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Effectiveness of the therapeutic-prophylactic complex in patients with bronchial asthma against the background of excessive body weight or obesity

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Abstract

Nowadays bronchial asthma (BA) is one of the leading problems along with cardiovascular and infectious diseases. The GINA edition of 2017 states that non-rational use of BASD drugs is a risk factor for acute asthma, and their excessive use is a risk factor for premature death from the disease itself. We examined 75 patients with a diagnosis of asthma. By the study design, all patients had EBW or obesity and the mean body mass index (BMI) in the examined patients was 31.76 kg / $m^{2.}$ the patients in the main group on an average lowered the body weight by 4.5 kg, and BMI from 32.00 kg / m^2 changed by 29.7 kg / m^2 ($p<0.05$). We observed a significant decrease in the T- and B-lymphocyte and CIC in patients of the main group ($p<0.05$), however, 32 weeks after the use of TPC, it was noted that the immunograms returned to the baseline. patients in the main group had significantly better control of asthma than patients in the comparison and control groups ($p<0.05$). Also, attention should be attracted to the fact that the given figure shows average values for all severity courses of BA, that is, the group includes patients with mild to moderate and severe course of asthma. Thus, we found that 78% of patients in the main group with mild asthma got control of the disease during treatment and kept it for 32 weeks. After 32 weeks of the follow-up, the patients began to notice a decrease in asthma control, which was reflected in the results of the AST test, so in our opinion, it is rational to use the drug for 6 to 9 months. The patients with

asthma against the background of EBW or obesity have alternative ways to solve the problem of asthma control, namely, studying in asthma school against the background of pharmacological correction drugs bacterial lysate and inosine promobas (RRR = 0.75, NNT = 2.12).

Key words: bronchial asthma, excessive body weight, obesity, therapeutic-prophylactic complex, pharmacological correction, Asthma school.

Urgency of the study. Nowadays bronchial asthma (BA) is one of the leading problems along with cardiovascular and infectious diseases. According to WHO, released in December 2016, 383,000 deaths due to asthma were recorded in 2015. Despite the large number of studies and introduction of the newest methods of treatment, asthma control does not reach half of the patients with asthma [1].

According to the Ministry of Health of Ukraine, about 210 thousand patients with bronchial asthma are registered in the country in 2015 [2]. However, as estimated by the experts, official statistics data are much lower and do not reflect the actual picture. Also attention is called to the treatment of patients, despite reimbursing and implementing the "Available drugs" program, 70-75% of patients do not receive baseline therapy, but the use of ambulatory drugs in the form of β-2 agonists of short duration (BASD) increased [3, 4]

The GINA edition of 2017 states that non-rational use of BASD drugs is a risk factor for acute asthma, and their excessive use is a risk factor for premature death from the disease itself [5]. Similar data were presented in the report of the Royal College of Physicians, which was conducted among patients with asthma [6]. Thus, it was found that 39% of patients who used drugs to reduce symptoms, received 12 inhalers (BASD) at the time of death, and 4% of patients received more than 50 BASD inhalers per year.

Not the last place in the modern practice of family physician is comorbidity. Cardiovascular diseases such as arterial hypertension, ischemic heart disease, gastro-pathology, gastroesophagal-reflux disease and others can be attributed to pathologies that can complicate asthma. However, in today's world of hypodynamism and urbanization the first place is taken by obesity or excessive body weight (EBW). In support of this, the Global Association for Allergy and Asthma conducted a study among populations of 8 European countries in 2014, in which it has been verified that BA and obesity or EBW are pathologies that complicate each other and their pathogenesis is interconnected [5, 7] One more proof of this is that GINA has allocated BA against the background of EBW or obesity as a separate phenotype for several consecutive years.

The purpose of our study was to determine the effectiveness of the application of the developed therapeutic-prophylactic complex in patients with bronchial asthma against the background of overweight or obesity.

Materials and methods. We examined 75 patients (44 women and 31 men whose average age was 43.8 ± 1.14 years) who were treated on the basis of the Department of Family Medicine and General Practice of Odessa National Medical University with a diagnosis of asthma. The diagnosis was established in accordance with international approval documents. The studies were conducted according to inclusion / exclusion criteria. By the study design, all patients had EBW or obesity and the mean body mass index (BMI) in the examined patients was 31.76 kg / m^2. The distribution of patients into groups was carried out by simple randomization with elements of stratification. The main group included 30 patients with asthma against the background of EBW or obesity, which received additional therapeutic - prophylactic complex (TPC) in the baseline treatment, namely pharmacological correction, along with training in Asthma school; the comparison group included 30 patients with asthma with EBW or obesity on the back that were undergoing training in the Asthma school and 15 patients with asthma against the background of EBW or obesity formed a control group who refused to use the developed TPC.

The patients were asked to undergo a comprehensive examination, which included: anamnesis, routine physical examination, AST test, anthropometry, and the study of the component body composition using bioimpedansometry. To evaluate the function of external respiration, our study took into account one of the most common indices, namely FEV1 - the amount of forced exhalation per a second; indices of the cellular immunity of T-lymphocytes (CD3 +, CD19-), B-lymphocytes (CD3-, CD19 +) and circulating medium-caliber immune cells. The immunoglobulin study was carried out using the immunoturbidimetry method from the venous blood of patients, which was collected on an empty stomach from 8 to 10 a.m.

The therapeutic-prophylactic complex (TPC) developed by us included training under the conditions of the Asthma School and pharmacological correction against the background of the application of the generally accepted basic step-by-step therapy.

The Asthma School program included: a cycle of theoretical and practical classes where the patients receive theoretical and practical skills in diet therapy, respiratory gymnastics and physical education against the background of standard basic therapy. The developed program of classes includes 5 group and 9 individual classes.

Since in case of AD there are disturbances of a number of immunity indices, even more profound inhibition of the immune response may occur under the influence of an

infectious agent, caused by both exo- and endotoxins, which are released due to bacteriolysis. In this case, immunostimulation increased with the elevation in the number of pathogens, is opposed by immunosuppression. Along with the risk of recurrence, the likelihood of a transition from an acute form to a chronic one increases. In this regard, it seems quite appropriate to make immunostimulation by bacterial antigens deprived of the immunosuppressive component. Traditional therapy does not permit to eliminate the persistence of bacterial agents. Therefore, in our opinion, a drug that may have immunostimulating properties is bacterial lysate. In domestic and foreign publications there is evidence that the use of bacterial lysates it is bronchommunal in Ukraine and OM-85 abroad, has a positive dynamics in the course of asthma to improve the control of asthma [12, 14, 15].

In 2007, experts of the European Respiratory Society published a major review devoted to the mechanisms of asthma-induced virus, which contained references to 162 scientific publications. It should be admitted that the leading scientists failed to come to the exact conclusion about what were the main mechanisms of asthma exacerbations in viral infections - evidences proving such causation were weak, and the mechanisms were poorly understood. Scientists distinguish the most significant factors in these processes: genetic features, disturbance of the congenital and adaptive immune systems in response to viral infection [16].

Taking into account the above, the pharmacological correction proposed by us consisted in the use of the preparation of bacterial lysate daily in a dose of 7.5 mg for 28-30 days in combination with inosin preparations of pronebex in the dose of 1000 mg three times a day for 3-4 weeks, 2 courses every 9-12 months

Statistical analysis was carried out according to generally accepted methods of variation statistics. Validity was evaluated by the t criterion of the Student. Differences were recognized as significant at the significance level of $p \leq 0.05$. The correlation connection was established using the Spirman and Pearson correlation coefficients. The effectiveness of prevention and treatment by the developed program was analyzed according to indices: relative risk reduction (RRR), the number of patients neeled to be treated (NNT).

Results. Today, the concept of "integrative medical care", which includes patient-oriented care based on traditional and complementary therapy [11], is becoming increasingly relevant in the world.

When analyzing the data obtained from all patients, we found that 52% (n = 39) of the patients did not follow the technique of using devices, 67% (n = 50) independently broke the regimen and dosage of the baseline and additional therapy of asthma. The patients have

harmful smoking habits, and 15% of them do not know that smoking complicates the course of asthma.

It has been found that the patients included in our study had an uncontrolled course of asthma, but 53 patients (70.6%) believed that they controlled the course of asthma. The patients with asthma received drugs of the first aid without control, but did not take baseline therapy in 2/3 of cases, that is approximately 50 patients of the total.

When taking anamnesis, it was found that 38 patients (28.5%) took oral or injection corticosteroids for a year. Similar data were obtained by Price D., Fletcher M. and van der Molen T. in their study, which included 8,000 Europeans with BA [12].

In our study, all patients had EBW or obesity. It should be noted that the patients included in our study were well-informed in the methods for weight loss and lacked motivation. 61 (81.3%) patients were diagnosed with disorder in a stereotype of nutrition. A significant number of the patients examined in the main group used to eat only twice a day. Also, it was found that most patients eat a dry food and do not use enough fruit and vegetables and do not have balanced nutrition at all.

However, 88% (n = 66) of the patients noted that following the course of the lecture sessions, understanding of the problems of asthma, their treatment and control improved, and in turn, inclination to therapy and compliance with the doctor improved too.

Also, the patients in the main group on an average lowered the body weight by 4.5 kg, and BMI from 32.00 kg / m^2 changed by 29.7 kg / m^2 ($p<0.05$). The patients in the comparison group also had a positive result, namely, during the follow-up period, the patients lowered BMI from 31.88 kg / m^2 to 29.8 kg / m^2 ($p>0.05$), the patients in the control group did not have a change in BMI and even a small number of the patients (14%) increased body weight for 32 weeks of the follow-up. Details of the BMI and body composition are given in Table 1.

Table 1

Indices of the body mass index and body component in patients with bronchial asthma against the background of overweight or obesity

Index	Catamnesis stage	Main	Comparison	Control
IMT kg/м^2	Before	32.00±0.85	31.88±0.87	31.39±1.25
	After	29.7±0.74*	29.8±0.73	31.41±1.27
% fat	Before	38.68±1.40	39.2±1.30	38.91±1.77
	After	36.51±1.26	36.59±1.28	39.00±1.76
Visceral fat	Before	12.33±0.76	11.93±0.83	12.16±0.90
	After	11.50±0.57	11.53±0.71	12.26±0.90

Note: * $p_{\text{before-after}} <0.05$

The table 1 shows that patients in the main group and the comparison group showed a more dynamic movement towards body weight loss together with BMI and reduction of the visceral fat compared with the control group. The patients in the main group, on an average, reduced body weight by 4.5 kg, and BMI from 32.00 kg / m^2 changed by 29.7 kg / m^2 ($p<0.05$). The patients in the comparison group also had a positive result, namely, during the follow-up period, the patients lowered BMI from 31.32 kg / m^2 to 29.8 kg / m^2 ($p>0.05$), the patients in the control group did not have a change in BMI and even a small number of the patients (14%) increased body weight for 6 months of the follow-up. It is necessary to note the positive dynamics in reducing the body fat and visceral fat, although they were not probative ($p>0.05$).

It is well-known that controlled physical activity has a positive effect on the course of asthma. Our patients were aware of this, but did not keep to this postulate. According to the pedometer, at the beginning of our study, most patients walked at most 2,000 steps a day. When walking, attention should be paid to prolonged exhalation, which should be 1.5-2 times longer than breath, and gradually increase the distance. Starting from the usual walking mode, 3,000 steps per day gradually increase the load (500-1000 steps per week) to 8-10 thousand steps a day.

Table 2

The number of steps per day in the dynamics of the follow-up of the patients with bronchial asthma against the background of overweight or obesity

Groups	At the beginning	32 weeks of follow-up
Main	1800±0.17	7600±0.22*
Comparison	1930±0.16	5900±0.21*

Note: * $p_{\text{before-after}} <0.05$

The table 2 shows the positive dynamics and increase in physical activity in the patients of the main group and of the comparison group but it was noted that the patients in the comparison group walked fewer steps per day than the patients in the main group, which was associated with deterioration of the well-being, therefore, we had chosen tactics of maintenance the results obtained, rather than their increase due to the deterioration of patients' well-being.

To evaluate the effectiveness of the proposed TPC, we evaluated the following immunity indices:

Table 3

Some immunity indices in patients with bronchial asthma against the background of overweight or obesity

Index	Catamnesis stage	Main	Comparison
CIC of medium calibre	Beginning	91.13±1.77	89.46±1.86
	7 weeks	83.86±1.71*	87.29±1.93
	20 weeks	77.36±1.96*	88.25±2.29
	32 weeks	84.43±1.82*	88.33±2.10
T-lymphocytes (CD3+/ CD 19-)	Beginning	77.24±0.72	77.60±0.63
	7 weeks	73.61±0.58	78.15±0.64
	20 weeks	70.36±0,69*	78.09±0.67
	32 weeks	73.54±0.64*	78.32±0.66
B-lymphocytes (CD3-/ CD 19+)	Beginning	12.57±0.82	12.99±0.79
	7 weeks	11.49±0.53	12.87±0.86
	20 weeks	10.19±0.52*	13.36±0.96
	32 weeks	11.0±0.56	13.08±1.01

Note: * $p_{\text{before-after}} < 0.05$

During the follow-up period, we observed a significant decrease in the T- and B-lymphocyte and CIC in patients of the main group ($p<0.05$), however, 32 weeks after the use of TPC, it was noted that the immunograms returned to the baseline. We found that the patients in the main group who received pharmacological correction, along with asthma school education, had positive changes in immunogram indices, which in turn affected the course of asthma. Such conclusions can be made according to the AST test in the examined patients (Fig. 2).

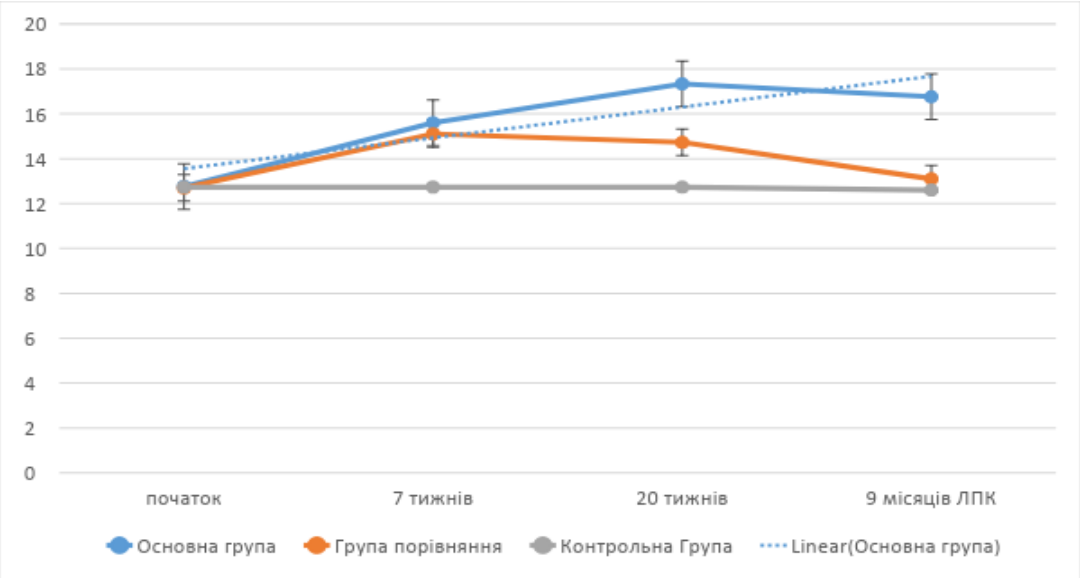

Fig.1 Results of the AST test in the examined patients at different stages of the study.

As shown in the figure, patients in the main group had significantly better control of asthma than patients in the comparison and control groups ($p<0.05$). Also, attention should be attracted to the fact that the given figure shows average values for all severity courses of BA, that is, the group includes patients with mild to moderate and severe course of asthma. Thus, we found that 78% of patients in the main group with mild asthma got control of the disease during treatment and kept it for 32 weeks. After 32 weeks of the follow-up, the patients began to notice a decrease in asthma control, which was reflected in the results of the AST test, so in our opinion, it is rational to use the drug for 6 to 9 months.

Also, spirography is one of the main criteria for diagnosis and control of treatment in patients with pulmonary profile.

We found that the patients in the main group received a significant increase in the indices of forced exhalation per the first second during treatment, and 20 weeks after the beginning of the study, they achieved results ($p<0.05$) corresponding to the mild course of asthma, that is, the patients achieved improvement in the course of asthma. The comparison group also noted positive dynamics, but not the same as the patients in the main group, and after 32 weeks from the beginning of the study, they obtained the same results as at the beginning of the investigation.

The patients with a severe course that only were trained at Asthma School did not achieve the desired results, but had a statistically significant difference in FEV_1 ($p<0.05$). In the main group, we had a more positive dynamics ($p<0.05$), however, 32 weeks after the beginning of the study there was a recurrence in the values of the spirograph, which again indicated that the proposed TPC should be repeated in certain patients.

Thus, there were obtained data that the patients with AD against the background of EBW or obesity have decreased physical activity, which in turn was a vicious circle, which included reduced physical activity, inadequate asthma control, and complicated asthma. The patients included in our study had inadequate compliance and inclination to therapy and used first aid drugs inappropriately, namely β-2 agonists of short duration. It has been found that patients with asthma against the background of EBW or obesity have disturbances of immunological reactivity, namely an elevated level of subpopulation of the T- and B-lymphocytes and circulating immune complexes. To handle this situation, we have proposed alternative ways to solve the asthma control problem in the course of asthma, namely, pharmacological correction and training at Asthma School.

Conclusions:

1) The problem of bronchial asthma is widespread in the world and in Ukraine, however, the lack of awareness of patients in the control and treatment of bronchial asthma does not allow the patient to have a controlled course and have adequate compliance with the attending physician.

2) Controlled dose-based walking is an assistant for improving asthma control in the patients with a different course of bronchial asthma, namely, increasing physical activity in the form of controlled dose-based walking significantly affects the patient's well-being and the course of asthma.

3) The patients from the main group who were trained at Asthma School, against the background of pharmacological correction with bacterial lysate and inosin promobex, had positive changes in immunohistochemistry and AST tests maintained for 32 weeks of the follow-up ($p<0.05$), and the comparison patients who received only baseline therapy and Asthma education had less positive results that they sustained for 20 weeks ($p>0.05$).

4) The patients with asthma against the background of EBW or obesity have alternative ways to solve the problem of asthma control, namely, studying in asthma school against the background of pharmacological correction drugs bacterial lysate and inosine promobas (RRR = 0.75, NNT = 2.12).

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