Immunological aspects of comorbid course of chronic obstructive pulmonary disease and chronic pancreatitis

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Persistent nature of inflammation in chronic diseases of internal organs leads to increased stress on the immune system, which turns the formation of secondary immune deficiency and decrease reactive properties of the body. Volume and characteristics of immune changes in each case due to several aspects: the nature of the disease, the presence or absence of foreign antigens, genetic factors, immune reactivity, volume and quality of the therapy and the severity of endogenous intoxication syndrome [1, 2, 4, 5]. The resulting endotoxins are responsible for the development of "metabolic imunodefektu" because it is a result of their pathogenic influence disrupt imunopoezu regulation, proliferation and metabolism of immune cells, autoregulation immune response [2, 4, 5].

Syndrome of endogenous intoxication for most clinical, biochemical and immunological manifestations in modern literature is considered as a non-specific process, caused by a mismatch between synthesis and excretion products of "normal" and abnormal metabolism [2, 3]. At its core, it is a natural consequence of violations of microcirculation, gas exchange, lipid peroxidation, leading to the accumulation in tissues and biological fluids products of tissue destruction and cell stress mediators. Intoxication syndrome — the main pathological syndrome that occurs in almost all diseases and is a nonspecific response for the pathology [2, 3]. However, despite its nonspecific, a variety of clinical situations, it is the presence of comorbidity makes this syndrome individual, specific features. Thus, the study of the mechanisms of formation of endogenous intoxication syndrome in terms of comorbid pathology is important.

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The aim of research is to identify ways to implement the autoimmune process in patients with combined course of chronic obstructive pulmonary disease (COPD) and chronic pancreatitis (CP).

Materials and methods. Under supervision there were 79 patients with COPD aged (44,7±4,9), and duration of history from 3 to 23 years. Among surveyed male patients prevailed — 58 (73.4%) patients. The main group consisted of 47 patients with COPD, which in previous stages of treatment were diagnosed with CP history lasting from 2 to 21 years. A comparison group presented 32 patients with isolated course of COPD. The control group included 20 healthy individuals of similar age and gender. Proliferative activity of peripheral blood lymphocytes were evaluated in response blasttransformation (RBTL), while using lymphocyte cultures: from phutohemoagglutinin (PHA), LPS (LPS) and monocultures without mitogen. Activity autoimmune processes — in response autologous lymphocyte rosette with their own

red blood cells. Expression of endotoxemia syndrome was evaluated in terms of the average molecular weight (IMS) by precipitation them from blood plasma. Level autosensibilization lymphocyte antigens relative to normal human tissues was determined in RBTL counting the number of lymphocytes proliferate at 100 percent of cells and proliferation.

Statistical analysis of the results was carried out using licensed software «Microsoft Excel» and «Statistica 6.0».

Results and discussion.

During the study, the functional activity of lymphocytes in RBTL found a significant reduction in the functional activity of T-lymphocytes compared with those of healthy individuals in both groups of patients on the background at the same time a substantial increase in activity of B-lymphocytes (Table. 1). At the same time revealed significant increase basic immunoregulatory factor (BIRF), indicating the formation of autoimmune processes [2].

Table 1

Indicators of functional activity of lymphocytes in RBTL in the patients examined

Studied indicators	**Patients with COPD (n=32)**	**Patients with COPD and CP (n=47)**	**Control group (n=20)**
FGA stimulation, %	35,67±1,2*	29,44±1,6*/**	42,23±2,57
GIPS stimulation, %	14,53±1,1*	18,22±0,9*/**	11,35±0,57
BIRF	1,57±0,03*	1,68±0,04*/**	1,40±0,05

Note. Here and afterwards p <0,05: * compared with those of the control group; ** compared with those of the comparison group.

The results indicate that the expressed deficiency of T lymphocytes and reduce their functional activity initiates infringement mechanisms regulating both cellular and humoral responses, resulting in the loss of tolerance in lymphocytes to avtoantyheniv and determines the possibility of avtoahresyvnyh reactions with high B-cell immune response as overproduction of autoantibodies [1, 4, 5]. Thus, lack of suppressor function of T-cells and B cell hyperactivity on avtoantyheniv can cause the development of autoimmune reactions in these patients.

During the research activity of lymphocytes in autologous rozetkoutvoreppi in COPD patients recorded a significant damaging effect of whole anthological serum for their own white blood cells (Table. 2). The research activity of various fractions of blood serum, transporting toxins, showed that the damaging action was common to all the factions, but the leading role played globulin fraction and the compounds of medium size (10-200 nm).

Table 2

Indicators of lymphocytes activity in autologous rosette in the patients examined

Studied indicators	**Patients with COPD (n=32)**	**Patients with COPD and CP (n=47)**	**Control group (n=20)**
Spontaneous reaction, %	22,45±0,97*	25,17±0,84*/**	15,22±0,89

Autologous blood serum, %	50,9±3,4*	61,7±2,7*/**	20,20±0,12
Albumin fraction, %	38,5±2,3*	62,6±2,7*/**	19,50±0,85
Globulin fraction, %	52,8±4,2*	68,9±3,4*/**	12,20±0,37
Fraction of medium-size compounds, %	56,8±2,7*	48,7±2,5*/**	15,20±0,39

Increased toxins medium-sized and major factions, transporting toxins in patients with COPD is seen as an indicator of the severity of endotoxemia syndrome which has arisen as a result of destabilization of cell membranes. High activity of these factions, apparently caused by the accumulation of serum avtoahresyvnyh damaging substances direct action and MSM.

In patients with COPD combined course and CP also determined performance increase cytolytic activity anthological serum for their own white blood cells. Although less intense accumulation of toxins of medium size, they contribute to the syndrome of endogenous intoxication rather significant. The research activity of various substances serum transporting toxins showed the presence of significant damaging action mainly albumin globulin fractions and serum. This redistribution active fractions, transporting toxins, as compared to the comparison group suggests significant decompensation of toxin-binding ability albumin and accumulation of tissue destruction.

The study found patients with isolated COPD flow increased content of MSM to 0,73±0,07 units. opt. density, which is 1.3 times higher than in controls and confirms the development of endogenous intoxication syndrome. Significant role in its formation played an increasing fraction of hydrophobic MSM figures which 2.8 times higher than control ($p < 0.05$) (Table. 3).

Table 3

The content of MSM and their factions in the patients examined

Studied indicators	**Patients with COPD (n=32)**	**Patients with COPD and CP (n=47)**	**Control group (n=20)**
MSM (common) units.opt. density	0,73±0,07*	0,89±0,05*	0,56±0,06
Hydrophobic units. opt.density	0,39±0,05*	0,57±0,05*	0,14±0,03
Hydrophilic units. opt.density	0,34±0,04*	0,32±0,03*	0,42±0,04

Patients with combined COPD and how IMS CP content was 0,89±0,05 units. opt. density, which is 1.6 times higher than the control value ($p < 0.05$). It also determined by increasing the content of MSM hydrophobic nature in 4.1 times compared with the values of healthy individuals.

The composition of the hydrophobic fraction pool MSM heterogeneous and can be represented phospholipids, cholesterol, free fatty acids, triglycerides and other

molecules that blood plasma circulates mainly in the form of complexes with albumin and low-density lipoprotein [1, 3]. The binding of MCM proteins gives them properties of initiating absorption of immune cells, which, in the end, makes modeling effect on the immune system.

Of the pool of MSM is hydrophobic protein degradation products with the most significant damaging effect of: contacting blood cells membranes and intracellular proteins, they lead to changes in their structure, increasing membrane permeability, inhibit enzyme activity. Have a significant impact on functional activity of phagocytic cells, leading to decompensation of function, inability to form adequate functional response to microbial antigens. Change of activity of intracellular enzymes microbicyde in these cells leads to disruption of phagocytosis that the later stages of the disease leads to deepening endogenous intoxication. This develops monocyte dysfunction, which causes disturbances in the system of antigen presentation to immune cells, thus ensuring the formation of autoimmune reactions in these patients.

High activity of lymphocytes in the spontaneous reaction reflects the significant level avtosensybilizatsiyi lymphocytes to own antigens, which was confirmed in the study of proliferative activity in the presence of tissue antigens of the lungs, liver and myocardium (Table. 4).

Table 4

Indicators of proliferative activity of lymphocytes in the presence of certain tissue antigens in examined patients

Tissue antigens	**Patients with COPD (n=32)**	**Patients with COPD and CP (n=47)**	**Control group (n=20)**
Liver, %	2,80±0,35*	4,70±0,37*»	1,34±0,22
Lungs, %	5,50±0,39*	4,20±0,43*»	1,67±0,45
Myocardium, %	5,90±0,31*	6,80±0,34**	2,45±0,22

However, if patients with COPD more immunogenicity revealed the presence of antigens and attack the lungs, then the comorbidity of COPD and the most important indicators of XP installed on myocardial antigens and liver.

Conclusions.

In patients with COPD exacerbation of the pathological process in bronchopulmonary system led to a pronounced deficiency of T cells, reducing their functional activity and lack of suppressor function, which initiated the breach of regulatory mechanisms of cellular and humoral immunity. The result was a loss of tolerance deviations of B-lymphocytes to avtoantyheniv, and as a result, the development of autoimmune reactions in patients in both groups. However, in the comorbidity severity of these changes significantly increased, which can be regarded as one of the additional factors of progression of disease.

Chronic recurrent nature of the pathological process in the bronchial tubes led to the formation of endogenous intoxication syndrome, the severity of which significantly intensified in the conditions of accession CP. This damaging effect of fractions of blood serum, transporting toxins in patients with COPD are more isolated

was caused by toxins pool of medium size and globulin fraction, increasing the overall level of MSM and redistribution of their constituents upward hydrophobic fraction. This, in turn, resulted in direct destruction of immune cells and may have been the cause of systemic inflammation.

When combined COPD and CP leading role in the formation of endotoxemia syndrome albuminoviy assigned globulin fractions and serum substances that transport toxins and significant strengthening of deviations in the composition of MSM. These changes were apparently associated with decompensation toxin-binding ability albumin autoagressive accumulation of substances and products of tissue destruction, which significantly increased the risk of autoimmune complications in patients with comorbid disorders. This thesis is confirmed by the survey proliferative activity of lymphocytes in the presence of tissue antigens: in comorbidity observed significantly higher immunogenicity lymphocyte antigen to your liver and myocardium that can be seen as a predictor of target organ damage.

Prospects for further research. One promising avenue is to study other immunological deviations in patients with COPD and comorbidity of CP and comparing the results obtained with the presented data.

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Objective. To identify ways to implement the autoimmune process in patients with combined course of chronic obstructive pulmonary disease (COPD) and chronic pancreatitis (CP).

Materials and methods. The study has been held for the peculiarities of the development of metabolic intoxication and formation of auto immune reactions in 79 patients with COPD and with combined course of COPD and CP.

Results and discussion. The presence of concomitant CP exacerbates the syndrome of endogenous intoxication and the imbalance oi regulatory mechanisms of both cellular and humoral immunity, which significantly increases the risk of autoimmune complications.

Conclusions. This fact allows us to consider the presence of concomitant CP in patients with COPD as unfavorable prognostic factor.