PECULIARITIES OF CERTAIN IMMUNITY INDICES IN PATIENTS WITH BRONCHIAL ASTHMA AGAINST THE BACKGROUND OF OVERWEIGHT OR OBESITY

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Annotation. Bronchial asthma is a common, potentially dangerous disease, which causes a significant burden for patients, their families and society as a whole. In the international Guidelines of Gina, there is an assumption that is most concisely suited to explain the factors that may affect the development of bronchial asthma (BA). We will not list all the components, but we would like to focus on those that are most interesting to us and the least studied in our population, namely obesity or excessive body mass (EBW) and immunity. The purpose of our study was to study the peculiarities of certain indices of immunity in patients with bronchial asthma against the background of overweight or obesity. 105 patients with the main diagnosis of bronchial asthma of various degree of severity were examined and treated on the basis of the Department of Family Medicine and General Practice of Odesa National Medical University. Patients in the main group had a body weight index on an average of 31.37 ± 0.49 kg / m2. It was found that all groups of patients did not have a reliably significant difference in the indices of the humoral immunity, namely levels of IgA, IgG, Ig. The level of the secretory Ig A has a direct strong association with the severity of the BA course (r = 1.0). Patients in the main and comparison groups have a lowered CD 14 level, in our opinion, this may be one of the leading components in the incidence of bacterial viral diseases and subsequent exacerbations of BA in our patients. Patients with bronchial asthma have a decreased level of CD14, which is one of the leading components in the exacerbation rate, provoked by bacterial and viral infections requiring immunocorrection in such a group of patients.

Key words: bronchial asthma, excessive body weight, obesity.

Bronchial asthma is a disease with clear clinical, physiological and morphological characteristics. Its most important clinical manifestations are episodes of suffocation, especially at night, accompanied by coughing [1]. Bronchial asthma is a common, potentially dangerous disease that causes a significant burden for patients, their families and society as a whole. Limitation of life, which reduces the patient's capacity to work, exacerbation of the respiratory symptoms, which sometimes require emergency care and can be fatal, here are the key problems of BA.

Factors influencing the risk of developing BA can be divided into those that determine the development of the disease and those that provoke the development of symptoms of exacerbation. Some factors are related to both groups. The first group consists of internal factors (first of all, genetic), the second one usually refers to external factors [1, 2]. However, the mechanisms of the influence of these factors on the development and

manifestation of BA are complex and interdependent. For example, the predisposition to BA is probably determined by the interaction of genes with each other, and their interaction with external factors [1, 3]. In addition, there is evidence that the peculiarities of human development may affect the risk of BA in genetically predisposed individuals [4, 5]. For example, maturation of the immune response system and the timing of contact with pathogens in the early years of life are important factors. In the international Guidelines of Gina, there is an assumption that is most concisely suited to explanation of the factors that may affect the development of BA. We will not list all the components but we would focus on those that are most interesting to us and the least studied in our population, namely obesity or excessive body mass (EBW) and immunity.

It is currently well-known that there is a relationship between BA and immunoglobin E (Ig E) as an allergic marker in the human body, but for others, namely immunoglobin A (IgA), immunoglobin (Ig G) and immunoglobulin M (IgM), we have a disappointing picture.

For over thirty years it has been known that the IgE molecule is a key ingredient in allergic responses. A direct correlation between IgE level and the development of bronchial asthma was proved, and, along with this, it has been proved that allergic rhinitis does not correlate with Ig E level and is associated with seasonal aeroallergens in patients. The cells such as CD4 and T regulate or organize most of the typical immune responses to foreign proteins in the human body, secreting cytokines such as interleukins (ILs) and interferons (IFNs), and can be classified as Th-0, Th-1 phenotypes, Th-2 [6].

The activation of Th2 and B-lymphocytes accounts for processes of sensitization to allergens in genetically predisposed people. The antigens treated with antigen presenting cells can be recognized by Th-2 cells. Interleukins that were released by activated Th-2 (IL-4, IL-13) cells enhance the production of IgE antibodies. These antibodies, in turn, get attached to other cells that have IgE receptor specificity.

In order to obtain more detailed information not only on the influence of the humoral immunity, but also on the influence of the cellular immunity on the course of BA, it is necessary to study this problem in detail in the population of comorbid patients.

The purpose of our study was to study the peculiarities of certain indices of immunity in patients with bronchial asthma against the background of overweight or obesity.

Materials and methods. We have examined 105 patients (72 women and 33 men whose average age was 41.19±1.05) who had the main diagnosis of bronchial asthma of various degree of severity and were treated on the basis of the Department of Family Medicine and General Practice of Odesa National Medical University. The diagnosis was established in accordance with international approval documents. Inclusion criteria were: agreement of the patient to participate in the study, age of patients over 18 years; BA of various degrees of severity, obesity or excessive body weight. Exclusion criteria: refusal to participate in the study, presence of acute infection, acute pathology and decompensation of any somatic accompanying pathology, endocrine obesity, metabolic syndrome, oncological pathology, mental disorders. The distribution of patients into groups was carried out by simple randomization with elements of stratification.

Patients were divided into two groups: the main group – patients with BA against the background of overweight or obesity (n = 75), the comparison group - patients with BA against the background of harmonic physical development (n = 30). Also, the study included 20 practically healthy individuals with harmonious physical development. All patients were able-bodied.

The patients were asked to make a comprehensive examination, which included: anamnesis, routine physical examination, ACT test, and anthropometry. To study the immune system indices, the indices of the humoral immunity, namely, IgA, IgE, IgG, IgM, and T lymphocyte cellular immunity (CD3 +, CD19-), T-helper / T-inductors (CD4 + .CD8-), T-suppressors / T-cytotoxic cells (CD4-, CD8 +), CD14 receptor monocytes / macrophages, NK-cells (CD3-, CD56 +), cytotoxic cells (CD3 +, CD56 +), B-lymphocytes (CD3-, CD19 +) and circulating immune cells of different calibre were investigated. The study was carried out by the method of immuno-turbidimetry from the patients' venous blood, which was taken on an empty stomach from 8 to 10 o'clock in the morning.

Statistical analysis was carried out according to generally accepted methods of variation statistics. Validity was evaluated for the t criterion of the Student. Differences were recognized as substantial at the significance level of $p \leq 0.05$. The correlation connection was established using the Spirman correlation coefficient.

Results. During our study, it was found that patients in the main group had a body-mass index on an average of 31.37 ± 0.49 kg / m2, a comparison group - of 22.65 ± 0.33 kg / m2 ($p < 0.05$), and in the control group, the average BMI was 22.64 ± 0.38 kg / m2 ($p < 0.05$).

In everyday clinical practice, successful treatment of BA remains rather insignificant. At the same time, a very significant impact on the results of the treatment of BA proves to be the correct assessment by physicians and patients of the present symptoms and the effectiveness of therapy given. According to the available data, most physicians and patients tend to underestimate the severity of clinical symptoms of BA and overestimate the outcome of treatment. It results in As inadequately low scope of therapy and inadequate control of the disease in a significant proportion of patients [7, 8].

Our study found that only 15 % of the total number of patients passed the ACT test while taking history. We received the following data: patients in the main group – 12.37 ± 3.10, patients in the comparison group – 17.63 ± 1.65 ($p < 0.05$), which does not reach the control indices of 20-25 points. That is, we can conclude that patients with comorbidity in the form of EBW or obesity have a less controlled course of BA than patients with harmonious physical development.

Since Ig G that accounts for about 75% of serum immunoglobulins and 10-20 % of the total serum protein of the blood, is synthesized by mature B-lymphocytes and is the main antibodies that are produced in response to secondary contact with the antigen, its antibodies are involved in the neutralization of the bacterial, viral toxins, phagocytosis stimulation, complement binding reactions. Immunoglobulin M is synthesized by the plasma cells, accounting for 5-10 % of the total number of immunoglobulins in

the serum. Ig M includes isohemagglutinins, antibacterial, heterophilic antibodies, rheumatoid factor. Antibodies have high complementary activity, and Ig M molecules bind complement more effectively than IgG. B-lymphocytes have superficial receptors to Ig M and are the first to secrete Ig M. Following the transformation of B-lymphocytes into a plasma cell, subsequent stimulation by the same antigen causes a pronounced "secondary response" with the secretion of Ig G. Thus, we have found that patients in all groups did not have a reliably significant difference in the indices of the humoral immunity, namely, Ig A, IgG, Ig M.

In our study, we did not focus on Ig E levels, but we found that 55% of the patients in the main group and 60% of the patients in the comparison group had an elevated IgE level. We did not find the relationship between the Ig E level and the severity of the BA course ($r = 0.32$).

The data presented in the Table 1 reflects the evaluation of subpopulation of T-lymphocytes in the examined groups.

Table 1

Evaluation of subpopulations of T-lymphocytes in the examined groups

Group	CD3+,CD19-%	CD4+,CD8-%	CD4-,CD8+%
Main	**77.67±0.43	**52.07±0.54*	**24.67±0.57
Comparison	74.63±4.42	48.18±0.79	25.18±0.83^
Control	69.13±1.73	45.56±1.27	27.47±0.67

*Note: *p о-n<0.05*
***p о-к<0.05*
^ p n-к<0.05

Subpopulations of T-lymphocytes have drawn our attention, so it was found that the patients in the main group had an elevated level of T-helper / T-inductors (CD4 + .CD8-) ($p<0.05$), compared with the control and comparison groups, and elevated level of T -lymphocytes (CD3 +, CD19-) compared with the control group ($p<0.05$), and the lower level of T-suppressors / T-cytotoxic cells (CD4-, CD8 +) in the main group and the comparison group relative to the control group ($p<0.05$).

The main function of the serum Ig A is a protection of the respiratory, urinary and gastrointestinal tracts from infection. The secretory IgA has a dimeric structure and is resistant to enzymes due to its structural features. The IgA secretory antibodies block the attachment of bacteria to the surface of the epithelial cells, preventing their adhesion, and, accordingly, damaging the cell and penetrating through the mucous membrane. We found that patients in the main group had a large difference in the levels of the secretory Ig A, but when we evaluated its level according to the severity, it turned out that the more severe was the course of asthma, the lower was the indices of the secretory Ig A, i.e., when a correlation analysis was performed between the level of the secretory Ig A and the severity of the BA course there was a direct strong bond ($r = 1.0$). In the analysis of the secretory Ig A in the control and comparison groups, it was found that in the comparison group, this figure was higher, namely 52.66 ± 1.68 μg / ml versus $83.68 \pm$

3.68 μg / ml in the control group (p 0.05).

The formation of the circulating immune complexes (CIC) is physiological for a human body, and it should result in the neutralization and elimination of the antigen. However, under certain conditions, CIC may be fixed on the vessels and cause an inflammatory reaction. The greatest pathological potential is inherent in a soluble medium-sized CIC capable of activating a complement. CICs are capable of activating a large number of cells, including eosinophils and basophils. Eosinophilic granulocytes activated by CIC have cytotoxic properties. Basophile granulocytes are able to bind Ig E, which are fixed on their surface. Therefore, we paid attention to the level of CIC in the patients being examined. We detected differences in the level of CIC in patient groups. The data is given in the Table 2

Table 2

The level of circulating immune cells in the examined groups

Groups	Large opt.unit	Middle opt.unit	Small opt.unit
Main	**10.89±0.38*	**86.65±1.36*	**176.09±1.19*
Comparison	8.10±0.28^	79.77±1.61^	182.2±1.05^
Control	8.25±0.38	69.0±1.51	145.3±1.65

*Note: *p о-п<0.05*
***p о-к<0.05*
^ p п-к<0.05

It is well known that mononuclear macrophages, namely tissue macrophages and monocytes, are one of the key components of the congenital immunity. They take part in the direct protection of the body from foreign substances, mainly due to phagocytosis and antibody-dependent cleansing. Along with this, the cells of the macrophage monocyte system are able to interact with the lymphoid cells, "activating" and regulating the mechanisms of the specific adaptive immunity. It is estimated that 14.9% of the daily dose of monocytes leaving the bloodstream gets into the lungs, so we can not forget about these cells in the study of BA. In our opinion, the balance in the macrophage monocyte system is an important component in the human immunity with BA and we have to investigate it in detail. Along with the CD14 receptor, our attention was attracted by NK-cells (CD3-, CD56 +), cytotoxic cells (CD3 +, CD56 +), B-lymphocytes (CD3-, CD19 +). More detailed information on these receptors is given in the Table 3.

The table 3 shows that the patients in the main and comparison groups have a lowered CD 14 level; in our opinion, this may be one of the leading components in the incidence of bacterial viral diseases and subsequent exacerbations of BA in our patients. This is confirmed by case histories of the patients included in our study. It was found that patients in the main and comparison groups were significantly more likely to be infected with bacterial and viral infections than the control group (p<0.05), and 81% of the patients noted an exacerbation of the symptoms of BA when bacterial and viral diseases developed. This is due to the fact that the CD 14 molecule recognizes the lipopolysaccharides of bacteria and viruses that are in the human body, and the

deficiency of these receptors leads to insufficient recognition that triggers the cascade of mechanisms, and the macrophage itself can not phagocyte the foreign molecule, and it infects the body and develops infection, which in turn leads to exacerbation of BA and its more severe course.

Overall, the study showed that patients with a comorbid overweight or obesity pathology have lower asthma control and have greater changes in the cellular and humoral immunity, requiring further immunocorrective therapy.

Table 3

Separate indices of the cellular immunity in the examined groups

Groups	CD 14%	CD3-,CD56+%	CD3+,CD56+%
Main	**5.70±0.15	**8.47±0.55*	**5.17±0.43*
Comparison	⌐5.57±0.09	11.12±0.53	3.61±0.16
Control	7.83±0.22	10.47±0.38	3.96±0.13

*Note: *p о-п<0.05*
**р о-к<0.05
∧ р п-к<0.05

Conclusions. 1. The patients in the main group have a less controlled course of bronchial asthma due to comorbid abnormality in the form of excessive body mass or obesity.

2. The patients in the main group have a decreased level of the secretory Ig A, which may be a criterion for more severe course of bronchial asthma in patients with excessive body weight or obesity in case asthma control is not achieved.

3. All patients suffering from bronchial asthma have an elevated level of the circulating immune complexes, which suggests persistence of chronic inflammation in such patients.

4. The patients with bronchial asthma have a decreased level of CD14, which is one of the leading components in the occurrence of exacerbations, provoked by bacterial and viral infections requiring immunocorrection in such a group of patients.

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