The trophological status of patients with osteoarthrosis and excretory insufficiency of pancreas

**Abstract.** Background. Studies found a high incidence of the gastrointestinal tract (GI) diseases in patients with OA, especially those that are accompanied by a violation of the excretory insufficiency of pancreas (EIP), which also contributes to the activation of proteolysis. The EIP in patients with OA is formed at the comorbid pathologies: chronic pancreatitis (CP) with EIP and increatory insufficiency in the form of diabetes mellitus (DM), functional biliary disorders, diseases of the liver and bile-excreting system, diseases of the gastroduodenal zones, enterocolitis and colon dysbiosis (CD); as a result of long-term treatment of OA using the non-steroidal anti-inflammatory drugs, steroids, chondroprotectors and chondrostimulators, etc. The purpose of the work was to study the state of the excretory insufficiency system and immune status (IS), the presence and depth of the CD in patients with primary OA against a violation of their EIP. Materials and methods. There were 64 outpatients with primary OA (group 1) and 74 patients with primary OA in combination with diseases associated with EIP (group 2). The control group consisted of 30 healthy people. Results. It was proved that there is a deeper excitation of the excretory function of the pancreas (severe) in patient with OA and comorbid pathologies of the gastrointestinal tract with EIP, as well as the presence of EIP in patients with mild OA without the clinically available EIP. In patients with primary OA that went through the isolation or in combination with the diseases accompanied by the EIP, a statistically significant activation of the total proteolysis by the level of PRA was established. Also, the analysis showed the presence of an increase in specific proteolysis, or kininogenesis, by the level of proteolytic enzyme KiK. In the examination of patients, dysbiotic changes of varying degrees were detected in both groups of the study: group 1 in 25 (39.06%) patients, the CD was 1 gr., in 18 (28.13%) - CD was 2 gr. In group 2 CD 1 gr. was in 35 (47.30%) patients, in 24 (32.43%) - CD 2 gr. In group 2, dysbiotic changes were significantly deeper than in group 1. This indicates a statistically weaker course in patients in the comorbidity conditions of the primary OA and gastrointestinal tract diseases and with EIP. The obtained results indicate the presence of secondary immune deficiency in the patients under study (T-lymphocytopenia was detected in II degrees with a decrease in all subpopulations of T-lymphocytes) and non-specific activation of the humoral part of the immune system and the inflammatory process (depletion of the total hemolytic activity of the complement, statistically significant increase of B-lymphocytes level with growth of level of all classes Ig (more Ig A and Ig M), circulating immune complexes). However, statistically more significant changes were observed in group 2, indicating the progression of the detected changes in comorbidity conditions. Keywords: primary osteoarthrosis; excretory insufficiency of pancreas; trophological status; dysbiosis of colon

**Background.** Primary osteoarthrosis (OA) is a chronic progressive degenerative-dystrophic joint disease. It is characterized by degeneration of articular cartilage with subsequent changes in subchondral bone and the development of marginal osteophytes and is often accompanied by reactive synovitis. Studies also found a high incidence of the gastrointestinal tract (GI) diseases in patients with OA, especially those that are accompanied by a violation of the excretory insufficiency of pancreas (EIP), which also contributes to the activation of proteolysis. The EIP in patients with OA is formed at the comorbid pathologies: chronic pancreatitis (CP) with EIP and increatory insufficiency in the form of diabetes mellitus (DM), functional biliary disorders, diseases of the liver and bile-excreting system, diseases of the gastroduodenal zones, enterocolitis and colon dysbiosis (CD); as a result of long-term treatment of OA using the non-steroidal anti-inflammatory drugs, steroids, chondroprotectors and chondrostimulators etc [1, 3, 4].

To the processes of maldigestion and malabsorption in patients with EIP often develops DC. The presence and depth of the DC determines the severity of the diseases accompanied by EIP and primary OA, the severity of trophic disorders: multivitamin and polynuclear deficiency, secondary immunodeficiency, osteoporosis, anemia etc [5].

**The purpose** of the work was to study the state of the proteolytic system and immune status (IS), the presence and depth of the DC in patients with primary OA against a violation of their EIP.

Inflammation plays significant part in the pathogenesis of OA. The main mechanism of cartilage degradation are production of proinflammatory cytokines (IL-1β, IL-6, FNP-α, etc.). They release enzymes that damage collagen (collagenase, elastase, peptidase) and proteoglycans (metalloproteinases, stromelysin, cathepsins) and activate proteolytic activity. This leads to increased destruction of hyaluronic fibers and a decrease cartilage regeneration [2].
Materials and methods

There were 64 outpatients with primary OA (group 1) and 74 patients with primary OA in combination with diseases associated with EIP (group 2). The control group consisted of 30 healthy people.

The exclusion criteria were cancer diseases, acute and exacerbation of chronic pathologies of vital organs, severe diabetes mellitus type 2, diabetes mellitus type 1, active stomach and duodenum ulcers, viral hepatitis and liver cirrhosis, Crohn's disease, non-specific ulcerative colitis, cystic fibrosis.

The age of the patients ranged from 29 to 74 years. The diagnosis of primary OA was established on the basis of unified diagnostic criteria, the X-ray stage of the primary OA, according to J. H. Kellgren and J. S. Lawrence [6].

The level of EIP was determined by the level of faecal \( \alpha \)-elastase-1, using ELISA of the company Bioserv Elastase-1-ELISA. The proteolytic activity of the plasma (PKP) was determined by hydrolysis of protamine sulfate. The activity of the kallikrein (KK) was investigated using a method based on the determination of the amount of paranethianiline. Prekallikrein (PKK) was determined by the ‘Veremeenk’s’ method. The activity of the \( \alpha \)-proteinase inhibitor (\( \alpha \)-Pi) and \( \alpha \)-macroglobulin (\( \alpha \)-MG) was determined by the unified spectrophotometric method. Determination of kininase-II activity was performed by spectrophotometric Folk’ method. Colon dysbiosis was determined using method of R.V. Epstein-Litvak and F.L. Wilson. To assess the immune status, the cell and humoral components of CD3, CD22, CD4, CD8, CD16 were using ELISA with monoclonal antibodies; concentration of the main classes Ig (M, G, A) in the serum - by the G. Man- cini method of radial immunodiffusion of globulins; activity of complement system - by hemolytic test.

Results and discussion

The analysis of the obtained parameters of fecal \( \alpha \)-elastase-1 levels in the study groups showed the presence of EIP in both groups of study - correspondingly (153.83±5.34) \( \mu \)g/g and (58.65±4.73) \( \mu \)g/g - in comparison with the group control (185.83±5.34) \( \mu \)g/g in both groups of study - correspondingly (153.83±5.34) \( \mu \)g/g.

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Table 1. The level of proteolysis indexes in patients with OA and EIP

| Index of proteolysis | Control group (n=30) | 1-st group (n=64) | 2-nd group (n=74) |
|---------------------|----------------------|-------------------|-------------------|
| PAP, ml of arginine/(hl) | 30.41±1.71 | 43.36±2.54* | 48.42±2.28** |
| KK, \( \mu \)mol/(min) | 54.12±1.43 | 139.78±5.67* | 151.65±7.44** |
| PKK, \( \mu \)mol/(min) | 74.79±1.89 | 51.26±2.47* | 45.18±4.34** |
| \( \alpha \)-Pi, g/l | 1.43±0.02 | 1.68±0.03* | 1.74±0.04** |
| \( \alpha \)-MG, g/l | 1.45±0.02 | 0.95±0.03* | 0.85±0.06** |
| Kininase-II activity, \( \mu \)mol GC/(min) | 271.38±1.45 | 185.32±3.31* | 172.45±7.86** |

Note: 1. * - significant difference in the data related to the control group (p <0.05); 2. ** - significant difference in the data related to the 2-nd group to the 1-th group (p <0.05).

Conclusions

1. It was proved that there is a deeper excitation of the excretroy function of the pancreas (severe) in patient with osteoarthrosis and comorbid pathologies of the gastrointestinal tract with the excretroy insufficiency of pancreas, as well as the pres-
ence of the excretory insufficiency of pancreas in patients with primary osteoarthrosis without the clinically available the excretory insufficiency of pancreas.

2. In patients with primary osteoarthrosis that went through the isolation or in combination with the diseases accompanied by the excretory insufficiency of pancreas, a statistically significant activation of the total proteolysis by the level of the proteolytic activity of the plasma was established. Also, the analysis showed the presence of an increase in specific proteolysis, by the level of proteolytic enzyme kallikrein.

Reduced inactive precursor kallikrein - prekalikrein is established. There was an increased level of this indicator blocks the kinogenase action of the kallikrein and depletion of the inhibitory protection of the organism, because this indicator blocks the kinogenase action of the kallikrein and displays active proteinas of endo- and exogenous origin. Also, decreased activity of kininase-II was revealed, which indicates weakening of the protective reactions of the organism through hyperproduction of kinins (p <0.05).

3. In the examination of patients, dysbiotic changes of varying degrees were detected in both groups of the study: group 1 in 25 (39.06%) patients was grade 1 of the dysbiosis of colon, in 24 (32.43%) person was grade 2 of the dysbiosis of colon.

In group 2 grade 1 of the dysbiosis of colon was in 35 (47.30%) patients, in 24 (32.43%) person was grade 2 of the dysbiosis of colon. Dysbiotic changes of varying degrees were detected in both groups: in group 1 in 28 (85.30%) persons was grade 1 of the dysbiosis of colon, in 18 (55.29%) patients was grade 2 of the dysbiosis of colon.

In group 2 grade 1 of the dysbiosis of colon was in 35 (47.30%) patients, in 24 (32.43%) person was grade 2 of the dysbiosis of colon.

4. The obtained results indicate the presence of secondary immune deficiency in the patients under study (T-lymphocytopenia was detected in 1-ІII grade with a decrease in all subpopulations of T-lymphocytes) and non-specific activation of the humoral part of the immune system and the inflammatory process (depletion of the total hemolytic activity of the complement, statistically significant increase of B-lymphocytes level with growth of level of all classes Ig (more Ig A and Ig M), circulating immune complexes). However, statistically more significant changes were observed in group 2, indicating the progression of the detected changes in comorbidity conditions.

Conflicts of interests. Authors declare the absence of any conflicts of interests that might be construed to influence the results or interpretation of their manuscript.

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6. Unifikovannyy klinikny protokol persynnyho, tyorynnyho (spetsializovannyy) medytsyny dopomohy ta medytsyny reabilitatsiy [Unified clinical protocol of primary, secondary (specialized) medical aid and medical rehabilitation]. (2014). Ministry of Health of Ukraine, 638 [in Ukrainian].

Received 23.03.2019
Трофологический статус пациентов с остеоартрозом и экскреторной недостаточностью поджелудочной железы

Резюме. Актуальность. Исследования выявили высокую частоту при ОА заболеваний желудочно-кишечного тракта (ЖКТ), особенно тех, которые сопровождаются нарушением внешнесекреторной функции поджелудочной железы (ПЖ), что также способствует активации протеолиза. Внешнесекреторная недостаточность ПЖ (ВСНПЖ) при ОА формируется при коморбидных патологиях, для которых она присуща (хронический панкреатит (ХП) с недостаточностью поджелудочной железы) и формированием инкреторной недостаточности в форме сахарного диабета (СД), функциональные билиарные нарушения, заболевания печени и желчевыводящих путей, а также клинически значимые изменения, связанные с недостаточностью поджелудочной железы и формированием инкреторной недостаточности при ОА. В условиях коморбидности первичного ОА с заболеваниями ЖКТ, обнаружены более глубокие дисбактериозные нарушения экскреторной функции поджелудочной железы (ПЖ), что приводит к прогрессированию выявленных изменений.

Материалы и методы. Было обследовано 64 амбулаторных пациентов с первичным ОА (1 группа) и 74 с первичным ОА без клинической недостаточности поджелудочной железы (вторая группа). Контрольную группу составили 30 здоровых людей. У всех пациентов проводилось обследование на наличие ЗСНПЗ легкой степени, а также на наличие ЗСНПЗ легкой степени при ОА с коморбидными патологиями ЖКТ из ЗСНПЗ. Отмечено, что у второй группы больных более выражены изменения, связанные с недостаточностью поджелудочной железы и формированием инкреторной недостаточности.

Ключевые слова: первичный остеоартроз; экскреторная недостаточность поджелудочной железы; морфологические изменения; поджелудочная железа; заболевание ОА; заболевание ЖКТ; нефритическая недостаточность; образование иммунных комплексов; протеолитический фермент УК; уровень ПРА; уровень ИГ М.