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PECULIARITIES OF ASTHMA AND INSULIN RESISTANCE DEPENDING ON THE TYPES OF OBESITY

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The purpose of the study was to examine specific clinical and laboratory signs and peculiarities of fatty tissue distribution in patients with bronchial asthma associated with diabetes mellitus, and their effect on respiration function (RF).

Material and methods. 78 patients with noncontrolled severe-course asthma and diabetes mellitus type 2 were studied. The patients were divided into 2 groups, with android and gynoid obesity types, according to anthropometric signs. Blood chemistry panel was performed: glycated hemoglobin (HbAlc), glucose, triglycerides (TG), total cholesterol (CHOL), low density lipoproteins (LDL), high density lipoproteins (HDL), and insulin resistance index (HOMA-IR). Concentrations of total CHOL, TG, high density lipoproteins (HDL), and low density lipoproteins (LDL) were determined using enzymatic method via photometer Solar PM 2111. Expiratory reserve flow (ERF), forced vital capacity (FVC) and forced expiratory volume for 1st second (FEV1) condition was evaluated based on analysis on a spirograph Spirokom (Ukraine). Besides, the control level of asthma symptoms was considered using questionnaires ACQ-5.

Results and discussion. The android type patients were older and had longer disease history versus the patients with gynoid obesity type. The increase of abdominal fat depots in patients with android type obesity was associated with more pronounced changes in carbohydrate-fat metabolism parameters, which was manifested through elevated glucose, TG, LDL serum values and decreased HDL concentrations. HbAlc and HOMA-IR were reliably increased. Assessment of external respiration function via a spirometer showed that FEV1 % FVC % in patient groups with gynoid and android obesity types were different as well. In patients with android obesity type, FEV1 and FVC parameters were reliably lower than in the group with gynoid obesity type. Higher degree of ventilation disorders in individuals with high waist circumference thigh circumference index can be due to fatty tissue central topography type.

Conclusions. The obtained data are indicative of various carbohydrate metabolism disorders, depend-

ence of insulin resistance on obesity type, hormonal balance, and RF decrease. Nevertheless, further complex studies, aimed at investigation of clinical peculiarities and hormonal support of pathological processes in patients with the examined pathology are required.

Keywords: bronchial asthma, diabetes mellitus type 2, obesity.

Research relation to the plans, programs and department research themes. The study was carried out within the research work of the department of propaedeutics of internal medicine № 2 and the nursing of the Kharkiv National Medical University "Factors of formation, progression of various clinical phenotypes of bronchial asthma, COPD and hospitalized pneumonia: peculiarities of the course, comorbid states, their prognosis and prevention" (state registration number 0116U004984).

Introduction. Increase in prevalence of asthma, obesity, and diabetes mellitus type 2 has been observed during the last two decades [4, 11, 17, 22, 23, 25]. Literature data demonstrate that these co-morbid conditions can be associated with anatomic, inflammatory and combined mechanisms. In the last years, the problem of co-morbidity attracts the investigators' attention more and more, as the study of manifestations of combined pathology of various body systems can promote revelation of disease formation mechanisms and development of pathogenetically justified therapy [13].

Irrespective of the mechanisms involved in this process, the presence of diabetes mellitus or asthma in obese patients considerably deteriorates quality of life of this patient cohort [5, 10]. Conducted epidemiological studies have shown contradictory results versus the sufficiently accumulated database of patients with this disease [20]. Some authors showed that the evidence of relation between asthma, obesity, and diabetes mellitus type 2, associated with insulin resistance, were found in an examined group of children with obesity and asthma. Insulin resistance level was 1.5 times higher in children with obesity suffering from

asthma versus obese children without asthma [8, 18, 26, 27].

Recently, these results were replicated in adults, assuring the relation between inflammation of airways and insulin resistance [12, 13]. In examined adult cohort, a direct correlation was found between the body mass index (BMI) and asthma. Diabetes mellitus and obesity can affect asthma course and severity to a similar extent in men and women [9]. It is proven that diabetes and obesity can affect the course and severity of the disease [19, 24]. Further study of this relation would allow revealing the mechanisms of development and progression of this disease in patients.

While progression of epidemiology of obesity and asthma is observed, the mechanism of these relations remains unclear. It has been shown that both mechanical and inflammatory processes take place, associated with the decrease in tidal volume rate in respiratory system [11]. These mechanical changes are related with both body mass index and abdominal obesity. A study conducted in France has shown that metabolic syndrome in asthma patients was associated with pulmonary function disorders subsequent to control of body mass, age, sex, smoking status, alcohol consumption, physical activity in free time, as well as cardiovascular pathology. Hypoxia associated with abdominal obesity persisted in patients even after smoking control. The presence of these mechanical changes can result in increase of systemic hypoxia, as well as make a contribution into systemic inflammation, aggravating the disease [7].

Pulmonary hypertension with hypoventilation and sleep apnea syndrome is deemed to be associated with excessive body weight [2]. It was shown that obesity promoted bronchial hyperreactivity, caused by physical exercise both with and without asthma [11]. There are no reliable evidences of development of excessive body weight as affected by asthma, related with decreased physical activity and use of inhaled glucocorticoids [19].

However, relationship between the changes in the conditions of life and incidence of asthma was revealed. It was shown that improved living conditions contribute not only to obesity growth, but also to morbidity from asthma [1, 16]. This can be attributed to asthma of modernization disease, which increases the risk of nutrition and increase body weight not only limited weight gain [21]. According to several authors, obesity and excessive weight are independent risk factors in asthma, which is noted in global strategy of asthma treatment and prophylaxis 2015 [19].

The purpose of the study was to examine specific clinical and laboratory signs and peculiarities of fatty tissue distribution in patients with asthma associated with diabetes mellitus, and their effect on external respiration function (RF)

Material and methods. In bioethical aspect, the study was conducted in accordance with requirements of the European Convention for the Protection of Vertebrate Animals (Strasbourg, 18.03.1986), European Economic Area Council Directive for the Protection of Vertebrate Animals (Strasbourg, 24.11.1986), the Law of Ukraine "On Medicinal Products", 1996, articles 7, 8, 12, principles of ICH GCP (2008), GLP (2002), "Procedure of Medicinal Products Clinical Trials and Expert Evaluation of Clinical Trial Materials" and "Typical Provision on Ethics Commission", approved by the orders of the Ministry of Health of Ukraine No. 523 dated 12.07.2012 and No. 616 dated 03.08.2012. The study was conducted with minimum psychological losses for the patients. The patients were fully informed of the study methods and scope. The study compliance with modern international and national requirements to bioethical norms was approved by Ethics and Bioethics Commission of Kharkiv National Medical University (meeting minutes № 6 dated 03.06.2015).

The total of 78 patients with non-controlled severecourse asthma and diabetes mellitus type 2 were studied. Anthropometric examinations were conducted in accordance with conventional procedures. Obesity was evaluated according to the classification (WHO, 1997). The patients were divided into 2 groups depending on obesity type according to anthropometric signs. Fat deposition type was established by waist circumference (WC) in accordance with WHO recommendations. The android type included patients with waist circumference (WC)/thigh circumference (TC) index more than 0.9 in men and more than 0.85 in women. The gynoid type included men and women with WC/TC index less than 0.85. The first group diagnosed with gynoid type obesity included 43 patients, and the second group included 35 patients with android type obesity. Duration of the history of asthma in combination with diabetes mellitus type 2 was 2 to 14 years. Hyperglycemia level varied from 6.5 mmol/l to 7.8 mmol/l for 2-6 years. In order to verify the asthma diagnosis and establish the severity and control level of this disease, respiration function (RF) was examined, and the patients were tested using the questionnaire for control of asthma symptoms ACQ-5. GINA 2014 criteria were used in the assessment of the obtained data.

Exclusion criteria were severe endocrine diseases of thyroid gland, hypophysis, diabetes mellitus type 1, anemia, severe decompensated cardiac, hepatic, renal failure. Besides anthropometric ones, biochemical parameters were tested – HbAlc %, glucose, triglycerides (TG), cholesterol (CHOL), low density lipoproteins (LDL), high density lipoproteins (HDL). HOMA-IR index was calculated for diagnostics of insulin resistance. Concentrations of total CHOL, TG, HDL, and LDL were determined using enzymatic method through the photometer Solar PM 2111.

State of RF, FVC and FEV1 condition was evaluated based on analysis of forced expiration curve registered on a spirograph Spìrokom (Ukraine). Besides, the control level of asthma symptoms was considered using questionnaires ACQ-5. Pearson linear correlation coefficient (r) was used in statistical data processing for evaluation of interrelation between parameters. The differences were deemed statistically significant in p < 0.05. Statistical analysis was performed using the software package (MS Office 2007).

Results and discussion. The tested parameters showed almost no differences in men and women groups ($p \ge 0.05$), which is why we continued the analysis with patient groups including individuals of different sex.

Data analysis has shown that the android type patients were older and had longer disease history versus the patients with gynoid type obesity (table).

Table – Results of anthropometric, biochemical and functional tests depending on obesity type

Parameter	Gynoid type n = 43	Android type n = 35
Age, years	47,3 ± 2,45	52,31-3.12
Duration of disease history	8.21 ± 1.15	12,21 ± 2,01 *
BMI	32.3 ± 1.9	до 33,9 ± 2.3
WC, cm	$95,7 \pm 8,1$	107,1 ± 11.3 *
HW, cm	120 ± 12,9	117,9 ± 10.3
WC/HW	0.81 ± 0.01	0.94 ± 0,04 *
Glucose, mmol/l	4.45 ± 0.47	5.02 ± 0,34 *
HbAlc	$5,68 \pm 0,$	7.54 ± 0,34 *
HOMA-IR index	$3,67 \pm 0,36$	5.34 ± 0,45 *
Triglycerides, mmol/l	1.17 ± 0,41	1, 92 ± 0,55 *
HDL, mmol/l	1.45 ± 0,14	1.12 ± 0,01 *
LDL, mmol/l	3.12 ± 0.33	4.01 0,54 ± *
FEV1%	67 ± 5.23	57,68 3,56 ± *
FVC%	62,34 ± 4,54	58,71 ± 5.12 *
ACQ-5	16.7 ± 2.31	13,5 ± 1 *

Note: $p \ge 0.05$ – reliability of differences between the examined groups.

The increase of abdominal fat depots in patients with android type obesity was associated with more pronounced changes in carbohydrate-fat metabolism parameters, which was manifested through elevated glucose, triglycerides, LDL serum values and decreased HDL concentrations. HbAlc and Homeostasis Model Assesment of Insulin Resistance (HOMA-IR) index were reliably increased. According to many investigators, morphological and functional peculiarities of visceral fatty tissue are important factors in development of obesity complications [1, 3, 12]. Adipocytes of the visceral region compared to the adipocytes gluteofemoral region have a higher density and sensitivity to β 1, β 2, and β 3 adreno receptors, steroid and

androgen receptors, reducing the number and affinity to $\alpha 2$ adrenoreceptors and receptors for insulin. This provides an increased sensitivity of visceral adipocytes to the lipolytic effects of catecholamines and a higher mobilization of free fatty acids in the portal system [6, 15, 14, 16].

Assessment of external respiration function showed that FEV1 %, FVC % in patient groups with gynoid and android obesity types were also different. In patients with android obesity type, FEV1 and FVC parameters were reliably lower than in the group with gynoid obesity type. Higher degree of ventilation disorders in individuals with high waist circumference /hip width (WC/TC) index can be due to fatty tissue central topography type. It is known that fat deposition in thoracic and abdominal cavities in men is associated with decreased of FVC % and, to a lower degree, FEV1. Correlation analysis of the values of parameters registered during anthropometric examination of patients has shown that, in general, anthropometric indexes are reliably increased in the age-specific sample.

The highest values of correlation coefficients between age and WC/HW ratio were found (r = 0.52, p < 0.05), which are indicative of the increase of fat depots. Thus, one of the most sensitive anthropometric parameters associated with age is WC/HW ratio, which makes sense, as the patient cohort with the high WC/HW ratio has longer disease history.

Correlation analysis of RF and biochemical parameters: blood levels of glucose (r = 0.26, p < 0.05), TG (r = 0.27, p < 0.051), HOMA-IR index (r = 0.27, p < 0.05), ACQ(r = 0.33, p < 0.05) confirms essential influence of this factor in the change of carbohydrate-fat metabolism and quality of life. RF effect on insulin resistance is evidenced by negative correlation with HOMA-IR index (r = -0.20, p < 0.05).

Conclusions

- Factors indicating individualized asthma morbidity risk can include excessive body weight caused by disturbance of muscular and fatty body components, as well as centralization of fat deposits.
- Bronchial hyperreactivity is associated with inflammation and, possibly, hormonal balance and carbohydrate-fat metabolism disorders.
- Constitutional changes result in more pronounced respiratory disorders in asthma patients with diabetes mellitus type 2 and obesity.

Nevertheless, **further complex studies** aimed at investigation of clinical peculiarities and hormonal support of pathological processes in patients with the examined pathology are required.

Abbreviations: HOMA-IR – Homeostasis Model Assesment of Insulin; Resistance RF – respiratory function; FEV1 – Forced expiratory volume in 1 sec.; FVC – Forced vital capacity; CHOL – cholesterol; TG – triglycerides; HDL – high density lipoproteins; LDL – low density lipoproteins

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ОСОБЛИВОСТІ БРОНХІАЛЬНОЇ АСТМИ ТА ІНСУЛІНОРЕЗИСТЕНТНОСТІ В ЗАЛЕЖНОСТІ ВІД ТИПУ ОЖИРІННЯ

€рьоменко Г. В.

Резюме. *Метою роботи* було вивчити специфічні клінічні та лабораторні ознаки та особливості розподілу жирової тканини у пацієнтів з бронхіальною астмою, поєднаною з цукровим діабетом, та їх вплив на функцію зовнішнього дихання.

Матеріали і методи: Всього обстежено 78 пацієнтів з бронхіальною астмою тяжкого перебігу та цукровим діабетом типу 2. Пацієнтів було розділено на групи за андроїдними та гінеоїдними типами ожиріння. У крові визначали вміст: HbAlc, глюкози, тригліцеридів, холестерину загального, ліпопротеїнів низької щільності, ліпопротеїнів високої щільності, індексу інсулінорезистентності (HOMA-IR) фотометричним методом. Величини форсованої життєвої ємності легенів та форсованого видиху за 1-у секунду оцінено спірографічно.

Результати і обаоворення. Пацієнти андроїдного типу були старшими та мали більш тривалу історію захворювання у порівнянні з пацієнтами з гінеоїдним ожирінням. Зростання депо жиру у черевній порожнині в пацієнтів з ожирінням андроїдного типу пов'язано з більш вираженими змінами параметрів метаболізму вуглеводів і жирів із підвищенням рівня глюкози, тригліцеридів, ліпопротеїнів низької щільності та зниженням рівня ліпопротеїнів високої щільності, концентрації HbAlc та HOMA-IR були достовірно підвищені. У пацієнтів з андроїдним типом ожиріння показники форсованого видиху за 1-у секунду, форсованої життєвої ємності легенів були нижчими, ніж у групі з гіноїдним типом ожиріння.

Висновки. Встановлено різні розлади вуглеводного метаболізму, залежність резистентності до інсуліну від типу ожиріння, гормонального балансу та порушення функції зовнішнього дихання.

Ключові слова: бронхіальна астма, цукровий діабет 2 типу, ожиріння.

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ОСОБЕННОСТИ БРОНХИАЛЬНОЙ АСТМЫ И ИНСУЛИНОРЕЗИСТЕНТНОСТИ В ЗАВИСИМОСТИ ОТ ТИПА ОЖИРЕНИЯ

Еременко Г. В.

Резюме. Цель – изучить специфические клинические и лабораторные признаки и особенности распределения жировой ткани у пациентов с бронхиальной астмой, совмещенной с сахарным диабетом, и их влияние на функцию внешнего дыхания.

Материалы и методы. Всего обследовано 78 пациентов с бронхиальной астмой тяжелого течения и сахарным диабетом типа 2. Пациенты были разделены на группы по андроидному и гинеоидному типам ожирения. В крови определяли содержание: HbAlc, глюкозы, триглицеридов, холестерина общего, липопротеинов низкой плотности, липопротеинов высокой плотности, индекса инсулинорезистентности (HOMA-IR) фотометрическим методом. Величины форсированной жизненной емкости легких и форсированного выдоха за первую секунду оценены спирографически.

Результаты. Пациенты андроидного типа были старше и имели более длительную историю заболевания по сравнению с пациентами с гинеоидним ожирением. Рост депо жира в брюшной полости у пациентов с ожирением андроидного типа связано с более выраженными изменениями параметров метаболизма углеводов и жиров с повышением уровня глюкозы, триглицеридов, липопротеинов низкой плотности и снижением уровня липопротеинов высокой плотности, концентрации HbAlc и HOMA-IR были достоверно повышены. У пациентов с андроидным типом ожирения показатели форсированного выдоха за первую секунду, форсированной жизненной емкости легких были ниже, чем в группе с гиноидным типом ожирения.

Выводы. Установлены различные расстройства углеводного обмена, зависимость резистентности к инсулину от типа ожирения, гормонального баланса и нарушения функции внешнего дыхания.

Ключевые слова: бронхиальная астма, сахарный диабет 2 типа, ожирение.

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