THERAPY

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STATE OF HUMORAL IMMUNITY IN PATIENTS WITH ASTHMA COMBINED WITH OBESITY

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Abstract: It was found out in patients having asthma combined with obesity that in cases of a higher body mass index versus patients with asthma and healthy persons the "waist/hip volume" ratio was reliably increased. An examination of the state of humoral immunity indices in patients with asthma found out an increase of non-specific (with rising concentrations of immunoglobulins Ig A, M, G) and specific (with a rising level of Ig E) immunity. Patients with comorbidity of asthma and obesity revealed differently directed changes in the concentration of the main immunoglobulins: with a decrease in the levels of IgA and IgM there was a significant increase in the concentration of IgG. Those changes were accompanied by a significant reduction in the number of circulating immune complexes and an increasing concentration of lymphocyte antibodies in the blood of patients with comorbidity of asthma and obesity. This fact may indicate an aggravating effect of obesity on the course of asthma and a change in the direction of the pathological process to the autoimmune one that should be taken into consideration when treating such patients.

KeyWords: asthma, obesity, humoral immunity.

INTRODUCTION

In recent years the attention of researchers and doctors of different specialities is more and more attracted by the problem of comorbidity, which means a combination of several chronic diseases in one patient [9, 15]. Modern studies of the incidence of asthma in patients with different levels of an increased body mass index (BMI) have revealed a direct dependence of the increased rate of asthma development upon an increase of the BMI [12, 21]. Asthma and obesity are prevalent disorders, each with a significant public health impact, and a large and growing body of literature suggests an association between the two. Meanwhile it has been found out that overweight and obesity occur in asthma cases twice more frequently than in the population on an average [13].

GINA (2014) recommendations point out the necessity of the personalized approach with regard for individual peculiarities of the asthma course in each particular patient and draw a parallel between the success in achieving control over asthma and comorbid states, which can influence difficulties in diagnosis and efficacy of the given therapy [11, 14].

An imbalance of the subpopulation structure of T lymphocytes that underlies pathogenesis in asthma facilitates development of a chronic local inflammation with participation of cellular and humoral reactions [2, 18]. The current focus on the fatty tissue as the source of both energy and proinflammatory mediators, which are also mediated by T helpers (Th) type 2 [7, 17, 20], causes a more thorough study of the immune system in patients having asthma combined with obesity. Cellular immunity changes are accompanied with disorders in the humoral component of the immune system.

2 PURPOSES, SUBJECTS and METHODS:

2.1 Purpose of this work is to study to study the state of humoral immunity indices in patients having asthma combined with obesity.

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The study was conducted in compliance with the asthmasic plan of research and development (R&D) of the State Institution "Kharkiv National Medical University" and is a fragment of the R&D subject "Factors of the development and progression of different phenotypes of bronchial asthma, chronic obstructive pulmonary disease and community-acquired pneumonia: peculiarities in the course, comorbid states, their prognosis and prevention" (State registration No. 0113U002280).

2.2 Subjects & Methods

The research was conducted on 121 patients with a moderately severe course at the age of (51.6 ± 4.7) years, including 51 (42,2 %) men and 70 (57,8 %) women. Of the examined patients, there were 46 cases with ASTHMA and normal body weight (group I) and 75 cases having asthma combined with obesity (group II). The control group consisted of 21 healthy donors of the same age and gender. Asthma was diagnosed according to Order of the Ministry of Health of Ukraine No. 127 dated March 19, 2003; the presence of obesity was determined by calculation of the BMI. All the examinees had their waist circumference (WC) and hip circumference (HC) measured and WC/HC ratio calculated.

The performed studies involved the state of the cellular and humoral components of immunity and phagocytosis with help of revealing: subpopulations of T and B lymphocytes (CD3, CD4, CD8, CD16, CD22) in absolute and relative values using "NVL Granum" diagnosticum (Ukraine); levels of IgA, IgM and IgG of blood serum by the Mancini technique [16] with help of reagents of the Federal State Unitary Enterprise "Microgen Scientific Production Association" (Ministry of Health of the Russian Federation, Russia); circulating immune complexes (CIC) using the technique developed by V. Haskova et al. and modified by Yu.A. Grinevich and A.I. Alfiorov [1]. Phagocytosis indices (phagocyting neutrophils, phagocyte number and neutrophil activation index) were studied by the principle of the ability of polymorphonuclear leukocytes and monocytes of peripheral blood to bind on their surface, absorb and digest microbe test cultures, NBT test modified by B.S. Nagoev [5]. A computer data asthma of the obtained indices was created in Microsoft Excel. The study materials were statistically processed with use of SPSS 19 program for Windows. Infinite variables are shown in the form of the median (Me) and values 25-75 (Q25-Q75). The critical level of significance in checks of statistical hypotheses was accepted equal to 0.05. Dependencies between the variables were studied with use of the Spearman's rank correlation coefficient. The results are presented as (M±m), where M– is the mean value of the index and m– is the standard error. The reliability of the difference of mean values between the groups by quantitative indices during a distribution close to the normal one (the Kolmogorov-Smirnov test) for independent samples was calculated using the Student's t-test.

Conflict of interests

There is no conflict of interests.

3 RESULTS AND DISCUSSION

The BMI of the patients from group I averaged with Me = 23.4 (respectively, Q25-Q75 = 22.5-24.3; $p<0.001$) that was higher than the control values (Me = 21.7, Q25-Q75 = 21.3-22.8). No reliable difference in WC of the patients from group I versus the healthy persons was detected, though their HC (Me = 101 cm, Q25-Q75 = 98-103 cm) was reliably ($p<0.001$) less than the same index in the healthy people (Me = 111.6 cm, Q25-Q75 = 109.9-114.4 cm) by 9.0 % with the resultant increase of the WC/HC ratio in the patients from group I versus the practically healthy persons by 7 % ($p<0.001$). Despite the fact that BMI in the cases from group I did not exceed the limits of the generally accepted norm, those persons revealed a tendency to increase their body weight versus the practically healthy people. These data coincide with results of studies on an increased rate of excessive body mass in patients with asthma [10, 11, 19]. The cases from group II were diagnosed an excessive body mass with Me of the BMI value equal to 28.9 (respectively, Q25-Q75 = 27.9-30.1) that was reliably higher ($p<0.001$) than the value in group I. In the patients from group I, Me of the WC value was 78 cm (Q25-

Q75 = 75-84 cm, respectively), in group II it being 99.5 cm (respectively, Q25-Q75 = 89-102 cm), which was by 21.5 cm or 27.6 % higher than in group I. In the latter group, Me of the measurement of HC in the patients was 101 cm (Q25-Q75 = 98-103 cm, respectively), while in group II it was 115 cm (respectively, Q25-Q75 = 100-118 cm), which was on an average by 14 cm or 13.9 % higher than in group I. Increases of WC and HC in the patients from group II versus those from group I was also reflected on an increase of their WC/HC index 1.2 times ($p<0.001$); respectively, Me = 0.89 and Me = 0.77.

All the examinees did not reveal any significant differences in analyses of values of their clinical blood test and glucose content.

It should be noted that Me of the IgE level in the patients from group I was 140 IU/l (Q25-Q75 = 120-170 IU/l), it being 2.3 times reliably higher versus the control group (Me = 60 IU/l, Q25-Q75 = 50-65 IU/l). In cases from group II their concentration of IgE (Me = 250 IU/l, Q25-Q75 = 170-290 IU/l) exceeded the control one 4.2 times ($p<0.001$) and the same value in group I 1.8 times ($p<0.001$); this fact could reflect an increasing influence of the accompanying obesity on the state of the systemic allergic inflammation in ASTHMA [22].

Me of the content of IgA in blood of the patients from group I was 4.1 g/l (Q25-Q75 = 3.1-4.9 g/l) and was 1.4 times higher than the control values (Me = 2.9 g/l, Q25-Q75 = 2.8-3.0 g/l) ($p<0.001$). The concentration of IgM in blood of the patients from group I (Me = 1.9 g/l, Q25-Q75 = 1.7-1.9 g/l) exceeded the control one (Me = 1.5 g/l, Q25-Q75 = 1.45-1.6 g/l) too, but less significantly, 1.3 times ($p<0.001$).

The levels of IgA (Me = 3.12 g/l, Q25-Q75 = 2.23-3.56 g/l) and IgM (Me = 1.56 g/l, Q25-Q75 = 1.45-1.76 g/l) in the patients from group II were reliably lower than those from group I (IgA with Me = 4.10 g/l and IgM with Me = 1.90 g/l), respectively, by a factor of 1.3 and 1.2 ($p<0.001$). The value of IgG in cases with combined ASTHMA and obesity (group II: Me = 20 g/l, Q25-Q75 = 18-22 g/l) was 1.5 times higher than that of the control group (Me = 13 g/l, Q25-Q75 = 12-14 g/l), ($p<0.001$), though did not differ significantly from the similar value in the patients from group I (Me = 19 g/l, Q25-Q75 = 18-20 g/l).

The above fact demonstrated that asthma was characterized by an increase of nonspecific immune defence [3]. When asthma was combined with obesity, changes of the blood immunoglobulin levels had different directions: lowering levels of IgA and IgM versus a significant elevation of the concentration of IgG.

The number of lymphocyte autoantibodies in the patients from group I (Me = 11.0 %, Q25-Q75 = 10.0-13.0 %) exceeded the norm 3.7 times ($p<0.001$), and in group II (Me = 15.5 %, Q25-Q75 = 14.0-17.0 %) it was significantly (5.2 times, $p<0.001$) higher than the control value (Me = 3.0 %, Q25-Q75 = 2.0-4.0 %) and 1.4 times higher than the same index in group I ($p<0.001$). The increase in the number of autoantibodies versus lymphocytes, on the one hand, demonstrates the development of the autoimmune component of inflammation [4] in patients with asthma and its further stimulation by the presence of the accompanying obesity and, on the other hand, facilitates explanation of the nature of formation of the secondary immune deficiency at the expense of the cellular component of immunity in asthma [3], this deficiency being also detected in another pathology of internal organs in conditions of its combination with obesity [15].

The blood concentration of the total number of CIC in the patients with asthma (Me = 91 %, Q25-Q75 = 89-93 %) was reliably higher versus the practically healthy people (Me = 93 %, Q25-Q75 = 92-94 %). The above data confirm previously conducted studies of the content of CIC in asthma with different degrees of severity [3, 5] taking into consideration the biological role of these complexes [2]. Herewith the content of CIC in the patients from group I was higher than the similar one in asthma combined with obesity (Me = 89 %, Q25-Q75 = 87-91 %) by 2 % ($p<0.001$). Side by side with an increased number of lymphocyte autoantibodies, the tendency to a reduced content of CIC in patients having asthma combined with obesity can highlight pathogenetic changes in components of a chronic inflammation from immune complex to autoimmune as more aggressive. Such changes in mediators of the chronic

inflammatory process in asthma combined with obesity versus the same ones revealed in patients with asthma, can demonstrate, on the one hand, the aggravating effect of the accompanying obesity on the course of asthma [4, 6, 8] and a potential risk of the development of complications of the disease and, on the other hand, direct the rational and pathogenetically grounded medical influence.

CONCLUSIONS

1. BMI and WC/HC ratio in patients having asthma without obesity are found higher than in practically healthy people. BMI in cases with asthma and obesity reliably exceeded the same index both in the control group and in the patients with asthma.

2. In asthma, increases of the nonspecific and specific components of the humoral immune defence are observed. In combinations of asthma and obesity changes of blood immunoglobulin levels had different directions: with lowering levels of IgA and IgM the concentrations of IgG and IgE significantly rose.

3. Side by side with a reduction in the total number of CIC, a more significant elevation of the level of lymphocyte antibodies in the blood of patients having asthma combined with obesity versus asthma cases without obesity reveals formation of the autoimmune component of inflammation in the comorbidity of asthma and obesity and can affect changes in the cellular component of immunity.

Thus, asthma and obesity have a number of common potential formation mechanisms, among them immunological factors, systemic inflammation, mechanical factors and concomitant diseases.

Further researches will deal with a comparative in-depth study of peculiarities in the immune system mechanisms in patients having asthma and asthma combined with obesity.

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