UDC 616.248-002.1-008.9-056.25 https://doi.org/10.26641/2307-0404.2022.1.254359

T.V. Bezditko,
G.V. Yeryomenko *

FEATURES OF CARBOHYDRATE METABOLISM IN ASTHMA PATIENTS WITH OBESITY

Kharkiv National Medical University
Nauky av., 4, Kharkiv, 61022, Ukraine
Харківський національний медичний університет
пр. Науки, 4, Харків, 61022, Україна
**e-mail: galyna0512@ukr.net*

Цитування: Медичні перспективи. 2022. Т. 27, № 1. С. 92-96
Cited: Medicni perspektivi. 2022;27(1):92-96

Key words: *asthma, metabolic disorders, obesity*
Ключові слова: *бронхіальна астма, метаболічні розлади, ожиріння*
Ключевые слова: *бронхиальная астма, метаболические нарушения, ожирение*

Abstract. Features of carbohydrate metabolism in asthma patients with obesity. Bezditko T.V., Yeryomenko G.V. *Asthma (As) and metabolic disturbances are widespread and socially significant states, obesity (Ob) being also one of them. The comorbidity of As and Ob both affects physiological mechanisms of bronchial obstruction syndrome, the course and prognosis of these two diseases and significantly complicates their treatment. A combination of changes in ventilation and a complex architectonics of the bronchi may contribute to worsening control over As. The performed study deals with the problem of early diagnosis and progression of the course in patients with As and Ob comorbidity. The study involved 62 patients with As. Of them, there were 24 cases with the normal body mass (Group I) and 38 cases with As+Ob (Group II). Along with evaluation of respiratory function values and anthropometric examination, all the patients underwent controlling of carbohydrate metabolism. It was found out that As combined with Ob were accompanied by a cascade of metabolic disorders: hyperinsulinemia, insulin resistance, and higher levels of HbA1c and fasting glucose versus the control group ($p<0.05$). According to correlation analysis data, in Group II negative correlations between values of HOMA-IR and $40\leq FEV_1<50\%$ ($r= -0.53$; $p<0.05$), HOMA-IR and $50\%\leq FEV_1<60\%$ ($r= -0.49$; $p<0.05$), insulin level and $40\leq FEV_1<50\%$ ($r= -0.42$; $p<0.05$) as well as a positive correlation between HPMA-IR value and BMI ($r=0.39$; $p<0.05$) were revealed. Patients with As, degree 1 Ob and a disorder of $FEV_1\geq 60\%$ revealed hyperinsulinemia and an increased level of insulin resistance index; this fact can be regarded as a prognostic criterion for an improved diagnosis, prognostication of unfavorable consequences and optimization of treatment approaches. In order to detect carbohydrate metabolic disturbances in patients with As+Ob it is not enough to determine levels of glucose and glycated hemoglobin. The necessity of studying insulin resistance and insulin level for systematization and determination of development of concomitant metabolic disturbances in patients to whom iGCS are prescribed is proved.*

Реферат. Особенности углеводного обмена у больных бронхиальной астмой с ожирением. Бездетко Т.В., Ерёменко Г.В. *Бронхиальная астма (БА) и метаболические нарушения – широко распространенные и социально значимые состояния, как и ожирение. Коморбидность при БА и ожирении (Ож) негативно влияет как на физиологичные механизмы синдрома бронхиальной обструкции, течение и прогноз обоих заболеваний, так и существенно усложняет лечение. Сочетание комбинации изменений вентиляции и сложной архитектоники бронхов, вероятно, способствует ухудшению контроля над астмой. Проведенное исследование посвящено проблеме ранней диагностики и прогрессированию состояния у больных с коморбидным течением БА в сочетании с Ож. В исследование были включены 62 пациента, страдающих БА, среди которых с нормальной массой тела было 24 (I группа) и пациенты с БА, сочетанной с Ож, – 38 (II группа). У всех исследуемых наряду с измерением показателей функции внешнего дыхания и антропологическим обследованием был проведен контроль углеводного обмена. Установлено, что БА в сочетании с Ож сопровождается каскадом метаболических нарушений: гиперинсулинемией, инсулинорезистентностью, повышенным уровнем HbA1c и глюкозы натощак в сравнении с группой контроля ($p<0,05$). По данным корреляционного анализа, в группе 2 были выявлены обратные корреляционные связи между показателями HOMA-IR и $40\leq ОФВ_1<50\%$ ($r= -0,53$; $p<0,05$), HOMA-IR и $50\%\leq ОФВ_1<60\%$ ($r= -0,49$; $p<0,05$), уровнем инсулина и $40\leq ОФВ_1<50\%$ ($r= -0,42$; $p<0,05$), а также прямую корреляционную связь между показателем HOMA-IR и ИМТ ($r=0,39$; $p<0,05$). У больных БА с Ож I ст. и нарушением $ОФВ_1\geq 60\%$ наблюдались гиперинсулинемия и повышение уровня индекса инсулинорезистентности, что можно расценивать как прогностический критерий улучшения*

диагностики, прогнозирования неблагоприятных последствий и оптимизации лечебных подходов. Для определения нарушений углеводного обмена у больных БА+Ож недостаточно определения глюкозы и гликированного гемоглобина. Доказана необходимость исследования инсулинорезистентности и уровня инсулина для систематизации и определения развития сопутствующих метаболических нарушений у больных, которым назначают ИГКС.

Bronchial asthma (BA) and metabolic disorders are widespread and socially significant conditions. Literary data indicate that the development of such accompanying pathologies as arterial hypertension, diabetes, coronary heart disease in patients with BA, especially in the elderly, is often also associated with obesity or excess body weight [1, 12, 13]. Some authors even distinguish a special phenotype of the disease – BA with obesity, which is characterized by a later onset of clinical symptoms, a lower prevalence of atopy, a severe uncontrolled course and resistance to basic therapy [7, 11].

Most likely, ventilation disorders in BA with obesity are the result of pathomorphological manifestations of both diseases, which leads to worsening of control over BA symptoms [12, 13]. It should be noted that if, in general, only 20% of people with BA have control over their symptoms [10], then in the presence of accompanying obesity, the indicator decreases even more [2, 9]. In addition, metabolic imbalance in obesity, insufficient physical activity of patients, and an increase in their body weight can lead to remodeling of the respiratory tract [5]. The accumulation of visceral fat plays a major role in the formation of metabolic shifts, metabolic and cardiovascular complications associated with obesity [4, 8, 9].

Understanding the clinical and pathophysiological relationships between bronchial obstruction and pathological changes in the body caused by obesity is the first step to improving the results of patient management over a long period of time, and assessing the essence of the cause-and-effect relationships between the development of obesity and BA necessary to determine the further tactics of managing such a category of persons. In addition, according to the current recommendations of the European Respiratory Society and WHO, the principle of phenoendotyping is an integral part of a personalized approach to the diagnosis and treatment of patients with asthma [3, 13].

The purpose of the study is to establish the pathophysiological factors of the influence of excess body weight and obesity on the course of this disease based on the results of a comprehensive examination of patients with bronchial asthma.

MATERIALS AND METHODS OF RESEARCH

62 patients with moderate and severe course of partially controlled asthma aged 46.3±2.8 years, including 25 (40.32%) men and 37 (59.67%) women took part in the study. The duration of BA was 22.3±3.2 years, the manifestation of the disease mostly occurred at the age of 18-35 years.

The study was approved by the commission on biomedical ethics of the Kharkiv National Medical University and was conducted in accordance with the principles of bioethics set forth in the Helsinki Declaration "Ethical Principles of Medical Research Involving Humans" and the "General Declaration on Bioethics and Human Rights (UNESCO)".

Patients were divided into two groups depending on the presence of obesity. Group 1 included 24 individuals aged 44.2±2.7 years, of whom 11 (45.84%) were men and 13 (54.16%) were non-obese women (BMI was 21.4 [18, 2; 23.6] kg/m^2), and group 2 included 38 people aged 47.5±1.7 years, of whom 13 (34.21%) were men and 25 (65.79%) were women, with alimentary and constitutional obesity (BMI was 31.9 [29.3; 32.6] kg/m^2, which corresponds to obesity of the 1st degree; duration of obesity was 4.8±0.2 years). The groups of examinees did not differ in age and gender ($p>0.05$). The level of FEV_1 in the general group of patients was 65.9 [63.4; 74.1]% of the proper value.

In group 1, the frequency of hospitalization was 1.72±0.21 times per year, in group 2 – 2.34±0.12 times per year. During the last six years, all patients received basic therapy – inhaled glucocorticosteroids/long-acting ß2-agonists (IGCS/LABA) in a dose of 160/4.5 mcg 2 times a day, and in case of deterioration – additional short-acting ß2-agonists (SABA). The average inhalation dose of SABA in group 1 was 2.24±0.11times/day, in group 2 – 2.95±0.45 times/day.

The control group consisted of 20 practically healthy people of similar age and gender: men – 8 (40.0%), women – 12 (60.0%), age – 49.3±2.4 years, BMI – 19.2 [18.2; 20.1] kg/m^2.

The ventilation function of the lungs was assessed using the “SPIROCOM” spirographic complex (KhAI-Med, Ukraine): the forced vital capacity of the lungs (FVC), the forced expiratory volume in the first second (FEV_1) and the FEV_1/FVC ratio were determined. An anthropometric survey was conducted. To control indicators of carbohydrate metabolism, the level of glucose in the fasting blood serum, glycosylated hemoglobin (HbA1c), the concentration of insulin in the serum was determined using the "Insulin ELISA" kits ("DRG Diagnostics",

Germany), insulin resistance – according to the HOMA model IR (HOMA-IR = insulin concentration (μU/mL) × glucose (mmol/L)/22.5).

Statistical processing of the obtained results was carried out using standard methods and the "SPSS 19" software product (IBM, USA). Quantitative indicators were calculated by median (Me) and 25th and 75th percentiles ([25%; 75%]). Differences between independent samples were calculated using the Mann-Whitney U-test. Relationships between indicators were evaluated using the Spearman test (r) and the Chaddock scale.

RESULTS AND DISCUSSION

A decrease in volume and velocity indicators during the study of the ventilatory function of the lungs was observed in all patients. When the level of FVC in the control group was 98.3 [95.4; 99.5]% of the appropriate value, then in group 1 – 83.3 [77.4; 88.5]% of the appropriate value, and in group 2 – 67.6 [60.3; 69.8]% of the appropriate value, which was 1.18 and 1.45 times lower than in group 1 ($p<0.05$) and the control group ($p<0.05$), respectively ($p<0.05$). The level of FEV_1 in group 1 was 72.0 [70.3; 74.1]% of the appropriate value, in group 2 – 59.8 [49.8; 63.2]% of the appropriate value, which was 1.20 times lower than the indicator in group 1 and 1.43 times lower than the indicator in the control group (85.4 [82.1; 88.3]% of the appropriate values) ($p<0.05$). The ratio of FEV_1/FVC in group 1 was 0.86 [0.83; 0.87], in group 2 – 0.77 [0.75; 0.78], in the control group – 0.86 [0.84; 0.88] ($p<0.05$).

The levels of indicators of carbohydrate metabolism in groups of examined patients are presented in Table 1.

Table 1

Indicators of carbohydrate metabolism in groups of examined patients

Indicators	Groups of examined			p
	1 (n=24)	2 (n=38)	контрольна (n=20)	
HOMA-IR	**3.01 [2.45; 4.23]**	**6.31 [5.76; 6.59]**	**2.12 [1.87; 2.16]**	**p1-c>0.05 p2-c<0.05 p1-2<0.05**
HbA1c, %	**5.06 [4.83; 5.26]**	**6.69 [6.15; 6.91]**	**4.32 [4.28; 4.56]**	**p1-c>0.05 p2-c<0.05 p1-2<0.05**
Fasting glucose level, mmol/l	**4.85 [4.83; 5.22]**	**6.22 [5.78; 6.99]**	**4.93 [4.83; 5.22]**	**p1-c>0.05 p2-c<0.05 p1-2<0.05**
Fasting blood insulin level, μU/mL	**6.30 [5.81; 6.22]**	**22.8 [20.5; 26.5]**	**8.32 [7.47; 8.56]**	**p1-c>0.05 p2-c<0.05 p1-2<0.05**

Notes: p – significance of differences; 1, 2 – numbers of groups; c – control group.

The analysis of the obtained results showed that in group 1 the levels of indicators of carbohydrate metabolism did not differ from the levels of indicators of the control group ($p>0.05$). However, in group 2, the glucose level was significantly higher than in group 1 and the control group ($p<0.05$); diabetic level of HbA1c was determined only in 3 (12.5%) patients of group 1 and in 16 (31.6%) patients of group 2; the level of insulin in group 2 was 3.62 times higher than in group 1 ($p<0.05$); and the NOMA-IR index exceeded the level of the indicator in group 1 by 2.09 times ($p<0.05$). In addition, it should be noted that hyperinsulinemia, insulin resistance and increased levels of HbA1c and fasting glucose compared to the control group were found in all patients of group 2 ($p<0.05$).

To determine possible differences between the indicators of patients with different indicators of bronchial obstruction and carbohydrate metabolism, patients of group 2 were divided into three subgroups depending on the level of FEV_1: subgroup A – with an indicator level of $40\% \leq FEV_1 < 50\%$ of the appropriate value (average level – 46.3 [44.3; 49.3] % of the appropriate value); subgroup B – with an indicator level of $50\% \leq FEV_1 < 60\%$ of the appropriate value (55.8 [53.2; 59.3]% of the appropriate value), subgroup C – with a level of $FEV_1 \geq 60\%$ of the appropriate value (63.4 [61.3; 65.8]% of the appropriate value). The levels of indicators of carbohydrate metabolism and BMI in subgroups A, B and C are presented in Table 2.

Table 2

Levels of carbohydrate metabolism and BMI in subgroups A, B, C

Indicators	Control group	Subgroups of patients of group 2			
		A (n=11)	B (n=15)	C (n=12)	p
HOMA-IR	**2.12 [1.87; 2.16]**	**6.48 [6.31; 6.56]**	**6.33 [6.22; 6.45]**	**6.12 [5.56; 6.21]**	$p_{Ac}<0.05$ $p_{Bск}<0.05$ $p_{Cск}<0.05$ $p_{A-B}>0.05$ $p_{A-C}>0.05$ $p_{B-C}>0.05$
HbA1c, %	**4.32 [4.28; 4.56]**	**6.92 [6.66; 6.99]**	**6.65 [6.25; 6.73]**	**6.50 [6.01; 6.66]**	$p_{A-c}<0.05$ $p_{B-c}<0.05$ $p_{C-c}<0.05$ $p_{A-B}>0.05$ $p_{A-C}>0.05$ $p_{B-C}>0.05$
Fasting blood glucose level, mmol/l	**4.93 [4.83; 5.22]**	**6.88 [6.72; 6.99]**	**6.23 [6.12; 6.33]**	**5.56 [5.32; 5.73]**	$p_{A-c}<0.05$ $p_{B-c}<0.05$ $p_{C-c}<0.05$ $p_{A-B}>0.05$ $p_{A-C}>0.05$ $p_{B-C}<0.05$
Fasting blood insulin level, μU/mL	**8.32 [7.47; 8.56]**	**21.1 [20.6; 21.9]**	**22.8 [21.3; 24.2]**	**24.7 [22.3; 26.4]**	$p_{Aск}<0.05$ $p_{B-c}<0.05$ $p_{Cск}<0.05$ $p_{A-B}>0.05$ $p_{A-C}<0.05$ $p_{B-C}>0.05$
BMI, kg/m^2	**19.2 [18.2; 20.1]**	**32.1 [31.5; 33.1]**	**31.1 [29.9; 31.6]**	**29.1 [28.2; 30.3]**	$p_{Aск}<0.05$ $p_{Bск}<0.05$ $p_{C-c}<0.05$ $p_{A-B}>0.05$ $p_{A-C}>0.05$ $p_{B-C}>0.05$

Notes: p – significance of differences; A, B, C – groups of patients.

The analysis of the obtained results in subgroups showed that HOMA-IR index, HbA1c, and fasting glucose were elevated in all subgroups relative to the control group ($p<0.05$) and in the comparison of carbohydrate metabolism indicators between subgroups, significant changes between the glucose level in subgroups B and C ($p<0.05$) and the level of blood insulin in subgroups A and C ($p<0.05$) were found. BMI indicators in subgroups A, B and C were identical ($p>0.05$) (Table 2).

According to correlation analysis, in group 2 inverse correlations were found between HOMA-IR and $40\leq FEV_1<50\%$ ($r= -0.53$; $p<0.05$), HOMA-IR and $50\%\leq FEV_1<60\%$ ($r= -0.49$; $p<0.05$), insulin level and $40\leq FEV_1<50\%$ ($r= -0.42$; $p<0.05$), as well as a direct correlation between the indicator HOMA-IR and BMI ($r=0.39$; $p<0.05$).

CONCLUSIONS

1. Patients with bronchial asthma with obesity of the first degree with a disorder of FEV1≥60% had hyperinsulinemia and an increase in the level of the index of insulin resistance, which can be considered as a prognostic criterion for improving diagnostics, predicting adverse consequences and optimizing treatment approaches.

2. Determination of fasting glucose and glycosylated hemoglobin is not enough to determine disorders of carbohydrate metabolism in patients with bronchial asthma with obesity. The necessity of researching insulin resistance and insulin levels to systematize and determine the development of concomitant metabolic disorders in patients prescribed inhaled glucocorticosteroids has been proven.

Contributors:

Bezditko T.V. – resources, conceptualization, methodology, writing – reviewing and editing;

Yeryomenko G.V. – research, methodology, data curation, formal analysis, visualization, research, writing – original draft, management.

Funding. This research received no external funding.

Conflict of interests. The authors declare no conflict of interest.

REFERENCES

1. Konopkina LI. [Features of therapy in patients with bronchoobstructive diseases in conjunction with diabetes and obesity]. Astma ta alerhiia. 2016;4:61-62. Russian. Available from: http://www.ifp.kiev.ua/doc/journals/aa/16/pdf16-4/61.pdf

2. Pertseva TA. [Unresolved issues of asthma therapy]. Astma ta alerhiia. 2017;4:37-38. Russian. Available from: http://nbuv.gov.ua/UJRN/astm_2017_4_9

3. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. [Internet]; 2019 [cited 2020 Apr 16]. Available from: https://ginasthma.org/wp-content/uploads/2019/06/GINA-2019-main-report-June-2019-wms.pdf

4. Bernhardt V, Tony GB. Exertional dyspnoea in obesity. European respiratory review. 2016;25(142):487-95. doi: https://doi.org/10.1183/16000617.0081-2016

5. De Santi F, Zoppini G, Locatelli F, Finocchio E, Cappa V, Dauriz M, Verlato G. Type 2 diabetes is associated with an increased prevalence of respiratory symptoms as compared to the general population. PMID: 28716044 PMCID: PMC5513377. doi: https://doi.org/10.1186/s12890-017-0443-1

6. Dixon AE, Peters U. The effect of obesity on lung function. Expert Rev Respir Med. 2018 Sep;12(9):755-67. doi: https://doi.org/10.1080/17476348.2018.1506331

7. Maniscalco M, Fuschillo S, Paris D, Cutignanob A, Sanduzzic A, Mottabet A. Clinical metabolomics of exhaled breath condensate in chronic respiratory diseases. Adv Clin Chem. 2019;88:121-49. doi: https://doi.org/10.1016/bs.acc.2018.10.002

8. Muc M, Mota-Pinto A, Padez C. Association between obesity and asthma – Epidemiology, pathophysiology and clinical profile. Nutr Res Rev. 2016;29(2):194-201. doi: https://doi.org/10.1017/S0954422416000111

9. Pradhan AD. Sex differences in the metabolic syndrome: Implications for cardiovascular health in women. Clinical Chemistry. 2014;60(1):44-52. doi: https://doi.org/10.1373/clinchem.2013.202549

10. Price D, Fletcher M, Van Der Molen T. Asthma control and management in 8,000 European patients: The Recognise Asthma and Link to Symptoms and Experience (REALISE) survey. NPJ Prim Care Respir Med. 2014;24:14009. doi: https://doi.org/10.1038/npjpcrm.2014.9

11. Sharma N, Akkoyunlu M, Rabin RL. Macrophages – common culprit in obesity and asthma. European Journal of Allergy and Clinical Immunology. 2018;73:1196-205. doi: https://doi.org/10.1111/all.13369

12. Sun Y, Milne S, Jaw JE, et al. BMI is associated with FEV1 decline in chronic obstructive pulmonary disease: a meta-analysis of clinical trials. Respiratory Research. 2019;20(1):236. doi: https://doi.org/10.1186/s12931-019-1209-5

13. Suratt BT, Ubags NDJ, Rastogi D, Tantisira KG, Marsland BJ, Petrache I, et al. An Official American Thoracic Society Workshop Report: Obesity and Metabolism. An Emerging Frontier in Lung Health and Disease. Ann Am Thorac Soc. 2017 Jun;14(6):1050-9. doi: https://doi.org/10.1513/AnnalsATS.201703-263WS

Стаття надійшла до редакції
08.07.2020