RESEARCH ARTICLE

Alternative Ways to Improve Asthma Control in Obese Patients

Daria Lahoda[*1]

[1]Doctor of Philosophy in Medicine (PhD), Assistant Professor of the Department of Family Medicine and Polyclinic Therapy, Odesa National Medical University, ave. 2 Valikhovskyi St., Odesa, Ukraine 65000, 0966419743

* dlagoda19@gmail.com

ABSTRACT

Diseases of the respiratory tract occupy one of the leading places among pathologies in people of working age in the world. According to the data of world studies, it can be considered that these two comorbidities are mutually aggravating, but scientists do not have a unanimous opinion about whether this is a simple coincidence or whether these pathologies are pathogenetically related. There is considerable evidence that asthma patients do not achieve adequate asthma control worldwide. Yes, according to Maria Sandra Magnoni et al. 77.8% of patients with asthma have an uncontrolled course of asthma, although 68.4% of them believe that they have sufficient asthma control, and their treatment does not require correction. Therefore, taking into account all of the above and taking into account the low level of asthma control in patients with comorbid pathology who often suffer from bacterial and viral diseases, we believe that a more detailed study of the immunological status of these individuals is necessary in order to optimize treatment and prevention measures. Aim: to investigate the effectiveness of alternative ways of asthma control in patients with bronchial asthma against the background of overweight or obesity. Materials and methods. At the I stage, 255 patients with BA were examined. According to the study design, patients were selected according to the "inclusion/exclusion" criteria at this stage. The study was randomized. Allocation of patients into groups was carried out by the method of simple randomization with elements of stratification. Groups are statistically significant. Statistical processing of the results was carried out using parametric and non-parametric analysis methods. Resalts. Overweight or obese patients had a more severe course of bronchial asthma than patients with a normal body mass index. Overweight or obese patients were found to have higher levels of systemic inflammation, namely eosinophilic cationic protein levels and erythrocyte sedimentation rate, than patients with a normal body mass index. In addition, a close direct correlation was established between the severity of the course of bronchial asthma and indicators of eosinophil cationic protein ($r=0.97$; $p<0.001$). After pharmacological correction, there was an increase in asthma control in patients with different severity of the course ($p<0.001$; $p<0.001$; $p<0.001$, respectively), a decrease in the frequency of exacerbations ($p<0.05$), a reduction in the number of hospitalizations ($p<0, 05$) and the number of acute respiratory diseases ($p<0.05$) in patients with bronchial asthma against the background of excess body weight or obesity. The use of the developed treatment-prophylactic complex using the drug bacterial lysate and inosine pranobex together with training in the Asthma School and standard treatment contributes to increasing asthma control and compliance with the doctor, reducing the number of exacerbations and hospitalizations per year in patients with bronchial asthma against the background overweight or obesity.

Background

Diseases of the respiratory tract occupy one of the leading places among pathologies in people of working age in the world. Along with this, it was established that the most widespread and threatening disease among pulmonary pathologies is bronchial asthma[1]. According to the World Health Organization, 235 million people worldwide suffer from asthma. Asthma is a public health problem not only in high-income countries, it occurs in all countries regardless of the level of economic development. More than 80% of asthma deaths occur in low- and middle-income countries[2,3]. Studies on the prevalence of asthma have shown a tendency to increase the proportion of people with excess body weight (overweight) or obesity in the population among these patients[4,5,6].

According to the data of world studies, it can be considered that these two comorbidities are mutually aggravating, but scientists do not have a unanimous opinion about whether this is a simple coincidence or whether these pathologies are pathogenetically related[4,6,7]. Recent studies by Dixon A. et al. and Sideleva O. et al. showed that at least two different phenotypes are observed in patients with bronchial asthma against the background of hyperthyroidism or obesity, namely allergic asthma and so-called late onset asthma, which can be translated as "late onset asthma", which is more severe and has fatal consequences[8,9].

On the other hand, bacterial and viral infections are also an aggravating factor in the course of bronchial asthma, which, in turn, is manifested by the body's inability to resist infections that cause an exacerbation of bronchial asthma. Such a mechanism is triggered again and again, which aggravates the course and makes the disease less controlled[10,11,12,13,14].

There is considerable evidence that asthma patients do not achieve adequate asthma control worldwide[15,16,17]. Yes, according to Maria Sandra Magnoni et al. 77.8% of patients with asthma have an uncontrolled course of asthma, although 68.4% of them believe that they have sufficient asthma control, and their treatment does not require correction[18].

There are also data that do not indicate that lower asthma control and insufficient response to conventional therapy are precisely comorbid patients with hyperlipidemia or obesity. In a meta-analysis by Shannon Novosad (2013), data from at least 7 studies including 9,557 patients from different populations were provided, and the aggravating effect of overweight or obesity on the course of bronchial asthma was confirmed[19].

Taking into account insufficient asthma control in patients with comorbid pathology, namely with hyperthyroidism or obesity and frequent bacterial and viral infections, the initial need is to improve treatment and prevention measures.

Therefore, to solve this issue, it is advisable to use integrated medical supervision and drugs with immunomodulating properties, namely bacterial lysate and inosine pranobex in such patients. In his research, V. A. Bulgakov together with co-authors. proved the effectiveness of the use of inosine pranobex in children with asthma who often suffer from bacterial and viral infections[20]. Also, positive dynamics in achieving asthma control were obtained with the use of bacterial lysate preparations in children and adult populations and in other studies[21,22].

Today, patient-centered therapy, which is based on traditional or basic and complementary therapy, is gaining more and more relevance in the world. In our opinion, patients with bronchial asthma on the background of hyperthyroidism or obesity and often suffering from bacterial and viral infections need individualized medical care in case of insufficient control of the course of bronchial asthma.

Therefore, taking into account all of the above and taking into account the low level of asthma control in patients with comorbid pathology who often suffer from bacterial and viral diseases, we believe that a more detailed study of the immunological status of these individuals is necessary in order to optimize treatment and prevention measures.

Aim

To investigate the effectiveness of alternative ways of asthma control in patients with bronchial asthma against the background of overweight or obesity.

Materials and methods

At the I stage, 255 patients with BA were examined. According to the study design, patients were selected according to the "inclusion/exclusion" criteria at this stage.

Inclusion: consent to participate in the study, patients aged 18–60 years, hyperthyroidism or obesity, persistent AD of various degrees of severity.

Exclusions: refusal to participate in the study, presence of acute infection, acute somatic pathology and decompensation of any somatic concomitant pathology, endocrinological obesity, metabolic syndrome, oncological pathology, mental disorders, COPD, BA in the acute stage.

For comparative characteristics of some indicators, a control group of 20 healthy individuals was also formed.

The study was randomized. Allocation of patients into groups was carried out by the method of simple randomization with elements of stratification. Groups are statistically significant.

For prospective cohort research tasks, the work consisted of two stages: "Patients with BA against the background of overweight (OW) or obesity", which included 175 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 55 patients. A control group included 20 somatically persons with NBMI to determine reference values of some indices. At the 2nd stage of the study, a treatment-and-prevention complex (TPC) was administered to the main cohort group of the 1st stage, which was divided into the main group – 60 patients, the comparison group – 60 patients, control group – 55 patients that refused the proposed TPC.

At the 2nd stage of the clinical study there were used drugs of bacterial lysate, inosine pranobex during training at the Asthma School, which included recommendations for diet therapy, respiratory exercises and physical activities. Inclusion / Exclusion criteria for the 1st and 2nd stage respectively included – Inclusion: approval for the participation in the study, patients aged 18–60 with OW or obesity, persisting BA. Exclusion: refusal to participate in the study, the presence of acute infection, acute pathology and decompensation of any somatic concomitant pathology, endocrinological obesity, metabolic syndrome, oncologic pathology, mental disorders, COPD.

Clinical examination involves assessment of risk factors, analysis of complaints, medical history data, objective examination according to generally accepted methods, anthropometric measurement. A detailed study of the clinical and anamnestic features of the course of BA against the background of hyperthyroidism or obesity was carried out using a questionnaire method. Questionnaires were used to determine the subjective state of health and find out the characteristics of the lifestyle (nature of nutrition, level of physical activity, etc.).

Clinical examination included general clinical studies (full blood count), biochemical analysis (glycemia on an empty stomach, total cholesterol level, triglycerides, high density lipoprotein (HDL), low density lipoprotein (LDL), index of atherogenesis), liver function tests (AST, ALT), uric acid. To determine the level of the systemic inflammation there were checked the level of ECP, ESR, the level of C-reactive protein; in addition, the study of some immune indices was made, namely IgA, IgM, IgG, IgE, CD14, secretory IgA (sIgA), T-lymphocytes (CD3 +, CD19-), T-helper / T-inductors (CD4 +, CD8-), T-suppressors of the cytotoxic cells (CD4-, CD8+), NK-cells (CD3-, CD56+), cytotoxic cells (CD3+, CD56+), B-lymphocytes (CD3-, CD19 +).

Most laboratory methods of research were carried out by the method of flow immunoturbidimetry

Also, we digged in the anthropometric indices (mass, height, BMI), including the component composition of the body by the method of impedance measurement, namely, the percentage of fat and body weight. To estimate the proportion of fat and muscle mass, the method of bioelectrical impedance (BEI) was used, which was also performed on an OMRON BF 51 impedance scale (Japan).

To increase the accuracy of the measurement, it should be performed on the patient before eating and more than 1 hour after liquid intake, in a state of rest. The patient, standing on the impedance scale with bare feet on the electrode, holds the second electrode with his hands. The measurements take place as follows: a weak electric current with a frequency of 50 kHz and a strength of less than 500 μA, which cannot be felt, passes through the human body and measures the electrical conductivity of the tissues of the body, which is then converted into indicators of tissue impedance, that is, it shows the composition of the body: fat mass, m' ulcer mass and basic metabolism at rest.

Cases of increased BMI due to muscle mass, as well as cases of excessive visceral fat mass with normal BMI, were excluded.

To determine the function of external respiration, we determined the priority indices, such as the volume of forced exhalation for the first second (FEV_1), vital capacity of the lungs (VC), forced vital capacity of the lungs (FVC), and peak expiratory air velocity (PEF).

Dispersion, correlation, regression, and discriminant methods of analysis were used in the study. Statistical data processing was carried out using a software package.

Statistical processing of the results was carried out using parametric and non-parametric analysis methods. Descriptive (descriptive) characteristics for indicators measured on a quantitative scale were given by the median and mean value (position indicators). In the comparative analysis of independent groups, the

student's test was used for unpaired samples (with the conditions of homoscedasticity and normal data distribution) and the Mann-Whitney test (for heteroscedastic data with a different type of distribution).

The relationship between traits was studied using correlation analysis using the Spearman (r) method, and Pearson's χ^2 test was used to assess the relationship between qualitative and quantitative traits.

The study of the influence of risk factors was carried out by the method of factor analysis with the determination of the main components. To assess the diagnostic significance of the applied research methods, standard operating characteristics were calculated: sensitivity, specificity, predictiveness of positive and negative results, diagnostic accuracy.

The effectiveness of prevention and treatment according to the developed program was analyzed according to the indicators: relative risk (RR; relative risk), relative risk reduction (RRR – relative risk reduction), number of patients in need of treatment (NNT – number needed to be treated).

The research results were processed using licensed MS Excel 2018 software products.

Results

According to the anthropometric examination of 255 patients with BA (98 men and 157 women) it was revealed that 175 (71.42%) patients had OW or obesity (BMI (31.67±0.53) kg/m²) that were from the main group, and 55 (28.57%) patients had OW (BMI (22.67±0.33) kg/m²) who made the comparison group. The patients in the control group had an average BMI of (22.33±0.32) kg/m². The patients had varying severity of persistent asthma (table. 1).

Table 1: Anthropometric indicators and indicators of the component composition of the body of the examined patients

group	BMI, kg/m2	Body fat mass, %	Muscle mass of the body, %	Visceral fat
Main	30.91±0.51*, **	39.42±1.21*, **	28.73±1.53*, **	12.45±0.85*, **
comparison	22.84±0.63	28.43±1.13	28.31±1.74	5.46±1.15
control	21.98±0.42	25.94±1.63	31.73±1.84	5.70±0.83

Notes:
1.* – $p_{m-com}<0.001$;
2.** – $p_{m-con}<0.001$;
3.^ – $p_{com-con}<0.001$.

During the study, it was found that in the main group the patients with severe course of BA – 58 (33.14%), moderate 82 (46.29%) and mild form – 35 (20.00%) persons prevailed, while the patients in the comparison group had a milder course and only 18 (32.72%) patients out of 30 had a moderate course of BA and 37 (67.27%) had a mild course of BA (p<0.05).
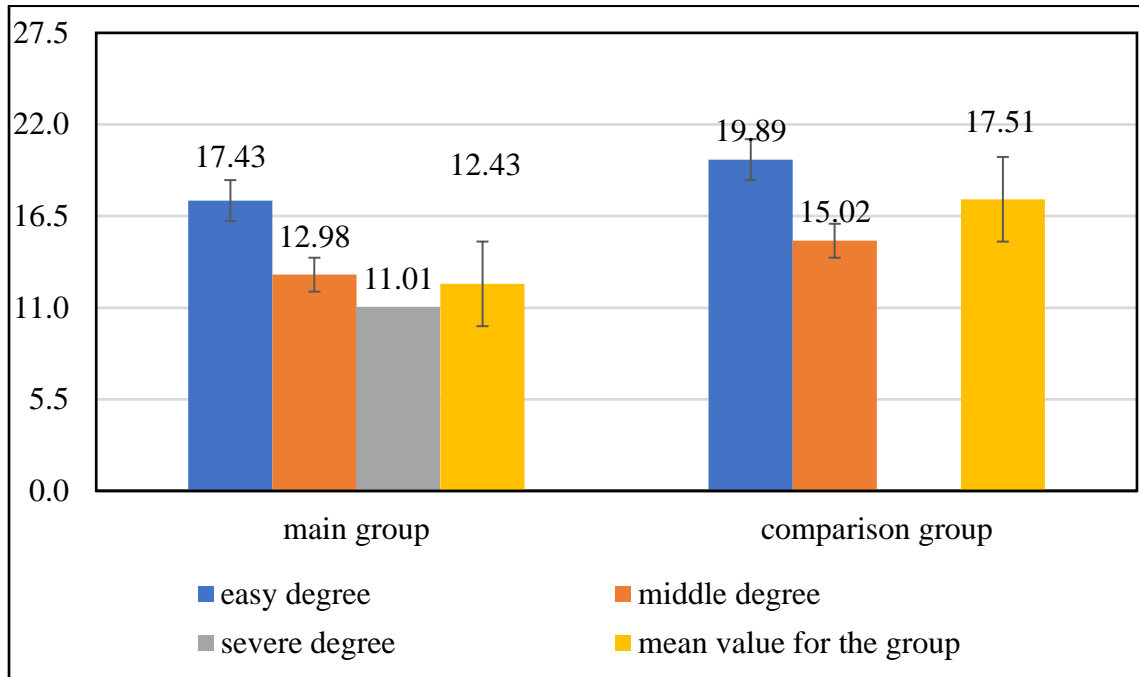
Fig. 1 Assessment of asthma control in patients of the examined groups

A correlation analysis revealed a correlation between BMI and the severity of BA, by Pearson (r=0.65), by Spearman (ρ=0.62). Accordingly, the body weight was also significantly higher in the patients of the main group (p<0.001) (fig 2).
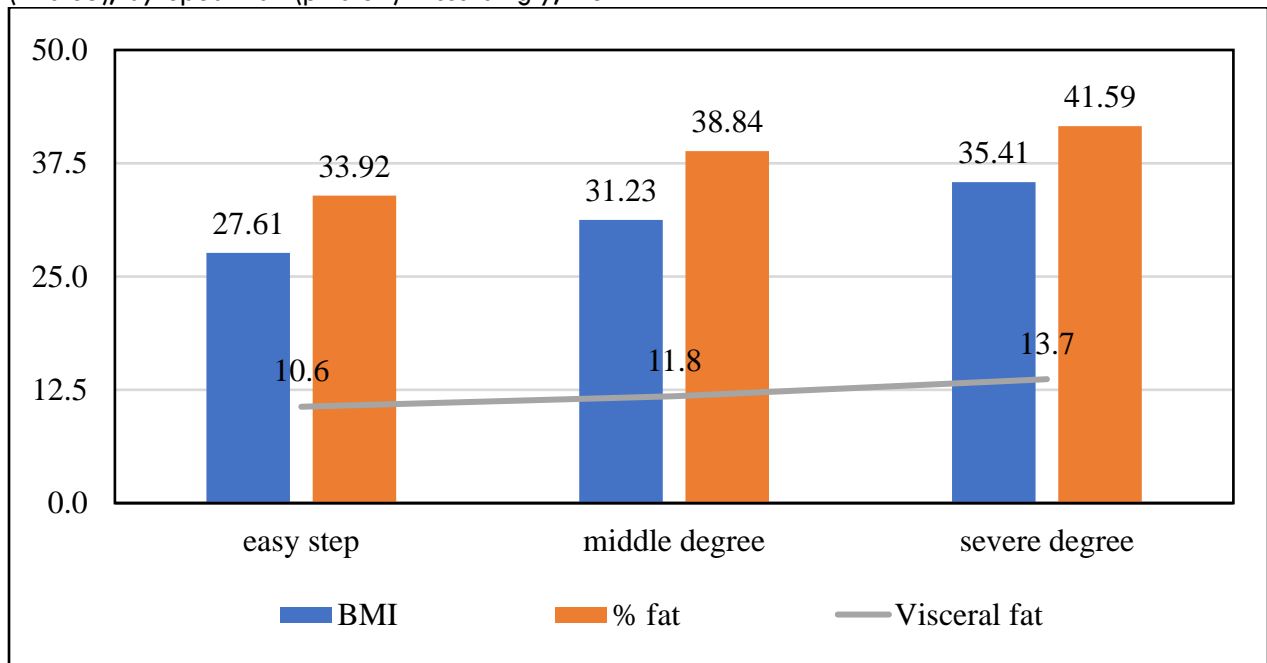
Fig. 2 Correlation between indicators of body mass index, percentage of fat and visceral fat depending on the severity of the course of bronchial asthma in patients of the main group.

When determining the level of systemic inflammation, it was found that patients had a significantly higher level of ECP in the main group, namely (31.72±4.91) ng/ml versus (18.54±2.71 ng/ml in the comparison group and (12.63±1.13) ng/ml in the control group (p<0.001; p<0.001, respectively). However, it was revealed that patients with BA against the background of OW or obesity with a severe course and the highest BMI had a higher level of systemic chronic inflammation, namely, ECP and ESR, and a close direct correlation by Pearson was established (r=0.97) (table. 2).

**Table 2:** Eosinophil cationic protein level and erythrocyte sedimentation rate in patients of the examined groups

Group	ECP level, ng/ml	ESR, mm/year	C-reactive protein, mg/l
Main	**31.72±4.91*	**14.84±0.64*	^^4.61±0.10^
Comparison	18.54±2.71^	12.72±0.97^	3.74±0.16
Control	12.63±1.13	7.42±0.62	3.62±0.19

Примітки:
1. * – p $_{m-com}$<0.001.
2. ** – p $_{m-con}$<0.001.
3. ^ – p $_{com-con}$<0.001.
4. ^ – p$_{m-com}$<0.05.
5. ^^ – p $_{m-con}$<0.05.

When calculating the average levels of sIgA in the examined patients, it was detected that the average value in the main group had a large standard deviation, so we performed sIgA analysis for the patients in the main group separately according to the severity of BA. The patients in the main group with mild course had a level of sIgA close to the control one, namely (82.51±2.25) µg/ml, in the patients with moderate severity course it was (35.92±3.61) µg/ml and in the patients with severe course – (22.58±1.74) µg/ml (p<0.001; p<0.001; p<0.001 respectively). A close reverse correlation was established between the sIgA level and the severity of BA by Spearman ρ=−1.0, and by Pierce r=−0.96. In the sIgA analysis of the control and comparison groups it was found that in the comparison group this index was lower, namely (53.62±1.57) µg/ml versus (82.73±2.97) µg/ml in the control one (p<0.001) (fig. 3).
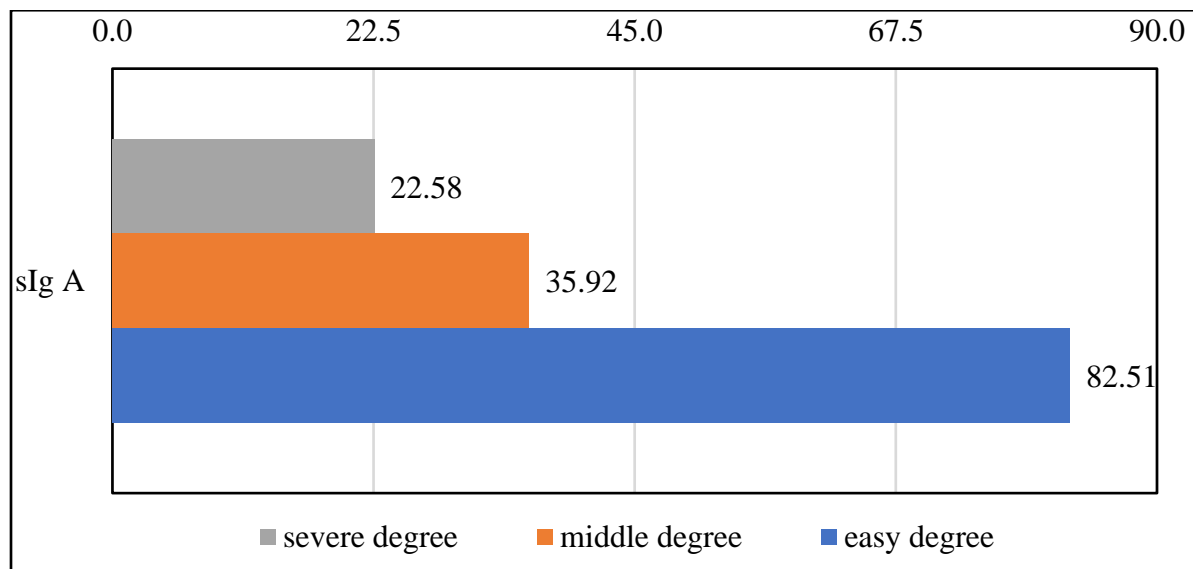
Fig. 3. The level of sIgA in patients of the main group according to the severity of the course of bronchial asthma

Thus, we have found that patients with OW or obesity have a more severe course of BA, changes in the immunity indices, systemic inflammation, which may affect the control of BA. Therefore, according to the design of our study, patients with BA and OW or obesity were included in the 2nd stage of our study.

We have developed and substantiated TPC for patients with BA against the background of OW or obesity, in addition to basic therapy training at

the Asthma school with pharmacological correction with a bacterial lysate in the dose of 7.0 mg for 30 days (according to the instructions) and inosine pranobex by 1000 mg for 30 days. The patients in the comparison group received only the study at the Asthma School in addition to basic treatment.

When evaluating the results of the AST test according to the severity of the course in the main group, we obtained the following data, namely the patients with a mild course improved their score from (15.49±0.26) to (20.63±0.51) points, with a moderate course – from (13.52±0.81) to (17.28±0.38) points, with a severe course – from (11.12±0.27) to (16.53±0.53) points (p<0.001; p<0.001; p<0.001 accordingly) (Fig. 4).
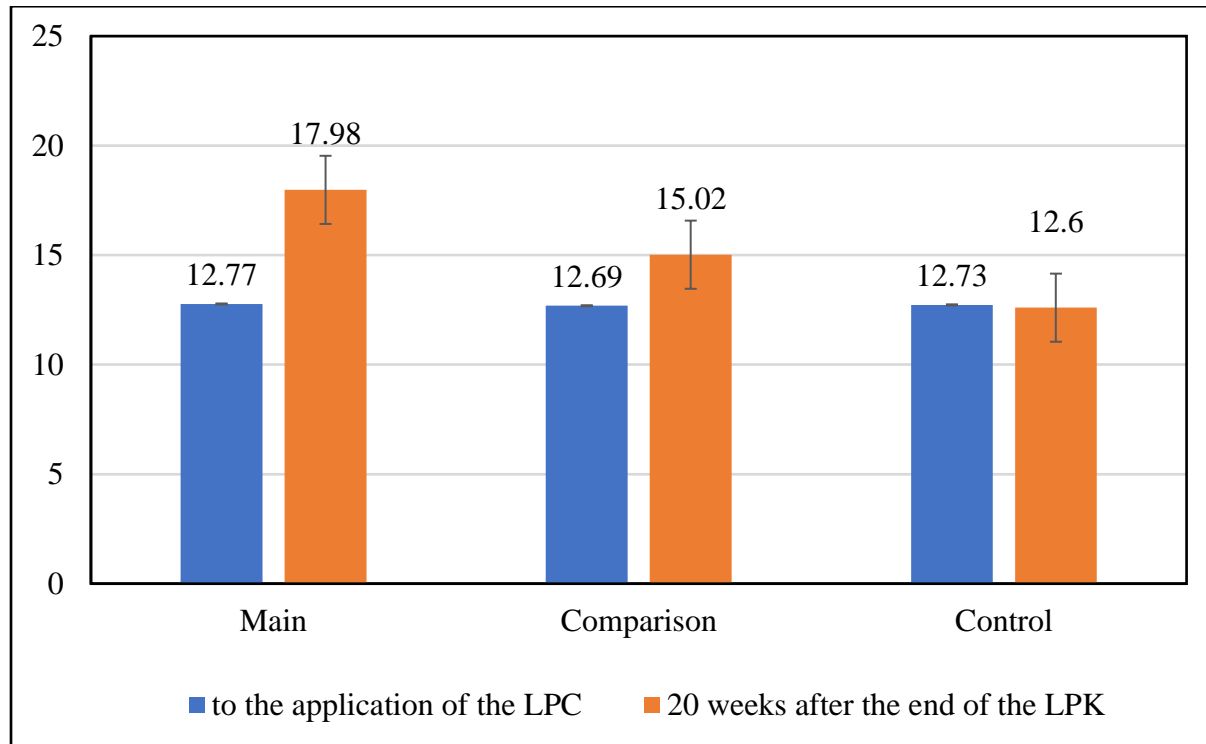
Fig. 4. Average values of the AST test in patients with bronchial asthma against the background of excess body weight or obesity during the use of the therapeutic and preventive complex

The patients of the main group had a significant increase in the level of sIgA against the background of the TPC use with the inclusion of bacterial lysate in combination with inosine pranobex against the background of training at the Asthma school, with receiving the basic treatment (p<0.05) (fig. 5).
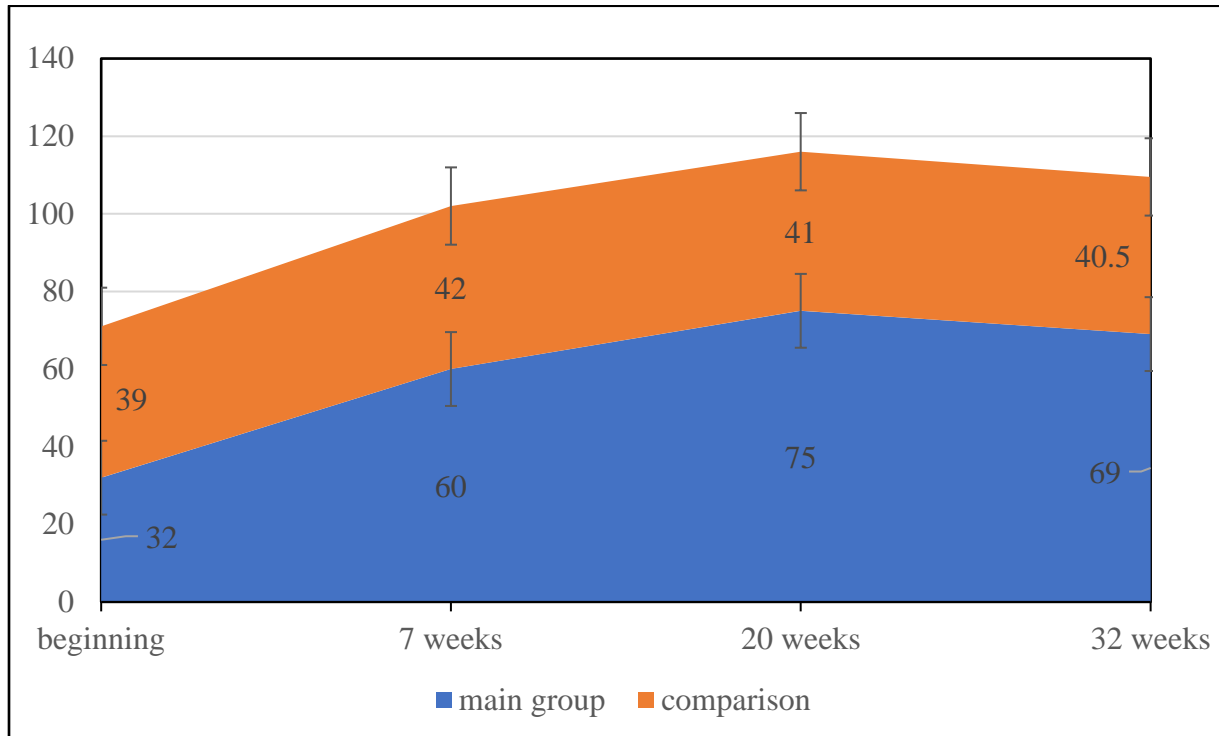
Fig. 5 The level of secretory immunoglobulin A in patients with bronchial asthma against the background of excess body weight or obesity during the use of the therapeutic and preventive complex

Besides, there was a shift in the immunogram indices, namely a reduced level of CD14; CD4-, CD8+; CD3+, CD56+ and elevated CD3+, CD19-; CD4+, CD8-; CD3-, CD56+ in the patient's BA and OW or obesity y (p<0.05). More pronounced shifts occurred in CD3-, CD56+ NK-cell indices in the patients with BA against the background of OW or obesity as compared to the patients with NBMI ((8.59±0.49)%; (11.52±0.46)%; p<0.05 respectively). The aforementioned immunological changes, in turn, affect the course of BA, making it less controllable, requiring increased pharmacological correction.

For the first time, a complex of therapeutic and preventive measures was developed and pathogenetically substantiated, and the effectiveness of pharmacological correction with bacterial lysate and inosine pranobex, together with training at the Asthma school, was proved due to the positive dynamics of some indices of immunity. Following the proposed treatment-and-preventive complex (TPC), stabilization of some immunological indices was noted. Namely, the normalization of T-lymphocyte (CD3+, CD19-) subpopulation from (77.41±0.69) to (70.18±0.19)% (p<0.05); (CD4+, CD8-) from (52.03±0.62) to (44.98±0.49)% (p<0.05) and (CD4, CD8+) at the beginning of the study and (24.37±0.29)% in 20 weeks after the termination of the application of TPC; this index changed

significantly and amounted to (28.94±0.59)% (p<0.05). Along with changes in the T-link, normalization of the marker of CD14 monocytes and macrophages from (6.36±0.26) to (7.51±0.14)% (p<0.05), NK-cells from (8.57±0.46) to (12.510.43)% (p<0.05) and B-lymphocytes from (12.17±0.52) to (10.38±0.12)% was observed. Positive dynamics was observed during treatment and after its cessation within 32 weeks.

All patients taking the proposed TPC improved asthma control. There was a decrease in the frequency of exacerbations from (5.41±0.42) to (2.39±0.36) per year (p<0.05), a decrease in the number of hospitalizations from (3.05±0.67) to (1.21±0.44) per year (p<0.05) and the amount of ARI from (6.34±0.15) to (3.31±0.61) per year (p<0.05) for the period of follow-up of the patients using the developed TPC. The data obtained had a positive effect on the course of BA, which in turn improved the physician-patient compliance, which was confirmed by the state patent of Ukraine for the utility model.

Conclusion

1. Overweight or obese patients had a more severe course of bronchial asthma than patients with a normal body mass index.

2. Overweight or obese patients were found to have higher levels of systemic inflammation, namely eosinophilic cationic protein levels and erythrocyte sedimentation rate, than patients with a normal body mass index. In addition, a close direct correlation was established between the severity of the course of bronchial asthma and indicators of eosinophil cationic protein (r=0.97; p<0.001).

3. After pharmacological correction, there was an increase in asthma control in patients with different severity of the course (p<0.001; p<0.001; p<0.001, respectively), a decrease in the frequency of exacerbations (p<0.05), a reduction in the number of hospitalizations (p<0, 05) and the number of acute respiratory diseases (p<0.05) in patients with bronchial asthma against the background of excess body weight or obesity.

4. The use of the developed treatment-prophylactic complex using the drug bacterial lysate and inosine pranobex together with training in the Asthma School and standard treatment contributes to increasing asthma control and compliance with the doctor, reducing the number of exacerbations and hospitalizations per year in patients with bronchial asthma against the background overweight or obesity (RR=0.37; RRR=0.63; NNT=2.14).

References

1. Global Asthma Report 2018 [Electronic resource]. Global Ashma Network. URL: http://www.globalasthmanetwork.org

2. The scale of the spread of asthma [Electronic resource].
World Health Organization. Access mode: http://www.who.int/respiratory/asthma/scope/ru

3. Health statistics and information systems [Electronic resource]. World Health Organization. URL:
http://www.int/healthinfo/global_burden_disease/
metrics_daly/en/

4. Solovieva I. A., Sobko E. A., Demko I. V., Kraposhina A. Yu. Bronchial asthma and obesity. Therapeutic archive. 2017. No. 89 (3). pp. 116–120.

5. Peters U., Dixon A. E., Forno E. Obesity and asthma. The Journal of Allergy and Immunology. 2018 Vol. 141, iss. 4. P. 1169–1179.

6. Role of adipokines and hormones of obesity in childhood asthma / H. Yuksel et al. Allergy, asthma & immunology research. 2012. Vol. 4. P. 98–103.

7. Baffi C. W., Winnica D. E., Holguin F. Asthma and obesity: mechanisms and clinical implications. Asthma Research and Practice. 2015. Vol. 1. P. 1.

8. Sideleva O., Black K., Dixon A. E. Effects of obesity and weight loss on respiratory tract physiology and asthma inflammation. Pulmonary pharmacology & therapeutics. 2013. Vol. 26, No. 4, pp. 455–458.

9. Sideleva O., Dixon A. The many faces asthma in obesity. Journal of cellular biochemistry. 2014. Vol. 115. P. 421–426.

10. Melnik O. B. Features of the transition and optimization of the treatment of bronchial asthma due to obesity Abstract of the thesis. dis. to-that honey. Sciences: 14.01.02 Bukovinian State Medical University. Chernivtsi, 2019: 67.

11. Osipova G. L. Bronchial asthma and viral infection. Asthma and allergies. 2014. No. 3. P. 3–7.

12. Castillo J. R., Peters S. P., Busse W. W. Asthma exacerbations: pathogenesis, prevention and treatment. The journal of allergy and clinical immunology. In practice. 2017 Vol. 5, No. 4, pp. 918–927.

13. Th1-related disease development during omalizumab treatment. P. Two cases with severe asthma / H. Hayashia et al. Allergology International. 2018 Vol. 67, iss. 3. P. 405–407.

14. Zhang Y., Zhang L. Prevalence of Allergic Rhinitis in China. Allergy, asthma & immunology research. 2014. Vol. 6, No. 2, pp. 105–113.

15. Arkhipov V. V., Grigorieva E. V., Gavrishina E. V. Control of bronchial asthma in Russia. Results of the NIKA multicenter observational study [Electronic resource]. Pulmonology. 2011. No. 6. P. 87–93. Access mode: https://doi.org/10.18093/0869-0189-2011-0-6-87-93

16. A bacterial extract of OM-85 Broncho-Vaxom prevents allergic rhinitis in mice / L. Han et al. Article in American Journal of Rhinology and Allergy. 2014. Vol. 28, No. 2, pp. 110–116. doi:10.2500/ajra.2013.27.4021

17. Gosavi S., Nadig P., Haran A. Factors Contributing Towards Poor Asthma Control in Patients on Regular Medication. Journal of Clinical and Diagnostic Research. 2016. Vol. 10, 6. P. OC31–35.

18. Asthma control in primary care: the results of an observational cross-sectional study in Italy and Spain / M. S. Magnoni et al. The World Allergy Organization journal. 2017 Vol. 10, N 1. P. 13.

19. Novosad S., Khan S., Wolfe B., Khan A. Role of Obesity in Asthma Control, the Obesity-Asthma Phenotype Journal of Allergy (Cairo). 2013. doi:10.1155/2013/538642.

20. Bulgakova V. A., Balabolkin I. I., Sedova M. S., Shmakova S. G. Clinical and immunological efficacy of inosine pronobex in acute respiratory infections in children with atopic bronchial asthma. Pediatric pharmacology. 2010. V. 7, No. 3. S. 98–105.

21. Lauener R. Genetics of asthma. Global Atlas of Asthma. European of Allergy and Clinical Immunology. 2013. P. 23–24

22. Marko M., Pawliczak R. Obesity and asthma: risk, control and treatment Postpy dermatologii i alergologii. 2018 Vol. 35, No. 6, pp. 563–571.

23. Martin R. J. Complementary, alternative, and integrative therapies for asthma [Electronic resource]. 2018. URL: https://www.uptodate.com/contents/complementary-alternative-and-integrative-therapies-for-asthma

24. Effects of weight loss on asthma control in obese patients with severe asthma / S. A. Dias-Júnior et al. *The European respiratory journal*. 2014. Vol. 43, N 5. P. 1368–1377. doi: 10.1183/09031936.00053413.

25. Cramer H., Posadzki P., Dobos G., Langhorst J. Yoga for asthma: a systematic review and meta-analysis. *Annals of Allergy, Asthma and Immunology*. 2014. Vol. 112. P. 503.

26. Body mass index and asthma severity in the National Asthma Survey / B. Taylor et al. *Thorax*. 2008. Vol. 63. P. 14–20.

27. Baffi C. W., Winnica D. E., Holguin F. Asthma and obesity: mechanisms and clinical implications. *Asthma Research and Practice*. 2015. Vol. 1. P. 1.

28. Asthma control in primary care: the results of an observational cross-sectional study in Italy and Spain / M. S. Magnoni et al. *The World Allergy Organization journal*. 2017. Vol. 10, N 1. P. 13.

29. Association of Obesity with Asthma Severity, Control and Quality of Life / S. Maalej et al. *Tanaffos*. 2012. Vol. 11, N 1. P. 38–43.

30. Sepiashvili R. I. Physiology of the immune system. Moscow: Medicine–Health. 2015. 352 p.