BLOKS/MOAKS system was used. According to it, the graph of the structure of the cartilage is given, and the size of the defect formed in it and the loss of its location in relation to the bone are taken into account. Comparison results of COMP, X-ray and MRI images of the knee joint are presented in Table 2. It can be seen that the mapping of the knee joint by MRT showed no disturbance in the location of the cartilage to the subchondral bone of the patients with OA, but when a defect of less than 5% was detected in the cartilage itself, an increase in COMP was observed in 95.8% of cases. Alternatively, the

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BLOKS/MOAKS system calculation on the other patients showed different degrees of decomposition of the cartilage. As can be seen from Table 2, the detection of OA symptoms on standard straight and lateral radiographs of the knee joint is limited even when there is less than 5% bone contact and up to 10% defect on its surface, i.e. only 27.3% of patients were diagnosed. It should be said that in this situation, 100% of patients had an increase in the amount of COMP. On the other hand, the location of the cartilage relative to the bone was not disturbed, but even when a defect of up to 15% was detected on its surface, X-ray examination was not characterized by high sensitivity in diagnosing OA, and only 30% of patients allowed to determine OA. Even in this situation, the amount of COMP was high in all 100% of patients. Interestingly, radiographic signs of OA were found in 69.2% of cases with <5% loss of bone-to-bone alignment and 10–50% defect size. Alternatively, radiographic OA was diagnosed in 88.9% of patients with <10% loss of bone-to-bone alignment and a defect size of up to 75%. Even in these situations, high concentrations of COMP were detected in all patients. Changes in the remaining volume of the cartilage allow the detection of OA by X-ray images.

Thus, when early changes in the structure of the joint in OA are observed in the knee joint, that is, small and sometimes medium-sized defects, radiological signs have low sensitivity in diagnosing the disease. An increase in the amount of COMP in the blood serum of patients indicates the development of OA, that is, the destruction of cartilage. On the other hand, during periods of OA, the location of the primary bone relative to the subchondral bone is preserved, but a defect of less than 5% is formed on the bone surface, an increase in the amount of COMP in the blood serum of patients is observed, expressed with a sensitivity of 95.8%.

It is known that severe bone destruction and underlying osteophytosis and changes in subchondral bone observed in the lower stages of OA are irreversible processes [2,11]. Therefore, endoprostheses are used today for radiological stages III-IV of OA. On the other hand, stopping the process by treating OA when a small defect of articular cartilage is formed is one of the urgent tasks of modern practical medicine. However, of scientific and practical interest is the influence of chondroprotectors on the dynamics of the number of COMP, as well as the study of drugs aimed at breaking one link in the chain of the pathogenic disease process in this direction.

The results of assessing the effectiveness of the complex treatment tactics used in our study show that clinical improvement and stabilization of the disease can be achieved by reducing the amount of COMP. As can be seen from Table 3, by the end of the 3rd month, depending on the treatment, there was a significant ($p < 0.05$) decrease in MCP in both groups. On the other hand, by the end of the 6th month of treatment, the amount of COMP in the main group significantly decreased to 903.6±92.7 ng/ml, and in the control group - to 1249.1±102.5 ng/ml ($p<0$,01). Here we can say that even if both groups had a positive trend in the number of COMP, the percentage of effectiveness in the main group was 71.3%, and it differed from the control group by 13.6%.

3 table

The dynamics of the amount of COMP on the basis of treatment in patients with OA

Groups	COMP, ng/мl			
	Before treatment	The end of 3 rd month	The end of 6 th month	Δ%
Main, n=37	3143,2±112,2	1787,6±103,2*	903,6±92,7**	71,3
Controle, n=33	2955,6±139,9	1928,4±143,4*	1249,1±102,5**	57,7

Note. Confidence level *p<0.05, **p<0.01, compared to pretreatment values.

According to the information published in literature sources the substance of garpagophytum, which is the basis of the composition of Sustavin, which we used in the treatment complex for the patients in the main group of our study, replaces the decrease in the amount of COMP in the blood by suppressing matrix metalloproteinase, which is considered to be an inflammatory enzyme, can be associated with by inhibiting COX-2, elastase, and the NO system [3, 9]. Consequently, in such a situation, an improvement in the inflammatory process is expected and, based on this, positive dynamics of the articular syndrome are expected. Indeed, it is known that by the end of the 1st month of treatment, the dynamics of joint pain

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syndrome according to VAS was significant in both the main and control groups - 41.8±3.9 mm ($p<0.02$) and 48.6 mm. Accordingly, ±4.4 mm decreased ($p <0.05$) and positive dynamics persisted until the end of the 6th month. However, the VAS index of the control group was significantly different from the main group from the 4th month of treatment and amounted to 18.2±4.1 mm, and the pain level remained at 9.5±1.1 mm until the end of the 6th month. Unlike the control group, VAS in the main group decreased to a minimum value of 1.2±0.9 mm ($p<0.0001$) by the end of the 6th month of treatment, and the percentage increase was 11.9%.

Based on the positive dynamics of the above indicators, the functional capabilities of the joints also changed. During treatment, the Lequesne index had positive dynamics in both groups and significantly decreased ($p<0.05$) compared to the indicators before treatment from the 1st month of treatment. Such positive dynamics persisted until the end of the 6th month, however, in the control group, by the end of the 3rd month of treatment, a slight negative change was observed, in contrast to the main group, and by the end of the 6th month it decreased to 6.1 ± 0.7. On the other hand, in the main group the Lequesne index decreased to 4.5±0.08 ($p<0.02$), the percentage increase was 15.8%.

The dynamics of the WOMAC index were explained by positive changes in both groups over 6 months during the treatment, and a convincing result compared with the indicators before treatment was observed by the end of the 3rd month. From the end of the 3rd month of treatment to the end of the 6th month, the dynamics remained in both groups, and in the control group it decreased to 29.8±7.2 points and in the main group - 17.3±6. 1 point. group. The percentage of growth based on joint addition was 16.5%.

Based on the treatment tactics, positive dynamics of a clearly convincing level were observed from the 3rd month of treatment according to the Lysholm assessment (LEI) indicators, in both groups there was a significant ($p<0.05$) decrease in scores by the end of the 3rd month (43.7±6.7 points and 38.9±5.4 points, respectively). In addition, by the end of the 6th month there was a statistically significant decrease in the LEI index in the main group to 27.9±3.2 points ($p<0.002$) and in the control group to 42.4±3.5 points ($p<0.002$). The percentage of growth based on joint addition was 19.1%.

On the other hand, the ability to flex the knee joint increased based on the treatment. In this case, the initial stages of destruction of the ankle joint and the treatment begun in a situation where a small defect had formed in it led to a change in the angle of flexion of the knee joint, the pre-treatment indicators of the main (137.1±10.1°) and control group (134.5±12.2°) by the end of the 6th month of treatment are based on the improvement in the functional activity of patients. knee joint, its flexion angle was 148.9±9.2° and expanded 143.2±9.1°, respectively.

Today, X-ray examination has not lost its practical importance in assessing the condition of the joint in OA, and with the help of this method it is possible to observe the dynamics of its changes. According to WHO/ILAR (World Health Organization/International League of Associations of Rheumatology) recommendations, measuring the width of the knee joint using X-rays can indirectly determine the development of degenerative disorders in the cartilage. On an x-ray taken a year later, the width of the gap of the knee joint in patients of the main and control groups is practically not narrowed, which indicates that the degenerative process has not increased in the ankle joint. In addition, when studying for comparison the radiographs (n=19) of patients with stages I and II of retrospective analysis, there was a clear change in the contrast index, and 5.3±0.09 mm was recorded. It was found that after a year the width of the incision narrowed to 3.1 ± 0.11 mm ($p < 0.05$). Consequently, this situation indicates an exacerbation of the process in OA.

Thus, the use of garbagafitum on the basis of traditional treatment in patients with OA of the knee joint at the initial radiological stages of 0-1, that is, with a defect of the articular surface of 5-10% or less, leads to a decrease in the number of COMP. Based on this, slowing down the development of changes in the articular structure has a positive effect on articular syndrome. In addition, it forces the knee joint to expand its angle of flexion to 150°, creating the basis for improved joint functionality.

Conclusion

In OA, the amount of COMP fluctuates widely due to changes in the structure of the joint. An increase in the amount of COMP in the blood serum of patients indicates the development of OA, that is, the destruction of cartilage. In this case, the increasing destruction of the knee joint is accompanied by an increase in the number of COMP. On the other hand, during periods of OA, the location of the primary bone relative to the

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subchondral bone is not disturbed, but a defect of less than 5% is formed on the bone surface, and the number of COMP is increased. observed in the blood serum of patients, expressed with a sensitivity of 95.8%. An increase in the amount of COMP is accompanied by a change in the articular syndrome, that is, pain and an exacerbation of the angle of flexion of the joints, while patients experience limited joint activity. The use of harpogaphytum based on traditional treatment (chondroprotectors) in patients with OA of the knee joint at the initial radiological stages I-II, that is, when a defect of 5-10% or less is observed in the articular cartilage, leads to a decrease in the amount of COMP. Based on this, slowing down the development of changes in the articular structure has a positive effect on articular syndrome. In addition, it forces the knee joint to expand its angle of flexion to 150°, creating the basis for improved joint functionality.

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