THE EFFECT OF ENDOTHOXICOSIS ON THE FORMATION OF THE PANCREAS EXOCRINE INSUFFICIENCY IN PATIENTS WITH PRIMARY OSTEOARTHRITIS

Abstract. Background. The development of endogenous intoxication (EI) leads to acute or chronic homeostasis disorders and leads to dysfunction of all organs and systems. Under the influence of endogenous toxins, microcirculatory disorders, hypotension, hypovolemia develop, which lead to hypoxia, dystrophy and hypofunction of all organs, including the pancreas. The purpose was to study EI syndrome in patients with pancreas exocrine insufficiency (PEI) with primary osteoarthritis and to analyze the possible correlation of indicators of this syndrome with other parameters. Materials and methods. There were 115 outpatients with PEI disorders and primary osteoarthritis examined. Diagnosis of primary osteoarthritis was determined based on diagnostic criteria, X-Ray stage - according J.H. Kellgren and J.S. Lawrence. Degree of exocrine pancreatic insufficiency was verified based on result of fecal elastase-1, which was done by Elisa test. The structural status of the pancreas was evaluated by the Cambridge Classification, assessing the severity of the process. To evaluate the process of endogenous intoxication in clinical practice used the method of determining the level of molecules of average mass (MAM) in the blood plasma in the modification of N. I. Habrielyana et al. The level of EI was judged by the level of sorption capacity of erythrocytes, which was determined according to the method A.A. Togaabaeva. Results. Analysis of the obtained indices of fecal elastase-1 levels in the study groups showed the presence of CHF in the study group - (58.65±4.73) mcg - compared with the control group (213±6.29 mcg) (p<0.05). The analysis showed statistically significant deepening of indicators of EI syndrome in patients with PEI with primary osteoartthritis of older age, indicating the progression of pathologies in these patients by age. It was found that between most pairs in the correlation analysis there are statistically significant moderately strong correlation relationships, and between the level of α-elastase and MAM, c.u. at 254 nm significant significant correlation relationship (p<0.05). Conclusions. The presence of pronounced PEI in the group of patients with primary osteoarthrits undergoing fecal elastase-1 was found to be statistically significantly lower and comparable to the control group (p<0.05). Patients with PEI and primary osteoarthritis have statistically significant increase in endotoxicosis control by MAM levels, which were increased by 43.19% and 54.26%, respectively, and LEI, which was increased by 95.93% (p<0.05). An analysis of changes in EI syndrome in patients with PEI and primary osteoartthritis by age was analyzed. The analysis showed a statistically significant deepening of EI syndrome in patients with PEI and primary osteoartritis of older age, indicating the progression of pathologies in these patients with age (p<0.001). It was found that between most pairs in the correlation analysis there are statistically significant moderately strong correlation relationships, and between the level of α-elastase and MAM, c.u. at 254 significant correlation relationship (p<0.05).

Keywords: osteoarthritis; exocrine pancreatic insufficiency; endotoxicosis

Introduction
Polyetiological and polypathogenetic syndrome, characterized by accumulation in tissues and biological fluids of endogenous toxic substances - excess products of normal or pathological metabolism is called endogenous intoxication (EI) syndrome. The development of EI leads to acute or chronic homeostasis disorders and leads to dysfunction of all organs and systems. Under the influence of endogenous toxins, microcirculatory disorders, hypotension, hypovolemia develop, which lead to hypoxia, dystrophy and hypo-

function of all organs, including the pancreas. By action at the level of cellular structures, endotoxins have a cytolitic effect; activate lysosomal enzymes; block energy processes in the mitochondria; initiate synthesis of free radicals; inhibit synthetic processes in ribosomes. Remote action of endotoxins is manifested by damage to the microcirculation system: impaired peripheral vascular tone, rheological state of the blood, transcapillary and transmembrane metabolism.

Endotoxins are a powerful stimulator of cytokine synthesis, in particular tumor necrosis factor, which activate the
functions of neutrophils, endothelial cells and the like. In addition, endotoxins cause the release of other mediators: platelet activation factor, complement components, kinin, histamine, endorphins. That is, against the background of endotoxicosis, the so-called "mediator chaos" with the development of cellular hypoxia, metabolic disorders, is formed. In view of the above, EI is now regarded as the basis for the emergence and progression of chronic diseases of the internal organs and, accordingly, as an important integral criterion for their severity [1-4].

The purpose was to study endogenous intoxication (EI) syndrome in patients with pancreas exocrine insufficiency (PEI) with primary osteoarthritis and to analyze the possible correlation of indicators of this syndrome with other parameters.

Materials and methods

There were 115 outpatients with PEI disorders and primary osteoarthritis examined. Average age of the patients was (51.3 ± 3.5) years (29 to 74 years); there were 68 (59.1%) and 47 (40.9%). Control group consisted of 30 healthy people. Excluding criteria: oncological diseases, acute and exacerbation of chronic disease of vital organs, severe diabetes mellitus type 2, diabetes mellitus type 1, gastric and duodenal ulcers, viral hepatitis and cirrhosis, Crohn's disease, ulcerative colitis, cystic fibrosis.

Diagnosis of primary osteoarthritis was determined based on diagnostic criteria, X-Ray stage - according J.H. Kellgren and J.S. Lawrence.

Degree of exocrine pancreatic insufficiency was verified based on result of fecal elastase-1, which was done by Elisa test. The structural status of the pancreas was evaluated by the Cambridge Classification, assessing the severity of the process. To evaluate the process of endogenous intoxication in clinical practice used the method of determining the level of molecules of average mass (MAM) in the blood plasma in the modification of N. I. Habrielyana et al.

The level of EI was judged by the level of sorption capacity of erythrocytes, which was determined according to the method AA. Togaibaeva.

In the parametric distribution, the Student’s t test was used (t-test). Non-parametric tests were used for sets whose distribution differed from "normal": to compare two independent samples, the Mann-Whitney U-test. The analysis of the relationship of the two traits in the presence of a normal distribution was estimated by the results of Pearson correlation analysis (r), the nonparametric Spearman rank correlation method (R) was used for the distribution other than normal.

Results and discussion

Analysis of the obtained indices of fecal elastase-1 levels in the study groups showed the presence of CHF in the study group - (58.65±4.73) mcg - compared with the control group (213±6.29 mcg) (p<0.05).

The analysis revealed the presence in patients with PEI with primary osteoarthritis statistically significant increase the endotoxicosis compared control group by MAM levels, which were increased by 43.19% and 54.26%, respectively, and LEI, which was increased by 95.93% (p <0.05) (Table 1).

Changes in indicators of EI in patients with PEI with primary osteoarthritis by age were analyzed.

The analysis showed statistically significant deepening of indicators of EI syndrome in patients with PEI with primary osteoarthritis of older age, indicating the progression of pathologies in these patients by age (p <0.001) (Table 2).

The data of the performed correlation analysis between the demonstrative EI of patients with PEI and primary osteoarthritis and the level of fecal α-elastase, as well as ultrasound criteria of pancreas are shown in table 3.

| Table 1. Indicators of EI syndrome in patients with PEI with primary osteoarthritis |
| El indicator | Control group (n=30) | Patients with PEI (n=115) |
|--------------|---------------------|--------------------------|
| MAM, с.u., at 254 nm | 334.10 ± 2.64 | 478.41 ± 7.35* |
| MAM, с.u, at 280 nm | 147.50 ± 1.23 | 227.54 ± 2.97* |
| LEI, % | 27.25 ± 1.22 | 53.39 ± 0.99* |

Note. * - statistically significant difference with respect to indicators of control group (p<0.05).

| Table 2. EI indicators in groups of patients with PEI with primary osteoarthritis of different ages |
| El indicator | Control group (n=30) | Group of patients with PEI by age |
|--------------|---------------------|-------------------------------|
|              | 30-45 y. (n=42) | 46-65 y. (n=52) | More than 65 y. (n=21) |
| MAM, c.u., at 254 nm | 334,10±2,64 | 422,67±7,34** | 471,94±9,45** |
|                  | p<0,001 | p<0,001 | p<0,001 |
| MAM, c.u, at 280 nm | 147,50±1,23 | 200,18±5,29** | 227,54±2,97** |
|                  | p<0,001 | p<0,001 | p<0,001 |
| LEI, % | 27,25±1,22 | 52,69±1,76** | 56,60±1,60** |
|                  | p<0,001 | p<0,05 | p<0,01 |

Note 1. * - statistically significant difference between the control group data (p<0,001); Note 2. p1-2 - statistically significant difference of data between the group up to 45 years and 46-65 years; Note 3. p1-3 - statistically significant difference of data between the group up to 45 years and >65 years; Note 4. p2-3 is a statistically significant difference between the 46-65 and >65 groups.
It was found that between most pairs in the correlation analysis there are statistically significant moderately strong correlation relationships, and between the level of α-elastase and MAM, c.u., at 254 nm significant correlation relationship (p<0,05).

Conclusions
1. The presence of pronounced PEI in the group of patients with primary osteoarthritis undergoing fecal elastase-1 was found to be statistically significantly lower and comparable to the control group (p<0,05).
2. Patients with PEI and primary osteoarthritis have statistically significant increase in endotoxosis control by MAM levels, which were increased by 43,19% and 54,26%, respectively, and LEI, which was increased by 95,93% (p<0,05).
3. An analysis of changes in EI syndrome in patients with PEI and primary osteoarthritis by age was analyzed. The analysis showed a statistically significant deepening of EI syndrome in patients with PEI and primary osteoarthritis of older age, indicating the progression of pathologies in these patients with age (p<0,001).
4. It was found that between most pairs in the correlation analysis there are statistically significant moderately strong correlation relationships, and between the level of α-elastase and MAM, c.u., at 254 nm significant correlation relationship (p<0,05).

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

References
1. Babinets L. S. Improvement of the complex medical treatment for the patients with chronic biliary pancreatitis./ L.S. Babinets, K.Y. Kysnai, Y.Y. Kotsaba, I.M. Halabitska, N.A. Melnyk, I.Y. Semenova, O.S. Zemlyak // Wiadomosci lekarskie. – 2017. – №2. – С.213-216.
2. Hochberg M. Osteoarthritis year 2012 in review: clinical / M. Hochberg // Osteoarthritis Cartilage. – 2012. – №20. – Р. 1465–1469.
3. Babinets’ L. S. Zovnishn’osekretorna nedostatnist’ pidshlunkovoi zalozy tu dysbalans systemy prooksydanty-antyoksydanty pry pervynnomu osteoartrozi z korobidnymy stanamy / L. S. Babinets’, I. M. Halabits ka, T.H. Mayevs ka // Zdobutka klinichnyi ta eksperimentalnoyi medytsyny. – 2017. – №3. – С. 22-25.
4. Unifikovanyi klinichny protokol pervynnyi, vidrówno-nyi (spetsializovanowyi) medychnyiy dopomohy ta medych-nyiy reabilitatsiyi / Ministerstvo okhorony zdorov’ya Ukrainy 10.09.2014, № 638.

Received 05.05.2019

| Couples in a regression | Age of patient, years (n=115) | The level of α-elastase, µg/g (n=115) | Ultrasound of pancreas, points (n=115) |
|-------------------------|-------------------------------|--------------------------------------|--------------------------------------|
| MAM, c.u., at 254 nm    | 0,387                         | -0,513                               | 0,385                                |
|                         | p<0,05                        | p<0,05                               | p<0,05                               |
| MAM, c.u., at 280 nm    | 0,417                         | -0,387                               | 0,439                                |
|                         | p<0,05                        | p<0,05                               |                                      |
| LEI, %                  | 0,382                         | -0,409                               | 0,380                                |
|                         | p<0,05                        | p<0,05                               |                                      |

Note 1. n is the number of pairs in the correlation analysis; Note 2. p - the degree of statistical significance of correlation dependence.

It is possible to establish relationships between the parameters of the syndrome with other diseases, and the relationship (p<0,05).
Влияние синдрома эндогенной интоксикации на развитие экзокринной недостаточности поджелудочной железы у пациентов с первичным остеоартрозом

Резюме. Актуальность. Развитие эндогенной интоксикации (ЭИ) приводит к острому или хроническому нарушению гомеостаза и ведет к дисфункции всех органов. Под действием эндогенных токсинов развиваются нарушения микроциркуляции, гипотония, гиповолемия, которые приводят к гипоксии, дистрофии и гипофункции всех органов, в том числе поджелудочной железы. Цель работы: провести исследование синдрома ЭИ у пациентов с внешнесекреторной недостаточностью поджелудочной железы (ВСН ПЖ) при первичном остеоартрозе и проанализировать возможные взаимосвязи показателей данного синдрома с другими параметрами. Материалы и методы. Было обследовано 115 амбулаторных пациентов с нарушениями нелестатичности поджелудочной железы в коморбидности с первичным остеоартрозом. Диагноз первичного остеоартроза был выставлен на основе диагностических критериев, рентгенологического обследования, согласно критериям Н. И. Габриэляна и соавт. Об уровне ЭИ судили по уровню молекул средней массы (МСМ) в плазме крови в методе 1-ELISA. Для оценки процесса эндогенной интоксикации использовали стандартные наборы фирмы BIOSERV ELASTASE-1. Результаты. Анализ показал наличие у пациентов с ВСН ПЖ с первичным остеоартрозом статистически значимого, относительно группы контроля, усиления эндотоксикоза по уровням МСМ, которые были повышены на 43,19 % и 54,26 %, соответственно, и УЭИ, что были повышены на 95,93 % (p<0,05). Анализ показал статистически значимое углубление показателей синдрома ЭИ у пациентов с ВСН ПЖ и первичным остеоартрозом старшего возраста, что свидетельствует о прогрессировании патологии у данных пациентов с возрастом (p<0,001). Было установлено, что большинством пар в корреляционном анализе имеются статистически значимые умеренной силы корреляционные связи, а между уровнем α-эластазы и МСМ, ум.од, при 254 нм значимые корреляционные связи (p<0,05). Выводы. Было выявлено наличие выраженной недостаточности поджелудочной железы в группе исследуемых пациентов по уровню фекальной эластазы-1, что свидетельствует о прогрессировании патологии у данных пациентов с возрастом (p<0,05). Анализ показал статистически значимое углубление показателей синдрома ЭИ у пациентов с ВСН ПЖ и первичным остеоартрозом старшего возраста, что свидетельствует о прогрессировании патологии у данных пациентов с возрастом (p<0,001). Было установлено, что большинством пар в корреляционном анализе имеются статистически значимые умеренной силы корреляционные связи, а между уровнем α-эластазы и МСМ, ум.од, при 254 нм значимые корреляционные связи (p<0,05).