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Features of Metabologram at Patients with Coronary Heart Disease and Obesity

ABSTRACT

Features of metabologram in patients with coronary heart disease and obesity according to indirect calorimetry were studied. It was revealed that the respiratory quotient (RQ) was significantly higher in patients with angina and obesity. Elevated levels of RQ can be seen as a predictor of cardiovascular risk and reflect a violation of fat oxidation.

Keywords: coronary heart disease, obesity, respiratory quotient, indirect calorimetry, fat oxidation, energy expenditure at rest.

INTRODUCTION

Cardiovascular disease (CVD) and obesity are actual problems of modern medicine. Coronary heart disease (CHD) is a major cause of morbidity and mortality worldwide [16]. More than 250 cardiovascular risk factors described in the literature [1, 2], one of which is obesity. Obesity is associated with the development of hypertension, dyslipidemia, type 2 diabetes, and becomes an independent risk factor for CHD at a BMI over 35 kg / m². [4] It is well known that an imbalance between energy intake and energy expenditure leads to weight gain. However, macronutrient oxidation may also play an important role in the development of obesity and associated diseases.

Metabolic status includes data about resting metabolic rate (RMR) and respiratory quotient (RQ) and could be evaluated with the indirect calorimetry. RQ - the ratio between oxygen consumption and carbon dioxide production reflecting the utilization of the macronutrients in a subject. RQ depends on the ratio of oxidized energy substrates (protein, fat and carbohydrate). The endogenous fat stores oxidation is associated to a decreased RQ, while a high level of RQ reflects the trend of reducing fat oxidation by increasing carbohydrate oxidation. The evaluation of macronutrient oxidation in patients with CVD and obesity is very important in connection with the results of recent studies. It was found that the reduced fat oxidation associated with a high rate of subsequent weight gain [10], hypertension [8], increased Carotid Intima-Media Thickness [11] and left ventricular concentric remodeling [14].

The aim of this study - to research the features of the metabolic status of patients with coronary heart disease and obesity according to indirect calorimetry.

MATERIALS AND METHODS

The study included 224 patients (89 men and 135 women) with class I-III obesity aged from 34 till 80 years. Patients were examined in the department of cardiovascular disease at the clinic of Institute of nutrition from October 2010 to August 2014. Patients were divided into 2 groups. The main group consisted of 112 obese patients with stable angina pectoris (I-IV functional class). The control group also included 112 obese individuals without concomitant angina. Patients in both groups were similar on clinical characteristics and receiving the same pharmacological and dietary treatment. Pharmacological treatment included angiotensin-converting enzyme inhibitor

or angiotensin receptor II, beta-blockers, calcium antagonists, peripheral prolonged action, aldosterone antagonists, acetylsalicylic acid.

The study excluded patients with clinically significant concomitant diseases (cancer, inflammatory diseases, anemia), endocrine disorders, organic cardiac disease (heart disease, cardiomyopathy), patients with myocardial infarction during the last year, and patients taking drugs that affect metabolic processes. Body composition was measured by bioelectrical impedance analysis (InBody 520, Korea). The metabolic status assessed by indirect calorimetry («Quark», company COSMED, Italy). Statistical analysis was performed in the program Statistica for Windows 6.1. Data are presented as the mean and standard deviations ($M \pm SD$). Between-group comparisons were analyzed with a Mann-Whitney U test, χ^2 -test. Relations between variables were sought by correlation analysis (Spearman's r). Statistical significance was set at $p < 0,05$.

RESULTS AND DISCUSSION

The patients in both groups were comparable by sex, height and body composition. Thus, the patients had no significant differences in body weight, body mass index, lean and fat body mass, muscle mass and total body water (Table 1), but there were differences in age ($p = 0,000$). The average age in the group of obese patients with angina pectoris was significantly higher - $59,44 \pm 7,9$ years than in obese patients without concomitant angina - $51,93 \pm 9,4$ years. This data can be explained by the fact that age is an important risk factor for CHD and frequency CHD increases with age. It was found that patients in the main group had greater area of the visceral fat ($243,8 \pm 49,0 \text{ cm}^2$) compared to patients in the control group ($229,6 \pm 57 \text{ cm}^2$), but these differences were not statistically significant ($p = 0,06$).

Data of resting metabolic rate and protein oxidation had no significant differences between groups. But RQ was significantly higher in obese patients with angina pectoris: $0,829 \pm 0,08$ vs. $0,796 \pm 0,05$ ($p = 0,003$). Since RQ reflects the ratio of fat and carbohydrate oxidation, the difference in RQ between the two groups resulted in significant differences in the rate of fat oxidation ($p = 0,000$) and carbohydrate oxidation ($p = 0,073$). Obese patients with angina pectoris had decreased fat oxidation ($96,91 \pm 59,0 \text{ g/day}$) and increased carbohydrate oxidation ($197,3 \pm 150,0 \text{ g/day}$) compared with control patients ($124,16 \pm 51,0 \text{ g/day}$ and $158,8 \pm 113 \text{ g/day}$, respectively) ($p < 0,05$). Trend continues in the analysis of macronutrients utilization in the percentage of RMR. The groups were comparable by the percentage of protein oxidation ($14,89 \pm 5,8\%$ against $14,87 \pm 3,9\%$, $p = 0,627$), but the percentage of fat oxidation ($46,34 \pm 25\%$ versus $56,55 \pm 18\%$, $p = 0,002$) and carbohydrate oxidation ($39,92 \pm 27\%$ versus $32,32 \pm 20\%$, $p = 0,048$) in the main and control groups were significantly different.

In our study the fat oxidation does not depend on the of the body composition, since the group did not differ in body mass index, as well as the fat and lean body mass. These findings are consistent with studies B. Ukropcova et al [6], which revealed that the differences in the metabolic status does not depend on the percentage of fat mass. They have been suggested that the level of fat oxidation is genetically determined, and not a result of obesity or insulin resistance.

On RQ, and on the fat oxidation can influence energy balance, macronutrient composition of the diet and the availability of substrate oxidation in the blood plasma (glucose, fatty acids) [7]. Fatty acids are available and the main source of energy in the absence of food intake during sleep, that is reflected in lowering RQ awakening. No reduction of RQ after an overnight fast (high fasting RQ) may reflect a violation of some of the mechanisms of fat oxidation [7, 9]. In our study, all patients received comparable dietary treatment. Measurement of the metabolic status conducted under the same conditions in the fasting between the hours of 7:00 am and 8:00 am. Thus, our

findings cannot be attributed to differences in macronutrient composition of the diet and energy balance, and most likely reveal a violation of fat oxidation in patients with angina pectoris.

The leading role in the development of CVD plays the atherosclerotic process. High RQ in patients with angina pectoris suggests that violation of fat oxidation can play an important role in the pathogenesis of CVD, participating in atherogenesis. This is confirmed by the fact that the increased RQ associated with an increased Carotid Intima-Media Thickness [14], hypertriglyceridemia [12] and other risk factors for CVD [8, 10]. Visceral obesity is also associated with the development of atherosclerosis [2, 3]. In our study, it was found a tendency to increase the level of visceral adipose tissue in patients with angina pectoris (Table 1). Correlation analysis showed direct correlation between the area of visceral fat and fat oxidation ($r=0,193$, $p=0,018$) (Picture 1), which may indicate the effect of a violation of fat oxidation in the distribution of adipose tissue, and thus reflect some mechanisms implementing violations of macronutrient oxidation in atherogenesis.

Different forms of CHD including angina pectoris, have a strong influence on the macronutrient oxidation in the myocardium and cardiac function. In a healthy heart β -oxidation of fatty acids is 60-80% of the ATP production [16] and the remaining 20-40% explained by oxidation of carbohydrates (glucose and lactate) and ketone bodies. Unlike normal heart, where the ratio of fat and carbohydrate oxidation is carefully regulated, process of ischemia and reperfusion violate these regulatory mechanisms [13, 16]. As a result, the metabolism of the myocardium at rest is totally dependent on the oxidation of free fatty acids received from the circulation [14]. Thus, myocardium becomes more sensitive to any change in the substrate oxidation. It is well known that the overall contribution of myocardial metabolism in RMR of the whole organism is less than the contribution of the internal organs such as liver, brain, and skeletal muscle. However, the rate of metabolism of the heart is approximately two times higher than the liver and the brain, and about 30 times greater than that of skeletal muscle [6]. Therefore, considering these facts, reduced fat oxidation according to indirect calorimetry may be accompanied by deficiency of substrate oxidation in the myocardium that leads to its subsequent morphological and functional disorders.

Thus, measurement of the metabolic status by indirect calorimetry in patients with angina pectoris and obesity is very important. Data of RMR and RQ can provide the necessary information for the selection of appropriate pharmacological and dietary treatment for each patient according to the macronutrient oxidation.

CONCLUSION

1. It was found that RQ was significantly higher in obese patients with angina pectoris.
2. Increased levels of respiratory quotient may be considered as a predictor of cardiovascular risk and reflect a violation of fat oxidation. High RQ in patients with angina pectoris suggests that the violation of fat oxidation can play an important role in the pathogenesis of CHD.
3. The data of metabolic status of the patients allows creating a personalized dietary treatment according to the macronutrient oxidation.

Table 1. Total characteristic of patients (M $\pm$ SD).

Indices	Control group (112 people)	Treatment group (112 people)	P
Sex (M/F)	48/64	41/71	P=0,339
Height, cm	167,6 $\pm$ 10,7	167,9 $\pm$ 10,5	P=0,833
Age	51,93 $\pm$ 9,4	59,44 $\pm$ 7,9	P=0,000
Body mass, kg	123,73 $\pm$ 29	125,11 $\pm$ 28	P=0,636
IMT, kg/m ²	43,82 $\pm$ 8	44,17 $\pm$ 8	P=0,585
Fatty mass, kg	59,00 $\pm$ 18	59,46 $\pm$ 16	P=0,612
Lean body mass, kg	64,66 $\pm$ 16	65,44 $\pm$ 16	P=0,62
Muscle mass, kg	34,69 $\pm$ 9	35,11 $\pm$ 8,5	P=0,61
General liquid, kg	47,66 $\pm$ 12	48,10 $\pm$ 12	P=0,643
Visceral fat area, cm ²	229,6 $\pm$ 57	243,8 $\pm$ 49	P=0,06

Table 2. Estimation of metabolism at patients with stenocardia and obesity (M±SD).

Indices	Control group (112 people)	Treatment group (112 people)	P
Energy expenditure of rest, kcal / a day	1973±499	1877±482	P=0,145
Oxidation of carbohydrates, g / a day	158,8±113	197,3±150	P=0,073
Fat oxidation, g / a day	124,16±51	96,91±59	P=0,000
Protein oxidation, g / a day	72±22,5	68±25,7	P=0,264
Respiratory ratio	0,796±0,05	0,829±0,08	P=0,003
% oxidation of carbohydrates	32,32±20	39,92±27	P=0,048
% fat oxidation	56,55±18	46,34±25	P=0,002
% protein oxidation	14,87±3,9	14,89±5,8	P=0,627

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