MEDICINE AND PHISIOLOGY

FEATURES OF THE REGULATORY SUPPORT OF THE CARDIOPULMONARY SYSTEM OF PATIENTS WITH PERSISTENT BRONCHIAL ASTHMA AND OBESITY

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Annotation. *The worldwide pandemic of obesity and its association with bronchial asthma (BA) is creating severe challenges for health care specialists. So, the investigation of mechanisms behind poor BA control in obese subjects is of great urgency.*

Blood pressure (BP) data and cardiointervalometry indicated deterioration of the cardiovascular function in the patients under study. Under the persistent course of BA there is a deterioration in the effectiveness of reduction of myocardium, regardless of body weight, deterioration of the processes of myocardial repolarization with its increase, and prevalence of parasympathetic effects on the heart rhythm. The general activity of free breathing is the lowest.

Key words: *obesity, uncontrolled bronchial asthma, persistent bronchial asthma, central hemodynamics, heart rhythm, respiration pattern.*

Introduction. Obesity is one of the main problems of health care around the world. It significantly increases the risk of various pathologies development, including type 2 diabetes, hypertension, chronic kidney disease, cardiovascular diseases, some types of cancer, depression, etc. Numerous epidemiological researches prove that there is a global epidemic of asthma and obesity that is concentrated in Westernized and developed countries [1, 2, 3] and increases in a parallel pace. In many cases it is an economic burden that prompts for effective counteraction search. It has been shown that the presence of obesity increases the risk of BA development, and BA is more common in people with obesity than in those of normal weight. Additionally, obesity can cause or even aggravate the course of asthma, which is reflected in the severe control of these patients [4-7].

Another problem is combination of metabolic syndrome and asthma that has grown rapidly over the past decades. Asthma is characterized by reversible episodic obstruction of the respiratory tract with hyperreactivity, whereas the metabolic syndrome is characterized by obesity, insulin resistance, dyslipidemia, hypertension, and intolerance to glucose. Studies made indicate that metabolic syndrome in association with impaired lung function may be a factor of BA formation. Among the components of the metabolic syndrome which are associated with asthma's risk, obesity is most palatable [8]. On the other hand, syndromes associated with an increase in blood pressure and blood glucose levels are considered as asthma' s important risk factors, while the comprehension of their relationship is not entirely convincing. Thus, in some researches it has been shown

that insulin resistance is a more significant factor in asthma symptoms occurring than weight gain or waist circumference, while according to others the risk of asthma is due to predominantly increased body weight in women. Therefore, it is unclear whether metabolic changes in obesity are independent risk factors for asthma development [9-12].

Although, according to some authors, some obese patients suffering from allergic asthma have a more severe inflammation in the bronchial tree than those with normal body mass. Besides, a significant phenotype of "obesity-asthma" is also found when the degree of severity does not depend on cell inflammation [11-13].

Therefore, the study of regulatory features, including those of cardiopulmonary system in BA with and without obesity is sufficiently important from the point of view of the definition of more subtle mechanisms of regulatory disorders [14].

The objective. To determine the peculiarities of cardiopulmonary system regulation in patients with persistent BA course and obesity.

Materials and methods. There were 69 patients aged 41.0±0.8 under study. They were divided into 4 groups. The main group (MG) included 20 persons (8 men and 12 women) who had clinically confirmed persistent asthma and obesity (BMI greater than 30 kg / m2). Taking into account BMI, comparative groups (CG1 and CG2) were formed, the first of which included 15 persons with BA persistent course and BMI 25.1 – 29.9 kg / m2, the second group included 24 patients with BA the same course and BMI up to 25.0 kg / m2. To determine the regulatory differences in view of BA severity, a control group (CG, n=10) was formed, in which BA intermittent course was observed together with obesity.

All the patients signed informed consent.

The patients were screened in the early hours, in fasting state. When put to the test, recording of cardio respiratory system performance using spiroarthriocardiorhytmography (SACRG) was applied. This method allows to make simultaneous registration of the regulatory effects activity on the heart rate, systolic and diastolic blood pressure, respiration [15].

Additionally, the clinical parameters of the BA course were analyzed and the physical development indicators were registered. The mass (MT, kg) and the body length (BL, cm), the circumference of the body and the limbs were determined. The routine methods for studying systolic (SBP), diastolic (DBP) and pulse (PBP) arterial pressure were carried out, as well as the calculation of a number of indices that characterize the functional state of the cardiopulmonary system and the body as a whole: Robinson's index (IR), Kerdo's index (KI) [16].

Regulatory influences were determined on the basis of spectral analysis of cardiac rhythm variability (HRV), blood pressure and respiration (ER). Spectral analysis was performed in three frequency bands: ultra-low frequency (VLF, 0-0.04 Hz), low frequency (LF, 0.04-0.15 Hz), and high frequency (HF, 0.15-0.4 Hz), which are measured in absolute values of power (ms2 - for CP, mm Hg2 for CBP and DBP, (l / min)2 - for uncontrolled breathing). The sensitivity of arterial baroreflex (BR) was determined. In this case, we analyzed α-coefficient separately calculated in the ranges of high (BRHF) and low (BRLF) frequencies.

The hemodynamic and minute volume of blood flow (MVBF, l) were determined based on ECG data in 1 withdrawal.

According to the ultrasonic spirometry, the indicators of the respiratory pattern – respiration volume (RV, l), the volume of inhalation and exhalation velocity - RV/ Tiv (l / s) and RV / Tev (l / s), the ratio of inhalation and exhalation phases Tiv/Tev, as well as the minute volume of breath - MRV, l. Parameters of cardiovascular and respiratory system synchronization – Hildebrandt's index (IH) and the ratio MVBF / RMV, which certify the frequency and volume components of synchronization of the cardiorespiratory system [17].

Non-parametric methods of statistical analysis with the definition of Man-Whitney criteria were used to evaluate the obtained results of the study. Statistical processing was carried out using statistical package STATISTICA 10.

We have concentrated our attention mostly on heart rate and breathing regulatory effects and performed an analysis of the differences in the indicators of CG, CG1, CG2 and MG.

The results obtained confirm the morphometric differences in patients with asthma based on BMI and are given in Table 1.

So, all the dimensions investigated in CG1 and GP2 ($p<0.01$), differ significantly from those in the MG, among which less significant were differences in body length and hip circumference ($p<0.05$). The majority of MG and CG indicators did not differ, except for significantly larger ($p <0.05$) chest circumference in MG 116.5 (112.5; 126.0) versus 112.0 (97.0; 117.0). The latter can testify to the more pronounced formation of emphysematous type of thoracic cell in MG. The predominance of the chest circumference in the CG in comparison with GP1 and GP2 may be due to the morphometric features of individuals with different body mass, which is significantly greater in the CG.

Table 1

The morphometric and BMI data of BA patients

Indicators	CG1	CG2	**MG**	CG
Body mass, kg	73,5 (68,7; 77,5)	81,2 (74,0; 84,0)	**92,5 (84,0; 102,0)**##**	94,2 (81,0; 102,0)
Body length, sm	167,5 (164,5; 170,5)	169,0 (165,0; 174,0)	**173,0 (166,0; 180,0)*#**	171,5 (165,0; 179,0)
IMT, kg/m2	24,2 (23,9; 24,9)	27,8 (27,0; 28,2)	**31,2 (30,4; 32,7)**##**	31,4 (30,5; 32,5)
Waist circumference, cm	73,0 (68,5; 76,0)	87,0 (82,0; 91,0)	**97,0 (95,0; 103,0)**##**	99,5 (96,0; 103,0)
Belly circumference, cm	87,5 (81,0; 90,5)	99,0 (94,0; 105,0)	**108,5 (102,5; 117,0)**##**	105,5 (100,0; 112,0)
Hip circumference, cm	46,0 (43,0; 48,0)	58,0 (54,0; 65,0)	**67,0 (62,0; 77,0)**#**	62,5 (58,0; 73,0)
Chest circumference, cm	96,5 (92,0; 98,5)	104,0 (102,0; 112,0)	**116,5 (112,5; 126,0)**##&**	112,0 (97,0; 117,0)

*, #, & - differences between MG & CG1; MG & CG2; MG & CG, correspondingly.

^, ^^, ^^^ - $p<0,05$, $p<0,01$, $p<0,001$, correspondingly.

Data of the fatty tissue content determination characterize the significant differences in main and control group of patients from those with normal body mass and overweight. While these patients did not differ on fat content, as well as BMI.

Additionally our patients underwent a number of regulated clinical examinations, clinical and biochemical blood tests, spirography.

The results of clinical blood analysis showed significantly higher ($p<0.05$) Hb's level in the MG patients, than in those from CG. Similar differences are in the values of Hb in other groups with persistent course of BA (CG1 and CG2), which suggests the development of a certain compensation of oxygen transport function, which develops under conditions of chronic hypoxia. However, this requires additional justification.

Biochemical examination of MG patients blood (Fig. 1), showed the increase of blood creatinine ($p<0.05$) in comparison with CG1 and CG2. This may indicate the catabolic processes inclusion, which is significant enough in BA patients with overweight. In the latter there is a sufficiently significant level of urea, which may indicate a development of metabolic dysfunctions associated with a violation of protein metabolism and detoxification.

Respiratory function (RF) in MG patients compared with that from CG is characterized by significant differences which relate both restrictive and obstructive disorders. The differences in inspiration are significant at the level of $p <0.05$, while on expiration they are more significant at the level of $p<0.01$. The data of RF at inspiration prove significant restrictive differences between main and control groups, which are related to lower vital capacity of lungs in MG patients ($p<0.05$). The same differences are typical for the patients of CG1 and CG2. Indicators of RF at expiration in all patients with persistent BA differ significantly from those in CG ($p<0.001$).

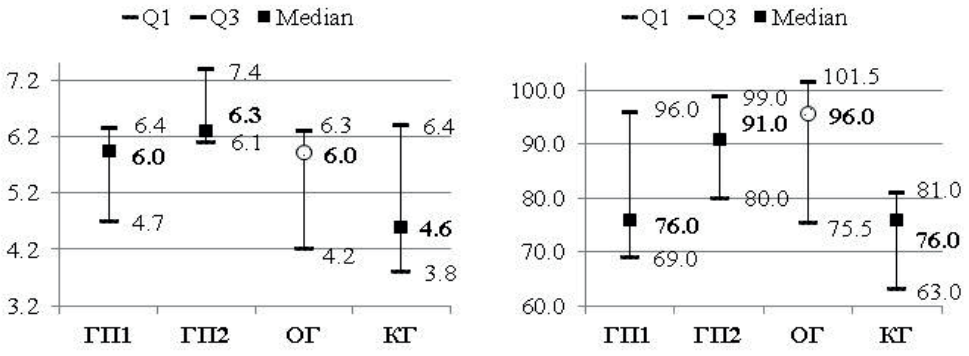

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Fig. 1. Differences in urea (a) and creatinine (b) blood values in patients with persistent asthma and obesity (MG) compared with CG, CG1 and CG2 patients

Analysis of blood pressure and cardiointervalometry allowed to note some features

of MG patients indicating deterioration of the cardiovascular system. Systolic BP data were the most intense in patients with excess body weight (CG2) Diastolic BP was the most intense in the MG. Cardiointervalometry data were significantly different in the main and control group ($p < 0.05$). It related the acceleration of atrioventricular conduction (PQ, c) 0.123 (0.112; 0.160) versus 0.152 (0.131; 0.164), delayed depolarization of the ventricles (QR, c) 0.093 (0.029; 0.037) versus 0.029 (0.028; 0.030) and delayed intraventricular conduction (QRS, c) 0.099 (0.089; 0.107) versus 0.086 (0.083; 0.098), which may characterize the desynchronization of the atrial and ventricular activity against the background of chronic hypoxia. Such differences are characteristic for other groups of patients with a persistent flow of asthma (CG1 and CG2). The indexes of heart rate did not differ significantly in all groups.

Changes in QTC (c) and ST (n.o.) indexes in the patients with BA persistent course confirm deterioration of myocardial recovery at the background of increased body weight (Fig. 2).

Indicators of autonomic heart rate (AHR) indicate significantly lower vegetative effect on the TP (ms2) in MG patients compared with CG ones - 1244 (408; 3914) versus 2190 (1444; 2830), $p < 0.05$ in the low-frequency (LF, ms2) and high-frequency (HF, ms2) ranges 453 (135; 1117) versus 742 (480; 1076), $p < 0.05$, and 221 (69; 803) against 988 (303; 1421), $p < 0.05$, respectively. These differences testifies the ones associated with uncontrolled and controlled course of asthma [24].

At the same time, there is little difference between data indicating the regulatory contribution of the sympathetic and parasympathetic regulatory branches (LFn and HFn) in MG, CG2 and CG, both in terms of proportion and ratio.

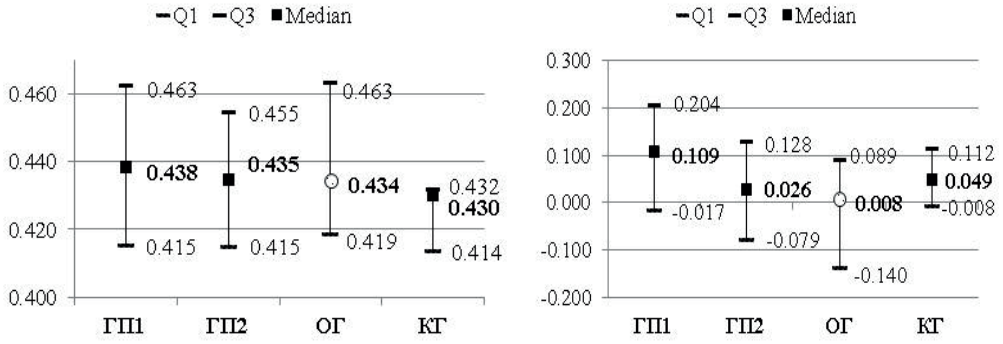

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Fig. 2. Differences between the average indicators QTC, c (a) and ST, b. (b) in patients with persistent asthma and obesity (MG) compared to patients with CG, CG1 and CG2.

The reduction of AHR in patients with persistent course of BA is associated with both the controllability of the pathological process and the patients' body weight. Obesity and even overweight significantly reduce the heart function reserves.

Variables of respiration indexes prove that in persistent course of asthma and obesity,

the total activity of regulatory influences on voluntary respiration is the lowest among all the groups under study. Along with it the intermittent course BA patients low activity of over-segmental (VLFbr) respiratory influences, which can characterize obesity and metabolic syndrome.

The data on the sensitivity of the arterial baroreflex in the low-frequency (BRLF) and high-frequency (BRHF) ranges indicate a certain dependence of these indices from BMI in patients with asthma and indicate a significant deterioration of the neuro-reflex mechanisms of central hemodynamics regulation, which can contribute to a significant increase in rigidity of the vessel wall and blood pressure.

The analysis of the respiratory pattern has shown that patients with uncontrolled asthma and obesity undergo a reorganization of the respiratory pattern, which resulted in a significant reduction of RMV due to reduction of RV, compared to a controlled course of the disease that is not compensated by an increase in respiratory rate, against the background of significant reduction of inhalation velocity volume and even more pronounced decrease in volumetric expiratory flow rate. The latter, in our opinion, can be a factor in the impossibility of compensation for hypoxia at the expense of the frequency of respiration, or lead to a more pronounced decrease in RV and tachypnea. So, the results obtained show that in patients with obesity and asthma's persistent course, in contrast to patients in other groups, there are more significant preconditions for the occurrence of dyspnea attacks that may be caused not only by obstructive but also restrictive factors.

The indicators of central hemodynamics in the patients under study prove about their less effective hemodynamic support.

The parameters of cardiopulmonary synchronization are given in Fig.3. They indicate that in patients with controlled asthma and obesity (MG) there is a significant difference in frequency synchronization (FS) from the patients with uncontrolled course, whereas in groups with a persistent course of BA this parameter does not differ significantly (Fig. 3, a). Significant differences are associated with BMI.

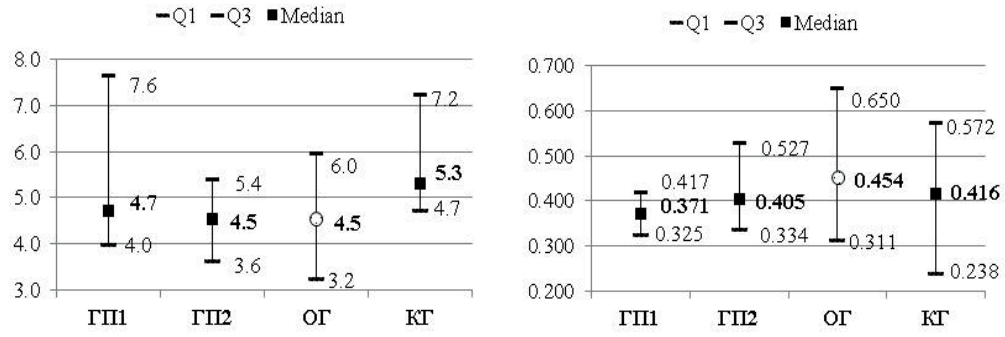

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Fig. 3. Average values of M (Q1; Q3) of the cardiorspiratory system synchronization in patients with persistent asthma and obesity (MG) compared to patients of CG, CG1 and CG2: FS (a), BMV / RMV (b).

Conclusions. 1. Asthma is an urgent health problem, and it is associated with a high incidence of obesity and poor quality of life.

2. With a combination of bronchial asthma and obesity / overweight there is a violation of pulmonary and cardiac microcirculation, the development of hypoxemia, pulmonary hypertension, the progression of heart failure and the early development of cardiorespiratory complications.

3. In BA patients, impaired hemodynamic and metabolic homeostasis as a result of significant damage to the vessels of lungs microcirculatory bed adversely affects the overall dynamics of the pathological process and is one of the mechanisms for its chronicity and progression.

4. Features of pulmonary ventilation and hemodynamic disorders in asthma take place in the form of prevalence of obstructive ventilation failure, early involvement in the pathological process the respiratory lung area with an increase of alveolar-capillary diffusion ineffectiveness on the background of clear manifestations of central, pulmonary and intracardiac hemodynamic changes .

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