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ORIGINAL PAPER

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Dynamics of changes in the level of IgA in patients with bronchial asthma against the background of excessive body weight or obesity

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ABSTRACT

Introduction. Among patients with asthma, a lot of attention is being given to, at the present time, to such comorbidity as excessive body mass (EBM) or obesity.

Aim. To evaluate the level of IgA in patients with bronchial asthma against the background of excessive body weight or obesity and to evaluate the effects of drug on the bacterial lysate and inosine pranobex.

Material and methods. According to the design, the study was conducted in two stages: the first stage – examination of 105 patients with asthma. 105 patients with a basic diagnosis of asthma were examined whose average age was 41.19 ± 1.05 years, 75 patients were found to have EBM or obesity (BMI 31.67 ± 0.53) who were included in the main group and 30 patients with NBMI (BMI 22.13 ± 0.32), which were the comparison group.

Results. The patients in the main group with a severe course had significantly lower serum IgA values than the patients in the comparison group ($p<0.05$), but the statistically significant difference between this index in the patients with a severe course in the main group and the control group was not revealed. The patients in the main group had a significant increase in the level of secret IgA against the background of the use of treatment-and-prophylactic complex (TPC) with the inclusion of a preparation of bacterial lysate in combination with inosine pranobex against the background of training in asthma school, receiving the basic treatment ($p<0.05$).

Conclusion. Patients with asthma who have large BMI have a more severe course of bronchial asthma. A Correlation relationship was established in the group of patients with bronchial asthma and with excessive body weight or obesity between the level of sIgA and the severity of the asthma course; there is a direct strong correlation. Patients in the main group had a significant increase in the level of sIgA against the background of the use of TPC with the addition of a basic treatment by the preparation of bacterial lysate together with inosine pranobex.

Keywords. bronchial asthma, excessive body weight, obesity

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Participation of co-authors: A – Author of the concept and objectives of paper; B – collection of data; C – implementation of research; D – elaborate, analysis and interpretation of data; E – statistical analysis; F – preparation of a manuscript; G – working out the literature; H – obtaining funds

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Introduction

Advanced studies of the 21st century have achieved significant success in understanding and treating bronchial asthma (BA). A deeper understanding of the mechanisms of the disease that was made possible by fundamental scientific investigations over the past twenty years has led to the development of highly specific methods of treatment. At the same time, publication of the results of clinical studies opened our eyes to the diversity of etiological, and pathogenetic mechanisms of development and the course of asthma. Due to the more advanced views on the pathophysiological mechanisms of asthma, the mechanisms that are not limited to allergic reactions and immune reactions of type II began to be studied.[1]

In the modern world, both the physician and the patient often need to solve the issues of comorbidity of pathologies. Among patients with asthma, a lot of attention is being given to such comorbidity as excessive body mass (EBM) or obesity.[2]

The study on adult obesity trends using NHANES I (1971-1975), II (1976-1980) and III (1988-1994) showed that BMI increased everywhere in adults with and without asthma; however, the prevalence of obesity was higher in the group of patients with asthma (21.3-32.8%) compared with that without asthma (14.6-22.8%).[3] A retrospective study involving 143 adult patients revealed a similar relationship between the prevalence of EBM or obesity and BA.[4] It has been shown that patients with asthma who had a comorbidity of EBM or obesity have a lower response to baseline therapy and have a more uncontrolled course of the disease and, therefore, this cohort of patients has a nearly fivefold risk of hospitalization due to exacerbations of the disease.[5]

Therefore, based on the data above, it is necessary to search for new diagnostic and therapeutic measures in patients with asthma against the background of EBM or obesity.

Among immunological parameters, IgE is the most studied in patients with asthma. However, our attention in this study was given to another immunoglobulin, namely serum and secretion IgA, which is less investigated, but in our opinion, has a significant effect on the course of asthma.

It is common knowledge that IgA is a gamma globulin fraction, synthesized mainly in the plasma mucosal cells in response to local antigen effects. The main function of the serum IgA is the protection of the respiratory, urinary tract and gastrointestinal tract from infection.[6]

Secret IgA (sIgA) has a dimeric structure and is resistant to enzymes due to its structural features. This immunoglobulin lives only for 5 days. Therefore, for its constant replenishment in the body, differentiation of B-lymphocytes into plasma cells occurs daily and plasma cells synthesize sIgA. Recent studies have suggested the possible role of the epithelial cells in an antigenic presentation. Dendritic cells in the airways epithelium can directly provide anti-B cells and thus stimulate them to differentiate with cytokines synthesized by the epithelial cells, into plasma and prior to the synthesis of sIgA.[7]

Thus, sIgA is responsible for local defense, and its regulatory role in combination with local synthesis, transport and secretion is distinguished by the immunity of mucous membranes from systemic immunity.[8] This immunoglobulin is not able to bind the complement or cause its activation. However, it fulfils various protective functions by interacting with different receptors of the immune system, which protects the mucous surfaces of the body from the penetration of microorganisms into tissues. sIgA can bind toxins and, together with lysozyme, exhibits bactericidal and antiviral activity. It acts as an agglutinator of microorganisms and a toxin neutralizer, inhibiting the binding of viruses and bacteria to the surface of the mucous membranes, thereby suppressing replication.[9,10]

In the domestic literature, at present, there are no researches on the correlation of IgA and BA, but in foreign sources of these studies are already available. Woo-Jin Kim and colleagues conducted a series of studies in adult asthma patients regarding IgA correlation and showed that IgA levels may have an association with age, gender, bronchial hyperresponsiveness and serum IgG levels.[11,12]

A characteristic feature of modern infectious pathology is the growth of chronic infectious and inflammatory diseases.[13,14]

Considerable experience has been accumulated in the use of drugs of bacterial origin with immunotonic properties for several decades, in chronic infectious pathology of various organs and systems, and in allergic diseases. A typical moment in the appointment of immune drugs is to include them in complex therapy along with anti-inflammatory drugs, which greatly increases the effectiveness of treatment and compliance of the patient with the doctor.[15]

Currently, the drug Broncho-munal from the firm Lek in Slovenia is popular among patients and doctors. The drug affects different parts of the immune response. [16,17]

Among immunomodulators with antiviral activity of interest is the drug Inosine pranobex, namely the drug Novirin, of Kiev vitamin plant, PAS, Kiev, Ukraine. Clinical studies have shown that it is well tolerated (practically non-immunogenic), which is probably due to the similarity ("affinity") of its compounds to substances found in the body [18,19]

Aim

To evaluate the level of IgA in patients with bronchial asthma against the background of excessive body weight or obesity and to evaluate the effects of bacterial lysate and inosine pranobex.

Material and methods

According to the design, the study was conducted in two stages. The first stage was examination of 105 patients with asthma based on the Department of Family Medicine and General Practice of Odessa National Medical University and the formation of the main cohort group according to inclusion/exclusion criteria "Patients with BA against the background of EBM or obesity", which included 75 patients, and a comparison group according to the inclusion/exclusion criteria "Patients with BA against the background of normal body mass index (NBMI)", which included 30 patients. At the 2nd stage of the study, a treatment-and-prophylactic complex (TPC) was administered to the main group of the main cohort group of the 1st stage (the main group - 30 patients and the comparison group - 30 patients, control group - 15 patients) to complete the clinical trial, namely the use of the preparations of bacterial lysate, inosine pranobex. The average course of treatment was 4 weeks.

Body mass was measured on the OMRON BF 51 scales impedance meter, measured in light clothing, on an empty stomach, measuring accuracy was 0.01 kg.

Body mass index was calculated by the formula: BMI = m/p^2, where BMI is the body mass index (kg/m^2); m - body weight (kg); p - height, elevated in square (m^2).

Studies of IgA levels were determined by flow cytometry, and the patient's blood was taken in the morning on an empty stomach. Reference values: IgA-0.70-4.00 g/l. The level of sIgA was determined by the method of immunoassay analysis. The material for the study was the patient's saliva. The reference values of sIgA are 40-170 μg/mL determined by flow cytometry on Cobas 6000, Roche Diagnostics (Switzerland).

The treatment and prophylaxis complex included in addition to the basic treatment includes bacterial lysate 7.5 mg daily for 28-30 days in combination with inosine pranobex at a dose of 1000 mg three times a day for 3-4 weeks.

A statistical analysis was carried out according to generally accepted methods of variation statistics. Validity was evaluated by Student's t test. Differences were recognized as essential at the significance level of $p \leq 0.05$. The correlation relationship was established using Spearman correlation criterion and Pearson correlation-regression analysis.

All patients signed a voluntary informative consent to participate in the investigation at the beginning of the study.

Results

105 patients with a basic diagnosis of asthma were examined, whose average age was 41.19 ± 1.05 years, of which there were 72 women and 33 men. According to the anthropometric study, 75 patients were found to have EBM or obesity (BMI 31.67 ± 0.53) who were included in the main group and 30 patients with NBMI (BMI 22.13 ± 0.32), which were the comparison group.

In the study, it was found that in the main group, patients with severe 25 (33.33%) and moderate 35 (46.67%) degrees of severity of asthma and mild 15 (20%), predominated, while patients in the comparison group had a milder degree of the course, and only 10 (33.33%) of patients within 30 had a moderate severity of asthma, and 20 (66.67%) patients had a mild BP ($p>0.05$). In the first and second stages of the study, all patients with severe asthma did not control the disease. The patients did not receive systemic steroids.

Patients with EBM or obesity had significantly lower control, namely on an average ACT-test with 12.73 ± 0.31 points. In the distribution of patients according to the severity of the course, we received the following data: with a mild degree of severity of the course 17.65 ± 0.23 points, with a moderate - 13.05 ± 0.17, with a severe - 10.9 ± 0.25 points. Patients with EBM had an average of 17.10 ± 0.34 points (15.33 ± 0.24 points in patients with moderate severity and 19.78 ± 0.37 in patients with mild) ($p \leq 0.001$). It is noted that the AST test correlates with the severity of the course in both groups according to Pierce r = 0.98 and r = 0.98, respectively.

In the study of serum IgA levels, it was noted that the values did not go beyond the reference values, more detailed data is presented in Table 1.

Table 1. Serum IgA level in the examined patients according to the severity of bronchial asthma

Group	Severity of the course	Level of serum IgA g/l
Main	Mild	2.54 ± 0.16**
	Moderate	2.36 ± 0.15
	Severe	1.87 ± 0.15*
Comparison	Mild	2.35 ± 0.16**
	Moderate	2.72 ± 0.48
Control	-	2.00 ± 0.20

Note:*$p_{m\text{-}comparison}<0.05$
**$p_{m\text{-}control}<0.05$
^$p_{comparison\text{-}control}<0.05$

The table above shows that the patients in the main group with a severe course had significantly lower serum IgA values than patients in the comparison group ($p < 0.05$), but the statistically significant difference between this index in the patients with a severe course in the main group and the control group was not revealed.

When calculating the mean values for sIgA in the examined patients, it was found that the mean value in the main group had a large standard deviation, so we conducted an analysis of sIgA for the patients in the main group separately according to the severity of BA (Fig. 1).

Figure 1 shows data indicating that patients with a mild course had a level of sIgA close to the control

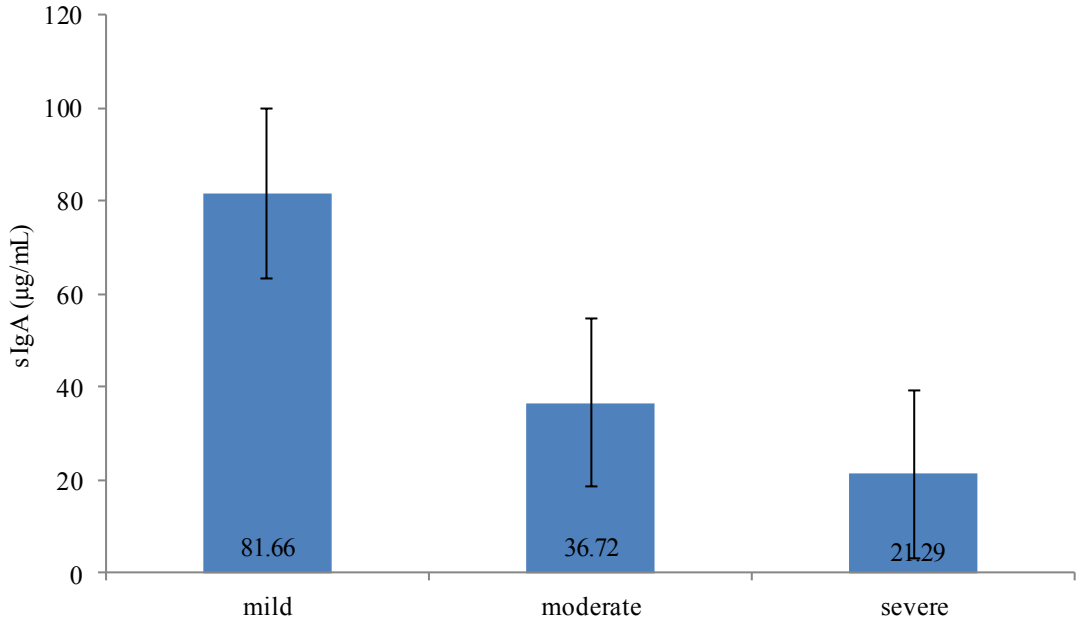

Fig. 1. The level of sIgA in the patients in the main group according to the severity of the course of bronchial asthma

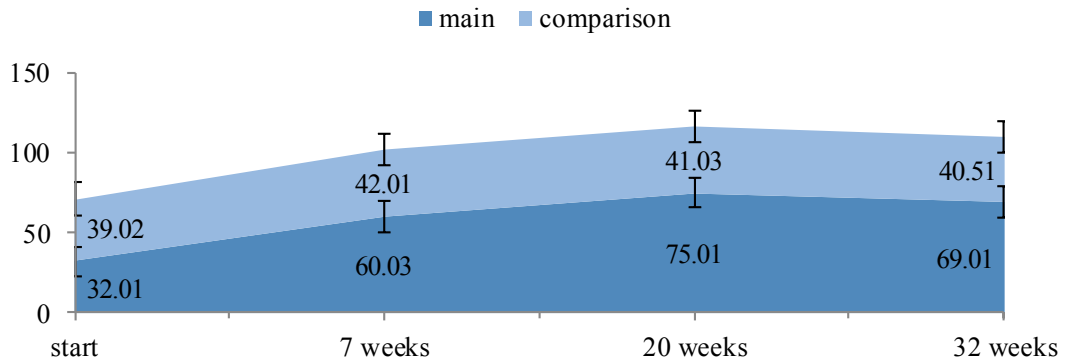

Fig. 2. The level of sIgA in the patients with bronchial asthma in the context of EBM or obesity in the use of the treatment and prevention complex

group, namely 81.66 ± 0.06 µg/mL, in the patients with an moderate severity – 36.72 ± 3.92 µg/mL, and in the patients with a severe course – 21.29 ± 0.01 µg/mL ($p<0.001$; $p<0.001$; $p < 0.001$, respectively). There was established a feedback close correlation relationship between the level of sIgA and the severity of the asthma course under by Spearman $\rho = -1.0$, according to Pearson $r = -0.96$. While analyzing sIgA in the control and comparison group, it was found that in the comparison group, this figure was lower, namely 52.66 ± 1.68 µg/mL versus 83.68 ± 3.68 µg/mL in the control group ($p<0.001$).

Therefore, it is established that the greater BMI, the lower is the level of sIgA, which can be explained by more frequent bacterial and viral infections in this cohort of patients, which further aggravates the course of asthma.

After examination, the second stage included patients from the main group of the first stage, that is, the patients with asthma against the background of EBM or obesity, which were given the proposed treatment.

The level of sIgA for the catamnesis period varied as follows (Fig. 2)

In Figure 2 it is evident that the patients in the main group had a significant increase in the level of sIgA against the background of the use of TPC with the inclusion of a preparation of bacterial lysate in combination with inosine pranobex against the background of training in Asthma school, receiving the basic treatment ($p < 0.05$).

In order to confirm the improvement of asthma control, all patients passed the ACT test before the start of the study and during the follow-up. Average figures in the groups are shown in Fig. 3.

Figure 3 shows that patients in the main group had a significant increase in asthma control, namely 17.98 ± 0.44 versus 12.77 ± 0.46 prior to the use of TPC

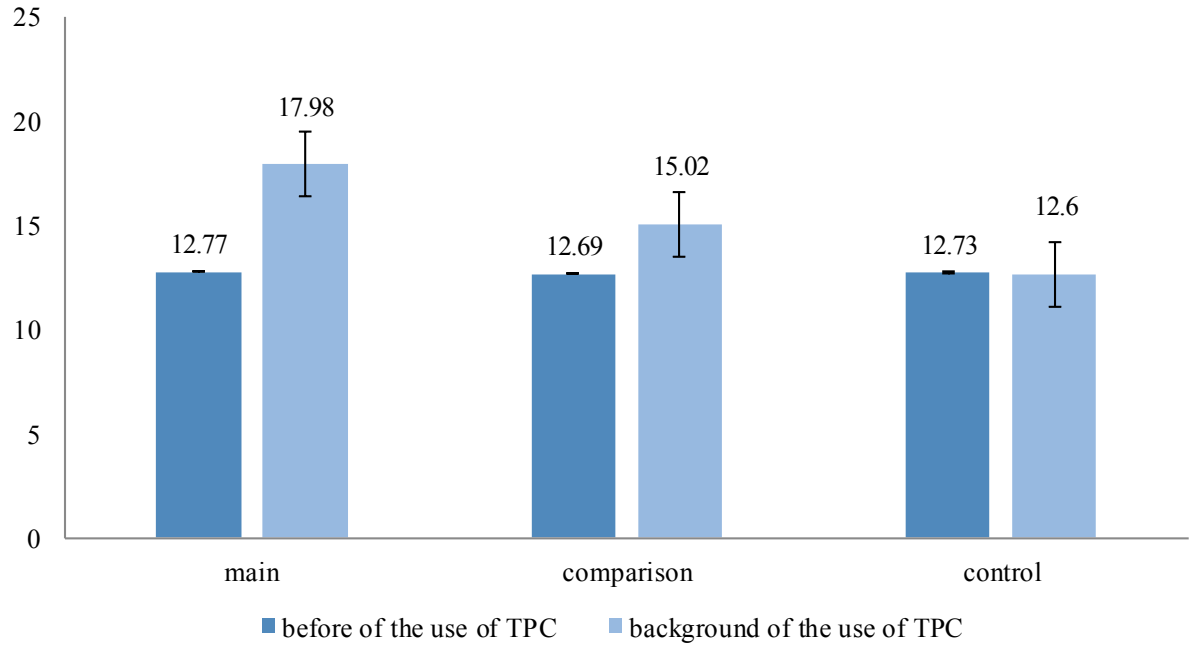

Fig. 3. Average values of the AST test in the patients with bronchial asthma in the presence of excessive body weight or obesity in the process of application of the treatment-and-prophylactic complex

($p < 0.001$). In the comparison group the patients who had undergone training at Asthma School also had improvements in asthma control, namely 15.02 ± 0.39 points versus 12.69 ± 0.56 points prior to training ($p < 0.01$). The patients in the control group who refused TPC and education at Asthma School did not have a statistically significant difference in the follow-up period, namely the pretest study 12.73 ± 0.74 versus 12.60 ± 0.79 points in 32 weeks ($p > 0.05$).

It should be noted that the data in the table corresponds to 20 weeks of the follow-up. During a re-examination on the 32nd weeks of the follow-up, the regression of spirographic parameters was detected in 17% of patients in the main group and in the comparison group.

As a result of the evaluation of the effectiveness of the developed TPC with the inclusion of pharmacological correction against the background of training at Asthma school the patients with asthma with EBM or obesity, it was found that the main group that used the above-mentioned TPC had the best results in improving Asthma control. The positive dynamics of increasing asthma control (RR = 0.38; RRR = 0.62; NNT = 2.12) is more reliable ($p < 0.05$) than in comparison groups (RR = 0.89, RRR = 0.11; NNT = 4.05) in patients with asthma against the background of EBM or obesity, which in turn affected the course of asthma by improving the compliance between the physician and the patient.

Discussion

The patients in the main group with severe asthma have a decreased level of sIgA ($p < 0.001$), which may be a criterion for the more severe course of bronchial asthma in patients with excessive body weight or obesity in the event that asthma control has not been achieved. Together with this, patients in the main group have a direct close correlation between the severity of the course and the level of sIgA ($r = 0.96$).

In analyzing similar studies, we did not find similar works. Woo-Jin Kim et al. in his study of the relationship between serum IgA level and allergy/asthma found a reduced sIgA level in only 12.2% of patients. However, it was not indicated how much body weight this patient population had.[11]

In another study, A. Gonzalez-Quintela et al. showed that obese patients had higher serum IgA levels than normal-weight people ($p = 0.006$) or overweight ($p = 0.005$).[20]

In 2018, Susanna Esposito demonstrated an increase in the production of IgA secretions of the nasopharynx and saliva when prescribing bacterial lysate to children with recurrent respiratory infections, wheezing and asthma.[21]

Bulgakova and co-workers also found that when inosine pranobex was used in children with asthma, humoral immunity returned to normal; while there was an increase in the concentration of IgG, IgA and IgM.[20]

In our study, the patients in the main group had a significant increase in the level of sIgA against the background of the use of TPC with the inclusion of a preparation of bacterial lysate in combination with inosine pranobex against the background of training in Asthma school, receiving the basic treatment ($p < 0.05$).

The data presented in this paper are intermediate and need further investigation.

Conclusion

Bronchial asthma is a widespread disease that often has confounding comorbidity as excessive body weight or obesity. Moreover, patients with asthma who have large BMI have a more severe course of bronchial asthma.

Correlation relationship was established in the group of patients with bronchial asthma and excessive body weight or obesity between the level of sIgA and the severity of the BA course; there is a direct strong Spearmen $\rho = 1.0$, and Pierce $r = 0.96$. Furthermore, patients in the main group had a significant increase in the level of sIgA against the background of the use of TPC with the addition of a basic treatment by the preparation of bacterial lysate together with inosine pranobex. The main group that used the above-mentioned TPC had the best results in improving asthma control.

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