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Peculiarities of bronchial asthma with obesity

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Abstract. In order to define the peculiarities of bronchial asthma with obesity there was carried out the analysis of the examination of 90 patients suffering from BA. The patients were divided in 3 groups: the first one consisted of 33 patients with normal body mass, the second one consisted of 29 patients with excessive body mass and the third one consisted of 28 patients with obesity. Bronchial asthma of the patients with obesity significantly more often was complicated by lung tissue pneumosclerosis and these patients more often were diagnosed the comorbid states - hypertensive heart disease and type 2 diabetes. The patients from group with obesity significantly rarely were diagnosed allergic rhinitis and eosinophilia.

Within analysis of the respiratory functions it was detected that the patients with obesity and excessive body mass had more expressive restrictive obstructions than the patients with normal body mass. Group with obesity included more women whose disease in comparison to man part was significantly more often complicated by pulmonary insufficiency of the third degree and pulmonary emphysema. In comparison to women men with obesity more often were suffering from type 2 diabetes mellitus.

Key words: bronchial asthma, phenotype, obesity.

Introduction. Bronchial asthma (BA) is one of the most common diseases (5-25% of general population) and its incidence has tendency to increase [3,11,13]. The frequency of the BA in Ukraine shall constitute 5-7% [1,2]. As of today approximately more than 300 million people suffer from the BA. However, as regards majority of the patients the BA is badly preventable or even unpreventable, that requires finding out new treatment approaches. Heterogeneity of the BA basing on the mechanisms, presentations and progress is considered one of reasons of bad preventability [8,16]. Lastly, the attention was drawn to the tries to phenotype and genotype the BA, i.e. define main variants basing on the clinical characteristics and genetic markers for understanding of pathophysiological basis of the disease and optimization of remedial measures [8,14,15,17]. Phenotyping of asthma is performed basing on the clinical characteristics (age, sex, duration, comorbid states), pathobiological inflammation appearances in sputum or bronchoscopic material [9,16] and response to

treatment. Phenotyping becomes particularly important to define the tactic of the treatment, namely while prescribing the systemic corticosteroids [15]. Obesity comprises one of the features under which the asthma is phenotyped and currently obesity turns to be the background of all diseases.

The **aim** of this paper is to analyse modern data regarding BA phenotyping considering obesity as well as findings obtained as a result of own observations.

According to the literature data, the attempts to combine all main criteria of phenotyping were not successful. The described inflammatory characteristics and peculiarities of the respiratory function that asthma with obesity comprises separate phenotype of bad preventability [18]. Patients with obesity suffer from non-eosinophilic asthma in the light-medium or severe (mostly women) form [5,12]. W.C. Moore et al. (2010) provided more detailed characteristics. They performed cluster analysis of the results of diagnostics and treatment of 726 adult patients suffering from BA and formed 5 groups united on the basis of common clinical and functional features, character of treatment and response to it [6,16]. According to their findings cluster consisting of 59 people (8%) united mostly older women aged 34-68 years (average age 50 years) with obesity appeared to be unique. Their asthma was featured with non-atopic character, late appearance and moderate reduction of the peak volumetric rate and frequent use of the gluco-corticosteroids for exacerbations treatment. 17% of such patients got systemic steroids. Notwithstanding the above, only 64% of them after treatment managed to reach the norm of peak expiratory flow rate by means of three or more medicines including one inhalant gluco-corticosteroid in high doses. It is important that the obesity degree of patients of this cluster is associated with the symptoms load. The history of such patients often revealed gastroesophageal reflux [4]. Asthma phenotyping is significantly important to define the tactic of treatment. While the patients with eosinophilic inflammation shall be prescribed with inhalant corticosteroids and prolonged beta$_2$-agonists [5], the patients

with non-eosinophilic neutrophilic inflammation would not respond to the therapy with inhalant and peroral corticosteroids and thus their first option shall be macrolide antibiotics [10]. Still most patients with the phenotyped of bad cases of asthma are resistant to standard therapy [7].

Materials and methods. In order to define the peculiarities of bronchial asthma with obesity there was performed analysis of the results of examining of 90 patients suffering from BA. The patients were divided into 3 groups basing on the criterion of body mass index (BMI): the first group consisted of 33 patients with normal body mass (BMI 18-24,9 kg/m^2), the second one consisted of 29 patients with excessive body mass (BMI 25-29,9 kg/m^2) and the third one consisted of 28 patients with obesity (BMI $\geq$30 kg/m^2). The age of the groups did not sufficiently differ; age medians were 41,5[25;54], 42[32;53], 51[45;52] years respectfully. However, the difference in gender composition of groups was significant, since the number of women in the group with obesity was larger (64,3±9,0% against 36,4±9,0% and 41,4±9,1% in group 1 and 2, p$_{3-1}$<0,05, p$_{3-2}$>0,05).

Results. While analysing the anamnesis data there was revealed that the disease of 93% of women with obesity appeared in the mature age, while only 60% (p=0,05) of men faced first symptoms in adulthood. Women with obesity more often suffer from pulmonary insufficiency of third degree (67%, p=0,05) and pulmonary emphysema (56%, p=0,047). Men with obesity suffered from the concomitant type 2 diabetes almost three times more often than women (60% against 22%, p=0,048).

Asthma with obesity is featured with inflammation of non-eosinophilic character that is confirmed by the fact that such patients significantly rarely suffered from allergic rhinitis (17,9±7,2%) than the patients with the excessive mass (46,4±9,3%, p=0,02) and normal mass (36,4±8,4%, p>0,05); and there was detected sufficiently lower level of eosinophils in peripheral blood (2[2;4]% against 4[2;5]%, p=0,009, while it was in case of excessive and

normal mass). At the same time the patients with obesity had significantly higher ESR index (7,5[6;12] mm/h, against 6 [4;6] mm/h and 7 [6;12] mm/h, p_{1-2}=0,05, p_{1-3}=0,049), that confirms that they had inflammation syndrome. Although the difference between the quantity of leukocytes and stab neutrophils was not significant, in case of obesity these indexes reached the maximum.

The BA of the patients with obesity significantly more often was complicated by lung tissue pneumosclerosis (21,3±7,7% against 3,5±3,4% in group 2, p=0,04); they were suffering from the comorbid states − hypertensive heart disease (42,9±9,4% against 12,1±5,7% in case of patients with normal mass, p<0,05 and 10,3±5,6%, p<0,05 in case of patients with excessive mass) and type 2 diabetes (42,9±9,4 % against 17,1±7,1 % p<0,05 in case of patients with excessive mass and 21,2±7,1% p>0,05 in case of patients with normal mass). The sub-group consisting of the patients with obesity had sufficiently higher indexes of blood glucose (5,6[4,7;6,1] mmol/l against 4,6[4,4;5,2] mmol/l and 4,9[4,5;5,2] mmol/l, p_{1-3}=0,01, p_{2-3}=0,02).

Some indexes of the respiratory functions (RF) sufficiently differ: inspiratory vital capacity (IVC) was significantly lower in case of the patients with excessive mass (58,2[42,3;73,8]%, p=0,009) and in case of the patients with obesity (60,8[38,4;66,5]%, p=0,02) in comparison to patients with normal body mass (74,3[61,5;82,1]%), that confirmed more expressed restrictive disorders. The patients with obesity had the lowest wheezing indexes such as FEV_1, FEV_1/FVC, FEF_{25-75}, MEF_{25}, MEF_{50} and MEF_{75}, however, these indexes did not reach the significance level.

Analysis of the RF indexes considering gender criterion demonstrated that in case of obesity women had significantly lower MEF_{75}, index that confirms the obstructive changes in bronchial tubes (34,9[24,4;35,8]% against 45,9[39,3;53,7]% and 55,9[24,5;61,0]% in case of patients with normal and excessive body mass, p_{1-3}=0,049; p_{2-3}=0,04). At the same time men

with excessive body mass and obesity were diagnosed significant changes of both volume and rate indexes. In case of obesity and excessive mass the indexes were sufficiently lower, as follows: forced VC (43,8[37,9;62,6]% and 47,7[43,8;68,7]% against 65,9[59,4;76,9]%, p_{1-2}=0,04, p_{1-3}=0,009), IVC (38,4[34,1;62,6]% and 43,0[40,4;58,0]% against 78,2[66,5;84,1]%, p_{1-2}=0,0005, $p_{1,3}$=0,002), Forced Expiratory Volume in 1 Second (FEV$_1$) (28,8[28,7;51,4]% and 33,5[31,0;49,6]% against 55[46,6;59,4]%, p_{1-2}=0,03, p_{1-3}=0,002), peak volumetric rate (22,6[17,6;28,0]% and 25,5[22,6;27,6]% against 45,8[32,9;66,1]%, p_{1-2}=0,008, p_{1-3}=0,007].

Thus, basing on the existing data only part of the patients suffering from the BA may be phenotyped. The division of the BA to clusters makes possible to individualize the diagnostic and treatment approaches. It is reasonable to allocate within the clinical characteristics the cluster of bronchial asthma with obesity, that is featured with non-eosinophilic inflammation, is more often faced by women (64,3%), and is accompanied with pneumosclerosis (21,3%), arterial hypertension (42,9%) and diabetes (42,9%), worse RF indexes and its prevention requires three or more medicines including one inhalant corticosteroids.

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