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THE CLINICAL ASTHMA COURSE AND NEUROHORMONAL STATUS AT PATIENTS WITH OBESITY

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Abstract:

The purpose of this study was to reveal the interrelation between neuropeptide Y level and particularity of clinical asthma course at patients with obesity and overweight. Materials and Methods: We examined 113 patients with asthma aged from 18 to 75 years. The asthma diagnosis was based on Global Strategy for Asthma Management and Prevention, GINA, updated 2018. We analysed the clinical (number of asthma exacerbations, ambulance calls, and hospital admissions, Asthma Control Test), instrumental and laboratory status of patients. The patients were divided into 3 groups. Group I included patients with standard weight, body mass index (BMI) was from 18.5 to 24.99; Group II included patients with overweight, BMI was from 25.0 to 29.99; Group III included patients with obesity, BMI was more then 30. All data was evaluated with STATGRAPHICS 5.1, Microsoft Office Excel, Statistica 8.0. Results: patients with asthma and obesity had statistically higher level of neuropeptide Y. It had inverse correlation with spirometrical data, asthma control and direct correlation with level of molecules general oxidizing damage. It demonstrates the possible pro-inflammatory effect of neuropeptide Y, promoting the unfavourable asthma course. Thus, the research of the interrelation between neuropeptide Y and asthma course is necessary for establishment of degree and mechanism of neurohormone influence on disease pathogenesis.

***Keywords**: asthma, obesity, neuropeptide Y, leptin, adiponectin*

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INTRODUCTION:

Asthma is the widespread disease leading to life quality impairment, disability and demanding considerable expenses in health care [1,2]. At the moment 300 million people worldwide, different age and race suffer from this disease. It is supposed that, with growth of urbanization, by 2025 the number of patients with asthma will reach a point in 400 million [3]. Distinctive characteristic of this disease are the heterogeneity and variability of clinical current. Now allocate asthma phenotypes. One of them is phenotype «asthma with obesity» [4,5]. Some researches revealed interrelation between asthma and obesity at the epidemiological level [6].

Thus, special attention to phenotype «asthma with obesity» is quite justified. Evealing of interrelation between neuropeptide Y level and particularity of clinical asthma course at patients with obesity and overweight is represented relevant.

In the present work, the goal has been set – to reveal interrelation between neuropeptide Y level and particularity of clinical asthma course at patients with obesity and overweight.

MATERIALS AND METHODS:

We examined 113 patients with asthma ((86/76.1% women and 27/23.9% men) aged from 18 to 75 years (mean age 57.81±13.05 years). The asthma diagnosis was based on Global Strategy for Asthma Management and Prevention, GINA, updated 2018. The study was approved by the Ethics Committee of Voronezh State Medical University named after N.N. Burdenko. Written informed consent was obtained from each patient.

A comprehensive clinical examination, functional and laboratory tests included the following procedures:

- Anthopometrical Reference Data: body mass index (BMI) was calculated using Quetelet's formula (in kg/m^2);
- Assessment of asthma severity included the number of exacerbations, ambulance calls, and hospital admissions for the past 12 months;
- Functional tests: spirometry;
- Assessment of asthma symptoms control by Asthma Control Test™ (ACT);
- Laboratory tests: leptin level, adiponectin level, neuropeptide Y level, and level of molecules general oxidizing damage (PerOx).

The patients were divided into 3 groups. Group I included patients with standard weight, BMI was from 18.5 to 24.99; Group II included patients with overweight, BMI was from 25.0 to 29.99; Group III included patients with obesity, BMI was more then 30.

All data was evaluated with STATGRAPHICS 5.1, Microsoft Office Excel, Statistica 8.0. Baseline characteristics were summarized as frequencies and percentages for categorical variables and as mean±SD for continuous variables. Student's unpaired t-test was used to compare two groups for data with normal distribution. A probability value of $P<0.05$ was considered statistically significant.

RESULTS AND DISCUSSION:

We analysed the clinical, instrumental and laboratory status of patients with asthma.

In patients with asthma and obesity (Group III) the number of asthma exacerbations, ambulance calls, and hospital admissions were significant more in comparison with patients with asthma and overweight (Group II), and patients with asthma and standard weight (Group I): 3.16±0.89; 2.76±1.02; 2.5±0.76 per year (F=21.28; p=0.0000), (F=35.94; p=0.0000), (F=10.03; p=0.0022).

Group III (patients with asthma and obesity) has control asthma symptoms by ACT significant lower in comparison with Group II (patients with asthma and overweight), and Group I (patients with asthma and standard weight). All patients (113/100.0%) with asthma have uncontrolled asthma symptoms. There were significant ACT value differences between Group III, Group II, and Group I: 13.97±0.83; 15.92±0.71 and 16.89±0.73 (F=4.44; p=0.035), (F=6.04; p=0.0165), (F=0.90; p=0.3454). Spirometry results were also significantly differences between Group III, Group II, and Group I. For example, FEV_1 in Group III was 60.45±6.17; in Group II and Group I – 66.03±6.70; 89.30±5.21 (F=7.42; p=0.0013), (F=7.70; p=0.0015), (F=7.20; p=0.0013); Index Tiffeneau was 76.87±3.92; 89.10±4.10; 97.46±3.63 (F=7.46; p=0.0011), (F=9.19; p=0.0004), (F=22.49; p=0.0000).

Adiponectin level was 23.66±11.03 mkg/ml in Group I, 23.40±11.29 mkg/ml in Group II, and 20.70±10.25 mkg/ml in Group III. There are not significantly differences of adiponectin level between compared groups ($p > 0.05$).

In patients with asthma and obesity (Group III) leptin level was significant more in comparison with patients with asthma and overweight (Group II), and patients with asthma and standard weight (Group I): 22.36±1.97; 13.01±1.97, 11.32±1.99 ng/ml (F=9.06; p=0.0002); (F=9.35; p=0.0000), (F=10.47; p=0.0005).

Neuropeptide Y level was 0.31±0.02 ng/ml in Group I (patients with asthma and standard weight), 0.48±0.02 ng/ml in Group II (patients with

asthma and overweight), and 1.19±0.25 ng/ml in Group III (patients with asthma and obesity). Neuropeptide Y level was significantly lower in patients with asthma and standard weight in comparison with patients with asthma and overweight, and patients with asthma and obesity (F=36.69; p=0.0000), (F=8.97; p=0.0037), (F=5.67; p=0.0000) (fig. 1).

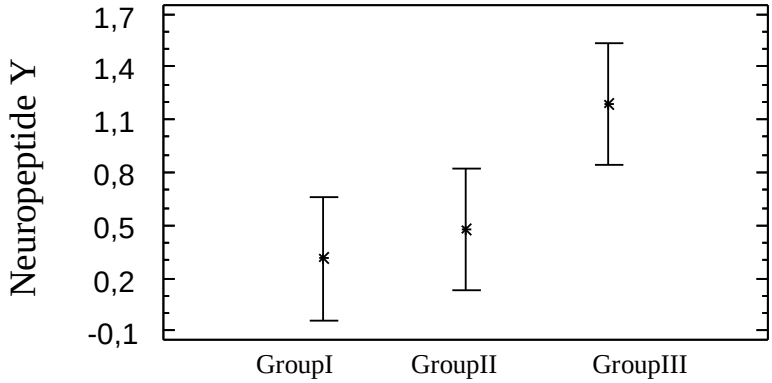

Fig. 1 Means of Neuropeptide Y level and 95.0 Persent LSD Intervals at patients with asthma and standard weight (Group I), patients with asthma and overweight (Group II), and patients with asthma and obesity (Group III)

PerOx level was 877.70±165.29 µmol/l in Group I (patients with asthma and standard weight), 1177.75±163.10 µmol/l in Group II (patients with asthma and overweight), and 1454.69±163.10 µmol/l in Group III (patients with asthma and obesity). There were no significantly differences between PerOx level at patients with asthma and standard weight and patients with asthma and overweight (F=2.34; p=0.1305). There were no significantly differences between PerOx level at patients with asthma and overweight and patients with asthma and obesity (F=1.11; p=0.2957). But PerOx level was significantly lower in patients with asthma and standard weight in comparison with patients with asthma and obesity (F=6.28; p=0.0144).

We carried out the correlation analysis (table 1).
Adiponectin level had average direct correlation with asthma exacerbations (r=0.51; p<0.05), Index Tiffeneau (r=0.51; p<0.05) and moderate direct correlation with MEF_{50} (r=0.37; p<0.05) and PEF (r=0.33; p<0.05), weak direct correlation with MEF_{75} (r=0.24; p<0.05).

Leptin level had average direct correlation with BMI (r=0.56; p<0.05), moderate direct correlation with asthma exacerbations (r=0.45; p<0.05), weak direct correlation with hospital admissions for the past 12 months (r=0.27; p<0.05), weak inverse correlation with FEV_1 (r=-0.28; p<0.05), FVC (r=-0.25; p <0.05), VC (r=-0.29; p<0.05) and MEF_{50} (r=-0.23; p<0.05).

Neuropeptide Y level had strong inverse correlation with VC (r=-0.75; p <0.05), average direct correlation with asthma exacerbations (r=0.55; p<0.05), average inverse correlation with FEV_1 (r=-0.57; p <0.05), MEF_{25} (r=-0.53; p <0.05), moderate inverse correlation with FVC (r=-0.45; p <0.05), Index Tiffeneau (r=-0.32; p<0.05), MEF_{50} (r=-0.41; p <0.05), PEF (r=-0.38; p <0.05), BMI (r=-0.38; p <0.05) and ACT (r=-0.37; p <0.05).

PerOx level had strong direct correlation with BMI (r=0.50; p <0.05), moderate direct correlation with asthma exacerbations (r=0.41; p<0.05), moderate inverse correlation with Index Tiffeneau (r=-0.43; p<0.05).

Table 1:The correlation analysis

	asthma exacerbations	ambulance calls	hospital admissions	FEV_1	FVC	VC	Index Tiffeneau	MEF_{25}	MEF_{50}	MEF_{75}	PEF	BMI	ACT
Adiponectin	**0.51**	0.14	-0.20	0.04	-0.08	-0.07	**0.51**	0.05	**0.37**	**0.24**	**0.33**	-0.06	-0.02
Leptin	**0.45**	0.08	**0.27**	**-0.28**	**-0.25**	**-0.29**	-0.18	-0.11	**-0.23**	-0.15	-0.15	**0.56**	0.13
Neuropeptide Y	**0.55**	0.25	-0.03	**-0.57**	**-0.45**	**-0.75**	**-0.32**	**-0.53**	**-0.41**	-0.18	**-0.38**	**-0.38**	**-0.37**
PerOx	**0.41**	0.09	0.21	0.23	0.22	0.07	**-0.43**	0.18	-0.08	0.04	-0.01	**0.50**	-0.01

Note: data are significant at $p<0.05$; strong correlation is at $r>0.70$; average correlation is at $0.50<r<0.69$; moderate correlation is at $0.30<r<0.49$; weak correlation is at $0.20<r<0.29$, very weak correlation is at $r<0.19$.

Thus, according to results of our investigation patients with asthma and obesity have more often asthma exacerbations, ambulance calls, hospital admissions, uncontrolled asthma symptoms, high Neuropeptide Y level and high PerOx level in comparison with patients with asthma and overweight and patients with asthma and standard weight.

These data is according to modern views on phenotype «asthma with obesity». Obesity is associated with high disease incidences and increased asthma mortality. About these interrelations it was reported both at women, and at men, among different races and all age groups [6-7]. As it was shown in a number of cross-section researches, increase of BMI considerably influences on asthma control and asthma severity [8]. At the moment in asthma pathogenesis at patients with obesity much attention is paid to adipose tissue as endocrine organ developing adipokines, such as leptin and adiponectin. Multiple researches showed that increase of body weight is connected with increase of leptin level and decrease of adiponectin level [9]. Leptin is also found in airways, it is higher at patients with asthma. Leptin level in airways increases depending on leptin level in plasma and BMI [6,10]. Airways epithelial cells express leptin receptors, which number decreases with increase of asthma severity [11].

In our investigation leptin level was significant high at patients with asthma and obesity, had direct correlation with BMI, asthma exacerbations, hospital admissions, and had inverse correlation with spirometry data. Our results demonstrate interrelation between high leptin levels and asthma severity.

In turn, adiponectin has protective action. It is also found in airways, but there no interrelation between adiponectin level in airways and BMI or adiponectin level in plasma [12]. At women higher adiponectin levels in plasma are associated with reduction of asthma development risk, however data of various researches are contradictory [13].

In our investigation direct correlation between adiponectin level and spirometry data demonstrate anti-inflammatory effect of adiponectin.

In recent years special attention is paid to Neuropeptide Y. Neuropeptide Y carries out extensive effects in a human organism by Y1, Y2, Y3, Y4, Y5, Y6 receptors. They are appetite, cardiovascular system, stress, cognitive processes regulation [14-15]. Neuropeptide Y significance is also investigated at the moment. Li S. et al. in the pilot study on mice showed that Neuropeptide Y produced by airways epithelium causes unstriated muscles contraction. It promotes airway hyperresponsiveness [16]. There are insufficient quantity of the researches devoted to studying of interrelation between Neuropeptide Y and asthma. But the results of the researches are demonstrating the negative impact of higher Neuropeptide Y levels on asthma clinical course.

In our investigation Neuropeptide Y level was significant low at patients with asthma and standard weight and significant high at patients with asthma and obesity. At the same time there was inverse correlation between Neuropeptide Y level and spirometry data, ACT, and direct correlation Neuropeptide Y level and PerOx level. It demonstrates the possible pro-inflammatory effect of Neuropeptide Y promoting the poor prognosis and heavier asthma course.

CONCLUSION:

Neuropeptide Y level correlated with asthma control, PerOx level and also with spirometry data, being associated with asthma clinical course. High associated with body weight increase.

Considering increase of Neuropeptide Y level, which associated with body weight increase, interrelation of Neuropeptide Y genotypes with asthma, participation of Y1 receptors in allergic inflammation it will be possible to considered Neuropeptide Y as a predictor of unfavorable course of asthma at patients with obesity.

It is necessary to conduct additional researches to establish the mechanism of Neuropeptide Y influence on asthma pathogenesis and itemize the variant of interrelations between Neuropeptide Y level and asthma clinical course.

Competing interests

The authors declare that they have no competing interests.

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