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PECULIARITIES OF THE BLOOD NEUTROPHILS REACTIVE RESPONSE IN ACUTE PANCREATITIS OF VARIOUS GENESIS

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The peculiarities of the reactive response of blood neutrophils in acute pancreatitis remain insufficiently studied, considering the etiological factor.

Objective – *to investigate the peculiarities of the relationships between the reactive response of blood neutrophils, the systemic inflammatory response and the protection, in patients with acute pancreatitis of alcoholic and biliary genesis.*

Materials and Methods. *189 patients were examined, including 45 (23.8%) women and 144 (76.2%) men, aged 23 to 77 years, with edematous form of acute pancreatitis. The control group consisted of 37 practically healthy individuals. The study did not include patients with necrotic forms of acute pancreatitis, sub-/uncompensated endocrine pathology, as well as during the period of exacerbation or unstable remission of diseases of any localization, including infectious diseases, acute vascular catastrophes, oncological pathology, the results of which could affect the reliability of the obtained data. The calculation of hematological indices and coefficients was carried out on the basis of an expanded general clinical blood test, which was performed on the CELL-DYN 3700 SL hematological analyzer (manufacturer – «Abbott Laboratories», USA) German-Ukrainian Laboratory «BUKINTERMED» with the assistance of the Cottbus Public Laboratory for Medicine, Microbiology and Infectious Epidemiology, Cottbus, Germany. The reactive response of blood neutrophils in patients with acute pancreatitis was assessed by the leukocyte and neutrophil shift index, neutrophil-lymphocyte ratio, neutrophil-monocyte ratio index, lymphocyte-granulocyte index, polymorphonuclear neutrophil reactive response index, leukocyte and lymphocyte index, general indicator of the ratio of the absolute number of leukocytes and the erythrocyte sedimentation rate and leukocyte intoxication index, nonspecific resistance index. The studies were performed in compliance with the basic provisions of GCP (1996), the Council of Europe Convention on Human Rights and Biomedicine (1997), the Declaration of Helsinki of the World Medical Association on the Ethical Principles of Conducting Scientific Medical Research Involving Human Subjects (1964-2008), and the Order of the Ministry of Health of Ukraine № 690 dated September 23, 2009 (as amended by the Order of the Ministry of Health of Ukraine № 523 dated July 12, 2012). The approval was received from the Bioethics Commission of the Bukovinian State Medical University (Protocol № 2 dated 02/09/2015). Statistical processing was performed using application programs: the MYSTAT 12 (Systat Software Inc., USA) and Scout 2008 Version 1.00.01 (U. S. Environmental Protection Agency, USA). The reliability of data for independent samples was calculated using the Student t-test (when the distribution of the arrays is close to normal), or the Wilcoxon-Mann-Whitney U-test (when the distribution is uneven). Analysis of qualitative features was performed using the χ2 criterion. The difference was considered significant at $p<0.05$.*

Results. *The occurrence of acute pancreatitis is characterized by 7.56 times increase of the neutrophil granulocytes reactive response, against the background of significant activation of innate factors and mechanisms of anti-infective defense with a lower response of adaptive specific immunity. In case of biliary genesis pancreatitis, the neutrophils reactive response was 95.29% higher compared to such in patients with alcoholic genesis pancreatitis. If biliary pancreatitis cellular anti-infective protection was provided mainly by monocytes/macrophages, then in alcoholic pancreatitis the microphage system dominated. Biliary pancreatitis was accompanied in 9 (12.5%) patients by vacuolization of the cytoplasm of peripheral blood neutrophils, which was not detected in alcoholic genesis pancreatitis. Toxigenic neutrophil granularity was observed in 54 (75%) patients with biliary pancreatitis, while in alcoholic genesis pancreatitis it was detected only in 36 (30.77%) patients.*

Conclusions. *It has been established that patients with biliary genesis pancreatitis have a stronger reactive response of peripheral blood neutrophil granulocytes and manifestations of intoxication, compared to alcoholic genesis pancreatitis.*

Key words:
pancreatitis, alcoholic pancreatitis, biliary, neutrophil granulocytes, nonspecific resistance.

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ОСОБЛИВОСТІ РЕАКТИВНОЇ ВІДПОВІДІ НЕЙТРОФІЛІВ КРОВІ ЗА ГОСТРОГО ПАНКРЕАТИТУ РІЗНОГО ҐЕНЕЗУ

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Особливості реактивної відповіді нейтрофілів крові за гострого панкреатиту зашаються недостатньо вивченими залежно від етіологічного чинника.

Ключові слова:
панкреатит алкогольний, біліарний, нейтрофільні гранулоцити, неспецифічна резистентність.

Клінічна та експериментальна патологія 2025. Т.24, №2 (92). С. 19-26.

Мета роботи *– дослідити особливості взаємозв'язків реактивної відповіді нейтрофілів крові, системної запальної відповіді і захисту, у хворих на гострий панкреатит алкогольного і біліарного ґенезу.*

Матеріал і методи. *Обстежено 189 хворих, серед яких – 45 (23,8%) жінок і 144 – (76,2%) чоловіків віком від 23 до 77 років, із набряковою формою гострого панкреатиту. Групу контролю сформували з 37 практично здорових осіб. У дослідження не включали хворих на некротичні форми ГП, суб-/некомпенсовану ендокринну патологію, а також у період загострення чи нестійкої ремісії захворювань будь-якої локалізації, у т.ч. – інфекційних, за гострих судинних катастроф, онкопатології, результати яких могли би вплинути на достовірність отриманих даних. Розрахунок гематологічних індексів і коефіцієнтів провели на підставі розширеного загально-клінічного аналізу крові, який виконувався на Аналізаторі гематологічному CELL-DYN 3700 SL (виробник – «Abbott Laboratories», США) Німецько-Української лабораторії «БУКІНТЕРМЕД» при сприянні Котбуської суспільної лабораторії медицини, мікробіології та інфекційної епідеміології, Коттбус, Німеччина. Реактивну відповідь нейтрофілів крові хворих із гострим панкреатитом оцінювали за індексом зсуву лейкоцитів і нейтрофілів, нейтрофільно-лімфоцитарним коефіцієнтом, індексом співвідношення нейтрофілів і моноцитів, лімфоцитарно-гранулоцитарним індексом, індексом реактивної відповіді поліморфноядерних нейтрофілів, лейкоцитарним і лімфоцитарним індексом, загальним показником співвідношення абсолютної кількості лейкоцитів і швидкості зсідання еритроцитів та лейкоцитарним індексом інтоксикації, індексом неспецифічної резистентності. Дослідження виконували з дотриманням основних положень GCP (1996 р.), Конвенції Ради Європи про права людини та біомедицину (1997 р.), Гельсінської декларації Всесвітньої медичної асоціації про етичні принципи проведення наукових медичних досліджень за участі людини (1964-2008 рр.), наказу МОЗ України № 690 від 23.09.2009 р. (зі змінами, внесеними згідно з Наказом Міністерства охорони здоров'я України № 523 від 12.07.2012 р.). Отримано схвалення Комісії з питань біоетики Буковинського державного медичного університету (Протокол № 2 від 9.02.2015 р.). Статистичну обробку виконували за допомогою прикладних програм MYSTAT 12 (Systat Software Inc., USA) і Scout 2008 Version 1.00.01 (U. S. Environmental Protection Agency, США). Достовірність даних для незалежних вибірок розраховували за t-критерієм Student (при розподілі масивів близькими до нормальних), чи U-критерію Wilcoxon-Mann-Whitney (при нерівномірному розподілі). Аналіз якісних ознак – за критерієм $\chi 2$. Різницю вважали достовірною при $p<0,05$.*

Результати. *Виникнення гострого панкреатиту характеризується зростанням реактивної відповіді нейтрофільних гранулоцитів у 7,56 раза на тлі вагомої активації вроджених факторів і механізмів протиінфекційного захисту та меншої реакції адаптивного специфічного імунітету. За біліарного ґенезу панкреатиту реактивна відповідь нейтрофілів виявилася на 95,29% вищою, ніж у пацієнтів із панкреатитом алкогольного ґенезу. Якщо за біліарного панкреатиту клітинний протиінфекційний захист забезпечувався переважно моноцитами/макрофагами, то за алкогольного панкреатиту домінувала мікрофагальна система. Біліарний панкреатит супроводжувався у 9 (12,5%) хворих вакуолізацією цитоплазми нейтрофілів периферійної крові, чого не було виявлено за панкреатиту алкогольного ґенезу. Токсигенну зернистість нейтрофілів спостерігали у 54 (75%) хворих на біліарний панкреатит, тоді як за алкогольного ґенезу вона виявлена лише у 36 (30,77%) хворих.*

Висновки. *Встановлено, що у хворих на панкреатит біліарного ґенезу спостерігається сильніша, порівняно з алкогольним панкреатитом, реактивна відповідь нейтрофільних гранулоцитів периферійної крові та прояви інтоксикації.*

Introduction

Acute pancreatitis (AP) and exacerbation of chronic pancreatitis remain a serious urgent problem over the past decades, occupying the second–third place in frequency in the structure of acute abdominal surgical pathology [1-4]. Despite the significant progress in the studying of the disease etiopathogenetic links, conducting of the complex intensive therapy and introducing minimally invasive surgical treatment methods against the background of rational antibiotic therapy, mortality continues to remain quite high and ranges from 3.9-20.0%, with a tendency to increase after surgical interventions for pancreatic necrosis [5-8].

The determining factors in the severity of the course of AP are, of course, the root cause, acinar cells' damage, intoxication, cellular reactivity of the organism, the level of the adaptive stress, the reactive response (especially in the early phases of the disease) of polymorphonuclear neutrophil granulocytes (PNG), monocytes/macrophages of peripheral blood, against the background of the immunological reactivity of the patient's organism [9-12].

Neutrophil granulocytes (NG) are the first of the immunocompetent cells, acting as sentinels, to contact pathogenic and conditionally pathogenic microorganisms that penetrate the organism protective barriers. At the slightest

changes in homeostasis, to which NG are very sensitive, the latter quickly leave the bloodstream, actively attacking microbes or other genetically foreign bodies anywhere and at any time. At the same time, NG, not having a reliable membrane regeneration system, die when overloaded with pathogenic or conditionally pathogenic microorganisms. In the case of severe microbial contamination, NG carry out excessive expression of free radicals in the microenvironment, which, in the case of the inability of the human body's antioxidant system to neutralize them, leads to the destruction of the producer cells themselves (NG) [13, 14].

Upon activation, NG secrete a wide range of pro– immune and immune cytokines (of the first and the second order), which enables NG influence on the stimulation of the activity of other immunocompetent cells and regulate the adaptive specific immune response. It is worth considering that with greater microbial contamination, neutrophils are forced to produce cytokines, free radicals and phagocytosis of microbial cells more intensively, forming effective anti– infective protection, often at the cost of their own existence.

Despite the known basic functions of this population of immunocompetent cells, the issues of the reactive response of polymorphonuclear NG in peripheral blood, especially in the early phases of the disease, in patients with AP, in the systemic inflammatory response, with various etiological factors, remain incompletely understood, and therefore require further research.

The aim of research

To investigate the features of systemic relationships between indicators of the reactive response of polymorphonuclear neutrophil granulocytes of peripheral blood and indicators of systemic inflammatory response and protection in patients with AP, with different etiological factors.

Research materials and methods

The study included 189 patients with acute pancreatitis and chronic pancreatitis exacerbation (edematous form), hospitalized in the emergency hospital of Chernivtsi during the last four years. The diagnosis of acute pancreatitis was made in accordance with the current domestic orders of the Ministry of Health of Ukraine and guidelines on the diagnosis and treatment of acute pancreatitis and chronic pancreatitis exacerbation [15, 16]. All patients signed an informed consent to participate in the study with the subsequent conduct of a complex of clinical, laboratory and diagnostic studies. The studies were performed in compliance with the basic provisions of GCP (1996), the Council of Europe Convention on Human Rights and Biomedicine (1997), the Declaration of Helsinki of the World Medical Association on the Ethical Principles of Conducting Scientific Medical Research Involving Human Subjects (1964-2008), and the Order of the Ministry of Health of Ukraine № . 690 dated September 23, 2009 (as amended by the Order of the Ministry of Health of Ukraine № . 523 dated July 12, 2012). The approval was received from the Bioethics Commission of the Bukovinian State Medical University (Protocol № . 2 dated 02.09.2015). Among the examined there were 45 (23.8%) women, 144 (76.2%) men. The average age of the patients was 45.1±5.19 years for men, 53.2±7.07 years for women (from 23 to 77 years). The control group consisted of 37 practically healthy individuals of the corresponding age and sex.

The calculation of hematological indices and coefficients was carried out on the basis of an expanded general clinical blood test, which was performed on the CELL–DYN 3700 SL hematological analyzer (manufacturer – «Abbott Laboratories», USA). The NG reactive response of patient organism with AP was assessed by the reactive response index of neutrophil polymorphonuclear leukocytes, the neutrophil–lymphocyte ratio, the shift index of neutrophils and leukocytes, lymphocytic–granulocyte index, neutrophil–monocyte ratio index, leukocyte and lymphocytic index, by the general indicator of the ratio of the absolute number of leukocytes and the erythrocyte sedimentation rate (ESR), total leukocyte, ESR and LII ratio indicator.

Statistical processing was performed using application programs: the MYSTAT 12 (Systat Software Inc., USA) and Scout 2008 Version 1.00.01 (U. S. Environmental Protection Agency, USA). The reliability of data for independent samples was calculated using the Student t–test (when the distribution of the arrays is close to normal), or the Wilcoxon–Mann–Whitney U–test (when the distribution is uneven). Analysis of qualitative features was performed using the $\chi 2$ criterion. The difference was considered significant at $p<0.05$.

The study was conducted as part of the comprehensive research project of the Family Medicine Department of BSMU, titled «Improvement of Diagnosis and Prediction of Hypertensive– Mediated Target Organ Damage and Symptom Control in Comorbid Pathology Considering Clinical–Metabolic and Molecular–Genetic Predictors» (State Registration Number 0124U002524, implementation period: 01.01.2024-31.12.2028).

Results and discussion

The results of the study of hematological indices and coefficients that characterize the reactive response of neutrophil granulocytes in peripheral blood of patients with acute pancreatitis are presented in Table 1.

The occurrence and course of AP is accompanied by a significant ($P<0.05$) increase (7.56 times) of the reactive response of NG, demonstrating a pronounced activation of innate factors and mechanisms of anti-infective defense to the inflammatory process in the pancreas. In addition, in patients with AP, the neutrophil-lymphocyte ratio increases by 2.53 times, which indicates an increase in the relative number of NG and the superiority of the activation of nonspecific factors in anti-infective protection over adaptive specific immunity. The value of the NG reactivity index indicates subcompensated intoxication of the patient body, which is caused by a microbial factor.

The increase of the leukocyte shift index in the peripheral blood of patients with AP by 2.52 times indicates the activation of the inflammatory process and the disruption of factors and mechanisms of nonspecific innate anti-infective and specific immune defense of AP patients with. This is also confirmed by 2.54 times decrease in the lymphocyte-granulocyte index. Enhanced activation of NG in patients with AP is demonstrated by 7.53 times increase of the neutrophil shift index during the inflammatory process with moderate intoxication.

Table 1

Reactive response of neutrophil leukocytes in peripheral blood of patients with acute pancreatitis

Indicators	Units of measurement	Patients with acute pancreatitis (n=189) M±m	Practically healthy individuals (n=37) M±m	p
Leukocyte Shift Index	c.u.	4,36±0,22	1,73±0,09	<0,001
Neutrophil Shift Index	c.u.	0,452±0,12	0,060±0,009	<0,05
Neutrophil-lymphocyte ratio	c.u.	5,53±0,47	2,19±0,27	<0,01
Neutrophil-Monocyte Ratio Index	c.u.	17,70±1,21	7,36±0,17	<0,01
Lymphocyte-granulocytic index	c.u.	1,75±0,18	4,44±0,31	<0,01
Neutrophil- granulocytes Reactive Response Index	c.u.	0,452±0,13	0,059±0,009	<0,05
Leukocyte and ESR ratio index	c.u.	0,33±0,05	1,44±0,11	<0,001
Leukocyte index	c.u.	0,18±0,02	0,46±0,04	<0,01
Lymphocyte index	c.u.	0,181±0,015	0,457±0,015	<0,001
Total leukocyte, ESR and LII ratio indicator	c.u.	4,65±0,27	6,43±0,47	<0,05
Nonspecific resistance index	c.u.	25,37±0,47	48,35±0,57	<0,001

Notes: ESR – erythrocyte sedimentation rate; LII – leukocyte intoxication index; c.u. – conditional units; p – probability of indicators differences between patients with acute pancreatitis and practically healthy individuals

A 4.36 times decrease of the ratio of the leukocytes absolute number and ESR, indicates moderate intoxication, which is mainly caused by an infectious process. A 2.56 times the leukocyte index decrease indicates the predominance of the cellular link of anti-infective defense (phagocytosis) in patients with AP at the initial stages of the inflammatory process development. A decrease of the total ratio of the leukocytes absolute number and ESR by 38.28% indicates the predominance of intoxication caused by microbial factors (endotoxins and exotoxins), although there is also an autoimmune process.

Thus, an increased level of intoxication (medium severity) minimizes the functionally stimulated activity of factors and mechanisms of nonspecific anti-infective defense of the organism with acute respiratory viral infection, as evidenced by the suppressive effect of intoxication on the overall level of nonspecific resistance of the patient body as a whole, which decreases 90.58%. That is why, conducting efferent detoxification correction in the early stages of treatment is a necessary immunological manipulation during this period.

The study results of the neutrophil granulocytes in peripheral blood reactive response of patients with alcoholic genesis pancreatitis (AGP) are presented in Table 2.

Table 2

Reactive response of neutrophil leukocytes in peripheral blood of patients with alcoholic genesis pancreatitis

Indicators	Units of measurement	Patients with alcoholic pancreatitis (n=117) M±m	Practically healthy individuals (n=37) M±m	p
Leukocyte Shift Index	c.u.	4,75±0,27	1,73±0,09	<0,001
Neutrophil Shift Index	c.u.	0,296±0,05	0,060±0,009	<0,01
Neutrophil-lymphocyte ratio	c.u.	6,79±0,48	2,19±0,27	<0,01
Neutrophil-Monocyte Ratio Index	c.u.	14,29±0,79	7,36±0,17	<0,01
Lymphocyte-granulocytic index	c.u.	1,42±0,15	4,44±0,31	<0,01
Neutrophil Reactive Response Index	c.u.	0,297±0,031	0,059±0,009	<0,01
Leukocyte and ESR ratio index	c.u.			
Nonspecific resistance index	c.u.	19,10±0,18	48,35±0,57	<0,001
Leukocyte index	c.u.	0,15±0,02	0,46±0,04	<0,01
Lymphocyte index	c.u.	0,147±0,015	0,457±0,015	<0,001
Total leukocyte, ESR and LII ratio indicator	c.u.	3,19±0,21	6,43±0,47	<0,01

Notes: ESR – erythrocyte sedimentation rate; LII – leukocyte intoxication index; c.u. – conditional units; p – probability of indicators differences between patients with alcoholic pancreatitis and practically healthy individuals

The occurrence, development and course of AGP is accompanied by a pronounced (5.05 times) activation of NG reactivity in peripheral blood. This is confirmed by the values and changes of other analytical immuno-hematological indices and coefficients. Thus, in patients with AGP, the value of the neutrophil-lymphocyte ratio significantly increases by 3.10 times, which indicates a significant advantage at the initial stage of AGP development of nonspecific protection due to NG activation. In contrast, «professional» immunocompetent lymphocytes do not show activity during this period and their concentration in peripheral blood does not change. Peripheral blood NG activity leads to a significant (4.93 times) increase in the shift of this population of immunocompetent cells (neutrophils).

The decrease of the leukocyte index by 3.07 times and the lymphocyte index by 3.11 times confirms that at this stage (the beginning of clinical manifestations of AGP), the cellular link of both nonspecific and specific anti-infective defense prevails over the activity of the humoral link of the immune system.

The 2.53 times decrease of the nonspecific resistance index, in our opinion, is due to organism intoxication of patients with AGP, caused mainly by an infectious and, to a lesser extent, autoimmune process, and also, not the least role in this process is played by alcohol consumption. All of the above indicates a decrease of the functional activity of factors and mechanisms of nonspecific anti-infective defense of the patients with AGP.

The results of the study of the reactive response of peripheral blood neutrophil granulocytes of patients with biliary genesis pancreatitis (BGP) are presented in Table 3.

In patients with BGP, there is a pronounced activation of neutrophil granulocytes according to the value of the NG reactive response index, which increases in these patients by 9.83 times, which is also confirmed by the increase of the neutrophil-lymphocyte ratio by 2.21 times.

The increase in the shift indices of leukocytes and neutrophils in peripheral blood of patients with BGP indicates a pronounced active progressive inflammatory process and impaired immunological reactivity (functional activity of factors and mechanisms of nonspecific and immune-specific protection).

Table 3

Reactive response of neutrophil leukocytes in peripheral blood of patients with biliary acute pancreatitis

Indicators	Units of measurement	Patients with biliary pancreatitis (n=72) M±m	Practically healthy individuals (n=37) M±m	p
Leukocyte Shift Index	c.u.	4,17±0,27	1,73±0,09	<0,001
Neutrophil Shift Index	c.u.	0,581±0,011	0,060±0,009	<0,001
Neutrophil-lymphocyte ratio	c.u.	4,83±0,47	2,19±0,27	<0,05
Neutrophil-Monocyte Ratio Index	c.u.	24,11±1,24	7,36±0,17	<0,001
Lymphocyte-granulocytic index	c.u.	2,20±0,17	4,44±0,31	<0,01
Neutrophil Reactive Response Index	c.u.	0,580±0,012	0,059±0,009	<0,001
Leukocyte and ESR ratio index	c.u.	0,25±0,01	1,44±0,11	<0,001
Nonspecific resistance index	c.u.	32,73±0,31	48,35±0,57	<0,001
Leukocyte index	c.u.	0,21±0,01	0,46±0,04	<0,01
Lymphocyte index	c.u.	0,207±0,014	0,457±0,015	<0,001
Total leukocyte, ESR and LII ratio indicator	c.u.	6,41±0,17	6,43±0,47	>0,05

Notes: ESR – erythrocyte sedimentation rate; LII – leukocyte intoxication index; c.u. – conditional units; p – probability of indicators differences between patients with biliary pancreatitis and practically healthy individuals

The lymphocytic-granulocyte index, which allows to differentiate autointoxication and bacterial intoxication of the patient body with BGP, decreases by 2.02 times, which indicates the predominance of infectious intoxication.

A significant increase (by 3.28 times) of the neutrophil-monocyte ratio index indicates a significantly pronounced activation of the microphage anti-infective defense system compared to the activity of the macrophage defense system. The latter, in addition to effective phagocytosis, participates in immunological recognition and presentation of T-lymphocytes antigens. All this is the evidence that the formation and development of BGP is accompanied by a pronounced activation of polymorphonuclear NG of the peripheral blood.

The decrease of the leukocyte index by 2.19 times and the lymphocyte index by 2.21 times allows us to say that in patients with BGP, the cellular link of anti-infective nonspecific and immune specific protection at the first stages of the disease prevails in its effectiveness over humoral defense mechanisms.

The presence of intoxication in patients with BGP, caused by an infectious process and, to a lesser extent, by autoimmune process, leads to the functional activity limitation of the factors and mechanisms of nonspecific innate and specific acquired immune anti-infective protection of the patient organism, which is confirmed by a 47.72% decrease in the index of the organism nonspecific resistance.

Thus, the formation, development and course of the first stages of manifestation of BGP are accompanied by a pronounced activation of the neutrophil polymorphic granulocytes in the peripheral blood reactive response of patients with BGP.

As indicated above, the peripheral blood neutrophils reactive response of patients with AGP was influenced by apoptosis. Therefore, these patients were diagnosed with infectious and autoimmune intoxication against a background of alcohol exposure. In order to identify differences in the influence (alcoholic and biliary) on the development of AP, we conducted a comparative analysis of the indicators of the peripheral blood NG reactive response in patients with AP of alcoholic and biliary genesis. The results of establishing the peripheral blood NG reactive response of patients with AP, in a comparative aspect, depending on the genesis, are presented in Table 4.

In patients with AGP, the neutrophil granulocytes reactive response is reduced 95.29% compared to such indicators in patients with BGP, and the neutrophil shift index is reduced 96.28%, which indicates an increase in the general intoxication of the patient body with AGP. This is confirmed by an increase of the leukocyte shift index 13.91%.

The decrease of the lymphocyte-granulocyte index 54.93% in patients with AGP indicates that in these patients infectious intoxication prevails over the autoimmune process intoxication, and a decrease in the neutrophil-monocyte ratio index indicates that in patients with BGP, the advantage in anti-infective protection belongs to monocytes/macrophages, and in patients with AGP, cellular anti-infective protection is due to a greater extent to the microphage system (neutrophils).

The increase of the ratio of the absolute leukocytes number and ESR 80.0% in patients with AGP confirms the idea a significant increase of exogenous intoxication (infectious and alcohol) of the patient body.

The decrease of leukocyte (40.0%) and lymphocyte (40.82%) indices in patients with AGP compared to such indicators in patients with BGP indicates that in the latter, cellular protection is carried out more effectively by monocytes/macrophages, and in patients with AGP – due to the activation of neutrophilic leukocytes. At the same time, in both groups of patients with AP, humoral factors of anti-infective protection show less activity and are ineffective.

Table 4

Comparative characteristics of the reactive response of neutrophil granulocytes in peripheral blood of patients with acute pancreatitis depending on the genesis

Indicators	Units of measurement	Patients with alcoholic pancreatitis (n=117) M±m	Patients with biliary pancreatitis (n=72) M±m	p
Leukocyte Shift Index	c.u.	4,75±0,27	4,17±0,27	>0,05
Neutrophil Shift Index	c.u.	0,296±0,05	0,581±0,011	<0,01
Neutrophil-lymphocyte ratio	c.u.	6,79±0,48	4,83±0,47	<0,05
Neutrophil-Monocyte Ratio Index	c.u.	14,29±0,79	24,11±1,24	<0,01
Lymphocyte-granulocytic index	c.u.	1,42±0,15	2,20±0,17	<0,05
Neutrophil Reactive Response Index	c.u.	0,297±0,031	0,580±0,012	<0,01
Leukocyte and ESR ratio index	c.u.	0,45±0,05	0,25±0,01	<0,05
Nonspecific resistance index	c.u.	19,10±0,18	32,73±0,31	<0,001
Leukocyte index	c.u.	0,15±0,02	0,21±0,01	<0,05
Lymphocyte index	c.u.	0,147±0,015	0,207±0,014	<0,05
Total leukocyte, ESR and LII ratio indicator	c.u.	3,19±0,21	6,41±0,17	<0,001

Notes: ESR – erythrocyte sedimentation rate; LII – leukocyte intoxication index; c.u. – conditional units; p – probability of indicators differences between patients with alcoholic and biliary pancreatitis

Thus, the above indicates that alcohol, which has become the trigger mechanism for the formation and course of AP, negatively affects the formation of the reactive the peripheral blood NG response of patients with AGP, minimizing the NG reactive response, which leads to a decrease in the nonspecific anti-infective defense of the patient body.

In terminally differentiated (segmentonuclear), short-lived NGs, upon activation, multidirectional actions are observed, which are associated with the activation of genes encoding the regulation of the various proteins synthesis that ensure the homeostasis stability of both humoral and cellular factors of anti-infective defense [17]. In addition to changes in gene expression, there are changes in mRNA levels in human neutrophils upon exposure to bacteria, which becomes important in the functional activation of NG for the synthesis of pro-immune and immune cytokines and chemokines, adhesion molecules; enzymes; substances that regulate the growth and apoptosis of immunocompetent and other cells. Such activation of NG function occurs in the peripheral blood of a healthy person and in the body of a person suffering from AP, in the presence of intoxication caused by an infectious and autoimmune process, while against the background of alcohol consumption, NG are negatively affected and the function of NG sensitivity to the changes in the sick person body is disrupted.

Neutrophil leukocytes respond to increased intoxication in the body with the appearance of toxigenic granularity and vacuolization of the neutrophil cytoplasm. Vacuolization of the peripheral blood neutrophils cytoplasm of patients with AGP was not detected in any patient, but it was observed in 9 (12.5%) patients with BGP.

Toxigenic granularity was detected in 36 (30.77%) patients with AGP. Of these, in 27 (23.08%) patients it was assessed as 1+, and in 9 (7.7.69%) it was assessed as 2+. At the same time, toxigenic granularity of NG was detected in 54 (75%) patients with BGP; it was assessed in 36 (50%) patients as 1+, in 9 (12.5%) as 2+, in the remaining 9 (12.5%) individuals as 3+.

Thus, in patients with AP, the level of peripheral blood NG reactive response increases, what directly depends on the etiological factor. The peripheral blood NG reactive response is more pronounced in patients with BGP, and less NG activation is observed in patients with AGP. From our point of view, the decrease in the level of NG reactive response in patients with AGP is due to the limiting effect of the latter on the functional activity of short-lived NG. At the same time, toxigenic granularity of NG is more pronounced in patients with BGP, and vacuolization of neutrophil cytoplasm is detected only in peripheral blood NG of patients with BGP.

The nature of the course and severity of the inflammatory process is determined by the degree of exogenous and endogenous intoxication and the immune reactivity of the patient body. The mentioned above, the level of adaptive stress, cellular reactivity of organism (degree of intoxication), the peripheral blood NG reactive response in patients with AP, depends on the genesis – alcoholic or biliary AP.

Conclusions

1. The functionally stimulated activity of factors and mechanisms of nonspecific anti-infective defense of patient body with acute pancreatitis (AP) is limited by the increased level of intoxication: the suppressive effect of intoxication on the general level of nonspecific resistance of patient body is generally reduced 90.58%.

2. The decrease of the nonspecific resistance index by 2.53 times in patients with alcoholic pancreatitis is due to the intoxication of organism, mainly due to the infectious process and alcohol.

3. In patients with BGP, intoxication is combined with limitation of the functional activity of factors and mechanisms of nonspecific innate and specific acquired immune anti-infective defense of the patient body, with a decrease of the index of nonspecific resistance of organism 47.72%.

4. In patients with BGP, the peripheral blood neutrophil granulocytes reactive response and their toxigenic granularity are more pronounced. Vacuolization of NG cytoplasm is present exclusively in patients with BGP, which indicates a stronger organism intoxication of this genesis.

Prospects

Establishing possible chronobiological relationships in the formation of acute pancreatitis, taking into account the etiological factor and gender.

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