HORMONAL REGULATION OF CARBOHYDRATE AND FAT METABOLISM IN WOMEN WITH DIFFERENT OBESITY TYPES IN THE FOOD DEPRIVATION TEST

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Abstract

Context. The dominant type of adipose tissue accumulation in the body is associated with the peculiarities of using key substrates in energy metabolism and their hormonal regulation. Hormonal and metabolic parameters were investigated in women with android and gynoid obesity before and after the short-term food deprivation test.

Results. At baseline, at gynoid obesity as compared to android obesity, the women's blood contained lower glucose and insulin levels and higher FFA levels. The reaction to food deprivation manifested by a decrease in glucose level and an increase in FFA level in the blood is less pronounced in women with gynoid obesity than in those with android obesity. At the same time, a similar (though varying in expression) decrease in insulin level and elevated levels of glucagon, growth hormone and thyroxine were revealed in women's blood in both groups. Blood cortisol level increased in women with gynoid obesity and remained unchanged in those with android obesity.

Conclusions. More pronounced activation of hormonal mechanisms for maintaining blood glucose levels at gynoid obesity as compared to android one suggests that glucose is the preferable substrate for energy metabolism at gynoid obesity in women.

Key words: women, obesity types, food deprivation test, glucose, free fatty acids, hormones.

INTRODUCTION

The prevalence of obesity in industrialized countries reaches 20 - 30%. Obesity increases the risk of cardiovascular diseases (CVD), atherosclerosis and diabetes mellitus type 2 (T2DM) (1) and can disrupt the balance of energy intake and expenditure. According to Randle hypothesis, glucose and free fatty acids (FFA) are key substrates for energy metabolism. They compete as substrates for oxidation and energy production (2), and the competition can be based on changes in blood levels of free and esterified fatty acids.

Such changes are accompanied by reduced functional activity of insulin-dependent glucose transporters and lower glucose utilization by cells (3).

Obesity varies in anthropometric and hormonal-metabolic characteristics. A high risk of cardiovascular and metabolic diseases is primarily posed by android obesity with abdominal type of adipose tissue accumulation, while individuals with gynoid obesity and gluteofemoral type of adipose tissue accumulation have a much lower risk (4).

We have previously shown that men and women with android and gynoid obesity have different frequencies of metabolic syndrome (MS) and its components with significantly higher frequency for android obesity (5, 6, 7). Men and women with gynoid obesity had no hyperglycemia (MS component), and the risk of insulin resistance, and T2DM was therefore minimal (5). Android obesity is characterized by insulin resistance (IR), which is an underlying condition for MS hypoadiponectinemia, increased risk of CVD with more severe metabolic disorders leading to T2DM (8). However, the metabolism of glucose and FFA as well as the hormonal regulation of carbohydrate and fat metabolism in individuals with android and gynoid obesity have been insufficiently studied.

To see how different substrates take part in energy metabolism, we used tests based on the administration of excess energy substrate, for example, glucose tolerance test (9) and, fat load test (10), and tests based on limited delivery of energy substrates, for example, food deprivation test (11).

The objective of our study was to analyze the hormonal and metabolic reactions in women with different obesity types in response to food deprivation.

SUBJECTS AND METHODS

A total of 54 women with primary alimentary-

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constitutional obesity (body mass index >30 kg/m², WHO criteria) and mean age of 30.3 ± 8.7 years were examined. The women were informed on study objectives and possible effects for body. All women gave an informed consent for participation.

Within 3 months prior to the study, all women were gynecologically healthy, had no menstrual irregularities, did not take oral contraceptives, hormonal drugs and medications affecting the metabolism. The women were anthropometrically examined including the measurement of body mass (kg), height (m) as well as waist and hip circumferences (cm). Body mass index (BMI) was calculated, and obesity type was determined by the waist-to-hip ratio (WHR). Women with WHR < 0.85 were classified to Group 1 (gynoid obesity) ($n=32$, WHR = 0.78 ± 0.03) and women with WHR ≥ 0.85 were classified to Group 2 (android obesity) ($n=22$, WHR = 0.87 ± 0.03) [5]. Groups 1 and 2 had similar BMIs (33.8 ± 5.3 kg/m² and 35.1 ± 4.9 kg/m², $p=0.12$) and age (29.9 ± 7.0 years old and 32.7 ± 10.7 years old, $p=0.095$), respectively.

Hormonal and biochemical blood parameters were measured twice, before and after three-day food deprivation during which women did not eat. Water consumption was not restricted, and women additionally received 1 liter of broth hips daily and were allowed to walk up to two hours a day. The levels of glucose, FFA, triglycerides (TG), total cholesterol (TC), cholesterol of high density lipoproteins (HDL cholesterol) and low density lipoproteins (LDL cholesterol) were determined by enzymatic methods in the serum collected in the morning on an empty stomach. The levels of serum hormones (immunoreactive insulin (IRI), glucagon, growth hormone (GH), thyroid stimulating hormone (TSH), thyroxine, triiodothyronine and cortisol) were determined by enzyme immunoassay using commercial

ELISA kits. The insulin resistance index HOMA-IR was calculated according to the formula: (Glucose (mM) * IRI (IU/mL) / 22.5. The presence of IR was recorded at HOMA-IR values > 2.77 .

Statistical processing was performed using “Statistica 10” (StatSoft, USA). The mean values of parameters in the text and tables are presented as $M \pm SD$. The intergroup differences were assessed using Mann-Whitney nonparametric tests; the dynamics of changes in the indicators was estimated using the paired t-test for dependent values. The minimum probability of validity of the null hypothesis was accepted at $p < 0.05$.

RESULTS

Significant differences in serum glucose levels were observed in women of both groups at the baseline (Table 1); the levels were higher in Group 2 (android obesity). In contrast, the highest serum FFA level was identified in Group 1 (gynoid obesity). It can be therefore supposed that carbohydrate oxidation dominates in energy supply of women with gynoid obesity in the morning on an empty stomach, while FFAs are mainly used in women with android obesity.

The analysis of the serum level of the transport form of substrates for lipid metabolism, namely TG and TC did not reveal any significant differences between the groups. The level of LDL cholesterol was significantly higher in Group 2, while the level of HDL cholesterol was significantly lower in Group 1. At the baseline, groups significantly differed only in IRI level, that was higher in Group 2 (Table 2). HOMA-IR value was also higher in Group 2, which indicated a high risk of insulin resistance syndrome in women with android obesity.

After a three-day food deprivation, both groups

Table 1. Carbohydrate and fat metabolism indices before and after the food deprivation test in women with different obesity types ($M \pm SD$)

Index	Group 1		Group 2		p
	Gynoid obesity type		Android obesity type		
	Before test	After test	Before test	After test	
	1	2	3	4	
Glucose, mM	4.23±0.37	3.23±0.43	5.00±0.49	3.43±0.53	1-2<0.0001
					1-3<0.0001
					3-4<0.0001
					1-2<0.0001
Free fatty acids, mM	0.72±0.29	1.14±0.32	0.55±0.28	1.11±0.33	1-3=0.0154
					3-4<0.0001
					1-2=0.0073
					—
Triglycerides, mM	0.79±0.31	1.01±0.27	0.91±0.43	1.05±0.42	1-2=0.0073
Total cholesterol, mM	5.34±1.08	5.74±1.23	5.63±1.16	5.72±1.08	—
HDL cholesterol, mM	1.41±0.20	1.31±0.21	1.22±0.25	1.18±0.20	1-3=0.0230
LDL cholesterol, mM	3.80±1.06	3.98±1.24	4.03±0.85	4.11±1.19	1-3=0.0371

HDL cholesterol – cholesterol of high density lipoproteins; LDL cholesterol – cholesterol of low density lipoproteins.

had significantly lower glucose levels and higher FFA levels. Glucose and FFA levels had a negative correlation in all women ($r = -0.41$, $p = 0.005$). Food deprivation cleared intergroup differences in glucose and FFA levels. As for the other serum biochemical indices, a significant increase in TG level was observed in both groups, and lower levels of HDL cholesterol were observed in Group 1 (Table 1).

After food deprivation, both groups had the same pattern of changes in hormonal regulation of energy metabolism. The changes were towards maintaining normoglycemia and had the following manifestations: pronounced reduction of serum IRI levels and increased levels of contrinsular hormones (glucocorticoids and glucagon); a significant increase in the level of serum GH enhancing lipolysis and an increase in serum FFA level. However, the intensity of these changes in the groups differed significantly (Table 2). For instance, glucagon and GH levels in Group 1 increased 2-fold (15.1 ± 7.00 to 31.7 ± 15.4 pg/mL, $p = 0.0011$), and 2.3-fold (from 1.9 ± 1.3 to 4.2 ± 2.4 ng/mL, $p = 0.0021$), respectively, whereas in Group 2 the levels increased by only 35% (from 18.8 ± 11.5 to 25.6 ± 9.5 pg/mL $p = 0.0069$) and 56% (from 2.4 ± 2.3 to 3.8 ± 1.3 , $p = 0.0028$), respectively. Cortisol level remained as at the baseline in Group 2 and decreased in Group 1, which indicates a pronounced stress reaction aimed to restore normoglycemia. Pituitary-thyroid system tended to demonstrate lower TSH levels, elevated

levels of thyroxine and decreased triiodothyronine in the serum. The severity of changes was higher in women with gynoid obesity (Group 1).

DISCUSSION

Initial differences of carbohydrate metabolism in two groups, such as elevated levels of blood glucose and insulin in women with android obesity compared to those with gynoid obesity, are consistent with previously described characteristics of carbohydrate metabolism in women with different obesity types in response to glucose load in different phases of circadian rhythm (12). Glucose load in women with gynoid obesity was accompanied by functional hyperinsulinemia and postprandial hypoglycemia, whereas women with android obesity had absolute hyperinsulinemia, insulin resistance and hyperglycemia irrespective of the time of the day (12). The examination of women with android obesity also revealed typical disturbances of lipid metabolism manifested by initially elevated levels of LDL cholesterol and a reduced levels of HDL cholesterol, which is consistent with other authors' findings (13).

Food deprivation response was manifested by the classical hormonal reaction aimed at maintaining homeostasis. The response was associated with decreased serum IRI levels and increased levels of contrinsular hormones (glucocorticoids and glucagon) required for

Table 2. Serum hormone levels and insulin resistance index before and after the food deprivation test in women with different obesity types (M $\pm$ SD)

Index	Group 1		Group 2		p
	Gynoid obesity type Before test 1	After test 2	Android obesity type Before test 3	After test 4	
Cortisol, nM	488.4 $\pm$ 230.4	668.4 $\pm$ 307.6	515.2 $\pm$ 166.1	441.3 $\pm$ 237.4	1-2=0.0055 1-2=0.0008
Insulin, μ U/mL	7.9 $\pm$ 4.3	3.8 $\pm$ 2.8	12.6 $\pm$ 7.1	8.2 $\pm$ 3.9	1-3=0.0072 2-4=0.0312 3-4=0.0427 1-2<0.0001
HOMA-IR, CU	1.42 $\pm$ 0.9	0.55 $\pm$ 0.39	1.77 $\pm$ 0.8	0.52 $\pm$ 0.45	1-3=0.0005 2-4=0.0081 3-4<0.0001
Glucagon, pg/mL	15.1 $\pm$ 7.00	31.7 $\pm$ 15.4	18.8 $\pm$ 11.5	25.6 $\pm$ 9.5	1-2=0.0011 3-4=0.0069
GH, ng/mL	1.9 $\pm$ 1.3	4.2 $\pm$ 2.4	2.4 $\pm$ 2.3	3.8 $\pm$ 1.3	1-2=0.0021 3-4=0.0028
TSH, mU/L	1.6 $\pm$ 0.8	1.2 $\pm$ 0.9	0.8 $\pm$ 0.6	0.7 $\pm$ 0.5	-
Thyroxine, nM	110.9 $\pm$ 40.8	161.3 $\pm$ 92.9	97.8 $\pm$ 25.7	113.2 $\pm$ 29.3	-
Triiodothyronine, nM	1.5 $\pm$ 0.6	0.9 $\pm$ 0.4	1.4 $\pm$ 0.3	1.0 $\pm$ 0.5	1-2=0.0020 3-4=0.0154

HOMA-IR – insulin resistance index; GH – growth hormone; TSH – thyroid stimulating hormone.

glycogenolysis, gluconeogenesis (14, 15) and lipolysis (16) as evidenced by a significant increase in GH serum level. As for the pituitary-thyroid system, a tendency of lower TSH levels, elevated levels of thyroxine and lower levels of triiodothyronine in the serum was revealed, which is consistent with published data (17).

Food deprivation test allowed us to identify the characteristics of hormonal regulation of carbohydrate and fat metabolism in women with different obesity types. Android obesity was associated with a higher insulin level in the blood, growing insulin resistance of peripheral tissues and, thus a predominant role of FFA as the preferable substrate for oxidation in energy metabolism.

Android obesity is characterized by growing visceral adipose tissue at a high metabolic activity and produces a large number of biologically active compounds: cytokines, adipokines, etc. (18). These compounds may predetermine the inert response of studied hormonal systems (adrenocortical and pituitary-thyroid systems as well as glucagon, GH systems) to experimental effects of food deprivation in android obesity.

In contrast, gynoid obesity demonstrates a strong food deprivation response of glucocorticoids, glucagon, GH, hormones of the pituitary-thyroid system, which is necessary to enhance carbohydrate and fat metabolism. A pronounced response to food deprivation in gynoid obesity shows continuous reactivity of hormonal systems to external influences, which, along with hypoadiponectinemia and a low index of visceral obesity (8), can be one of the mechanisms to support a low risk of metabolic disorders and obesity-associated diseases in gynoid obesity.

In recent years, special attention has been paid to the phenomenon of “metabolically healthy” obesity when the main metabolic indices in obese individuals are the same as in normal-weight individuals, and the risk of obesity-associated cardiovascular diseases, diabetes mellitus type 2 (T2DM) and atherosclerosis is therefore lower in such obese individuals (19, 20). Individuals with “metabolically healthy” obesity make up about 10 – 40% of the total obese population, and their prevalence was the highest among young men and women until the early menopausal period (21). The findings of this and previous (8) studies suggest that it is gynoid obesity type that can be classified as “metabolically healthy” obesity.

In conclusion, the study revealed different mechanisms of hormonal regulation in carbohydrate and fat metabolism. The mechanisms are most clearly seen

in food deprivation test. Women with gynoid obesity had a more pronounced activation of hormonal systems aimed at maintaining the blood glucose level, which allows us to consider glucose a preferable substrate for energy metabolism. In women with android obesity, insulin resistance predetermines the predominance of lipid-based metabolism and therefore a less pronounced reaction of hormonal systems to food limitation.

Conflict of interest

The authors declare that they have no conflict of interest.

Financial disclosure

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