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Comprehensive assessment of certain trace elements, hormones and enzymes in patients with exogenous-constitutional obesity in predicting transition to metabolic syndrome

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Abstract

Aim. To study the relationship between the trace element status (chromium, zinc and copper) and hormonal activity (insulin, leptin) in women with metabolically healthy and unhealthy obesity phenotypes, depending on the type and severity of obesity.

Methods. A cross-sectional study was conducted to compare 288 women with exogenous-constitutional obesity aged 25–45 years and healthy women of similar age (n=38). The comparative analysis was carried out in groups of patients with android and gynoid ECO types and varying degrees of obesity. The study was conducted in the NUZ "Department Clinical Hospital of the Kazan station of JSC Russian Railways" between 2016 and 2020. Along with clinical laboratory tests, the indicators of carbohydrate and lipid metabolism (including the determination of hormones), the activity of enzyme systems and trace element content were determined. The statistical significance of the differences was assessed by using the non-parametric Spearman's rank correlation test.

Results. It was revealed that the type of obesity associated with the indicators of lipid and carbohydrate metabolism, the activities of catalase and peroxidase, and trace element content. In patients with abdominal obesity, the concentration of copper was higher than in the comparison group, and chromium and zinc — lower than in patients with gynoid obesity and in the control group. In patients with android obesity, a high correlation was found between the serum copper level (r=0.98) and body fat percentage (r=0.74) compared with patients with gynoid type obesity. The correlation of chromium level with the level of blood glucose (r=0.58), triglycerides (r=0.66), cholesterol (r=0.60) and catalase enzyme activity (r=0.54) as well as correlation of zinc level with the level of blood glucose (r=0.74), cholesterol (r=0.77), triglycerides (r=0.90), catalase (r=0.57), and peroxidase (r=0.59) were revealed. Also, significant differences in the level of trace elements in patients with varying degrees of obesity were found.

Conclusion. An increase in copper concentration and a decrease in the concentration of chromium and zinc are unfavorable signs in obese patients associated with the activation of oxidative stress, hyperplastic processes and a high risk of developing a metabolic syndrome.

Keywords: microelements, exogenous-constitutional obesity, metabolic syndrome, activity of enzyme systems.

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Background. The special focus of the medical community on obesity is quite understandable. Obesity is known to be one of the significant risk factors for the development and progression of ischemic heart disease, arterial hypertension, type 2 diabetes mellitus, liver, kidney, reproductive system diseases, and oncological pathology, etc. [1, 2]. In addition, it has been shown that a progressive course characterizes the android (abdominal) type, a high risk of metabolic syndrome with subsequent damage to vital organs ("low-grade" obesity, or "metabolically unhealthy" obesity) [3, 4]. The rapid progression of abdominal obesity to metabolic syndrome is due to the high density of β-adrenergic receptors, glucocorticoid, and androgen receptors localized in the adipose tissue of the visceral region, which has abundant innervation and blood supply and determines its high metabolic activity [5].

Current concepts about the pathogenesis of most systemic diseases, such as obesity, imply the presence of complex mechanisms of interaction be-

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tween external and internal factors. Moreover, it encompasses cascade mechanisms of disorders and multilevel regulation of the most significant functions of the body. Thus, the problem involves a comprehensive data analysis, starting with subcellular structures and assessing functioning at the whole organism level [6].

In our opinion, one of the most important aspects of the problem of obesity is the study of the relationship of this disease with micronutrient and enzymatic disorders. According to some scientists, the lack of certain trace elements (Fe, Se, Cr, I, Zn, Cu, etc.) contributes to the formation of the metabolic syndrome. It is no less important than the oxidation of lipids by free radicals, especially if we consider the fact that the deficiency of micronutrients in the diet of a contemporary person is due to their low content in soil and agricultural products, as well as their significant loss during thermal processing of food products [6].

Trace elements, being the most important catalysts of biochemical reactions, contribute to the growth and development of the body, metabolism, and adaptation to the environment [7]. Their levels in the body indicate the state of morphophysiological systems and can be a predictor of a particular pathology. These data can be used in early diagnostics of certain diseases, particularly diseases associated with metabolic disorders [8].

Some studies discuss the prospects of using the assessment of micronutrient composition in prenosological diagnostics of several diseases [9, 10]. Moreover, some researchers used the determination of the levels of chemical elements in biological substrates even in assessing the level of functional reserves of the body [6]. This field is undoubtedly promising since any changes visible at the macroscopic level begin much earlier at the microscopic level [6].

In our current study, we paid particular attention to the micronutrients chromium (Cr), zinc (Zn), and copper (Cu) as they take the most active part in the formation of metabolic disorders. Cr is involved in regulating carbohydrate and fat metabolism, normalizing the permeability of cell membranes for glucose, and lowering serum cholesterol levels [11]. Cr also performs antioxidant effect [12]. Zn is included in more than 80 enzymes that regulate the activity of more than 200 enzyme systems and biologically active substances involved in the synthesis and breakdown of carbohydrates, fats, proteins, and nucleic acids, including the enzyme Zn-dependent superoxide dismutase. Zn is involved in the regulation of insulin secretion directly in the pancreatic β-cells [6]. In addition to active participation in the functioning of enzyme systems, Cu is closely associated with markers of inflammation. This helps identify the characteristic signs of aggressive forms of thyroid cancer at the subcellular level and predicts the development of vascular disorders. All these micronutrients protect the body from oxidative stress [13–18].

These micronutrients were selected when studying the metabolic parameters of the early stages of the metabolic syndrome and predicting its development in patients with obesity.

This work aimed to study the micronutrient status (for Cr, Zn, and Cu), hormonal activity (insulin, leptin) in women with exogenous-constitutional obesity (ECO), depending on the type and severity of obesity, and to assess the prospects for using these indicators in early diagnostics of metabolic syndrome.

Materials and methods. A one-stage cross-sectional study was conducted, including 288 women of fertile age (20–45 years) with ECO and 38 women with normal body weight who signed informed consent to participate in the study. All patients resided in a large industrial center, and their job was not associated with hard physical labor. They had good and satisfactory living conditions. Everyone was interested in obtaining results from obesity treatment.

The work was performed at the clinical site of the Departmental Clinical Hospital of Kazan Station of Russian Railways. The study was conducted in the period from 9 August 2016 to 5 April 2020.

The patients were distributed into three groups, namely the group with the abdominal type of ECO (ECO-AT) including 116 patients (average age 35.1 ± 4.48 years), the group with the gynoid ECO type (ECO-GT), which included 172 patients (average age 33.4 ± 6.11 years), and the control group which included 38 healthy women comparable in age (mean age 35.22 ± 4.17 years); there were no differences between the groups ($p > 0.05$). The study groups included patients with a body mass index (BMI) above 30 kg/m^2 (on average 32.3 ± 4.2 kg/m^2). The control group included patients aged 26–44 years without excessive body weight (BMI 27.1 ± 3.2 kg/m^2; $p < 0.05$).

The inclusion criteria were: criterion 1 was women aged from 20 to 45 years, criterion 2 women maintained a regular menstrual cycle, and criterion 3 was informed consent of the patient.

Exclusion criteria were secondary forms of obesity, menopause, somatic diseases with a complicated course and manifestations of functional impairment, acute pathology, and mental disorders.

A simple random sampling method was used to select patients for the study. Since the selection criterion for patients with obesity in the study was

20–45 years, the experimental groups were comparable in age. Hence, group 1 was with ECO-AT, and group 2 was with ECO-GT. The minimum sample size was calculated using the equation:

$$N = 2 \times (Z_{\alpha/2} + Z_{\beta})2 / (d / SD^2),$$

where N is the calculated sample size; $Z_{\alpha/2}$ and Z_{β} are the values of the normal distribution at probabilities $Z_{\alpha/2}$ and Z_{β}, respectively; d is the clinically significant difference in group mean values; SD is the standard deviation.

For a given significance level (0.05), test power (0.80), and d of 0.5, the minimum sample size (N) should have been at least 63 female patients for one group [19].

The study was one-center, one-stage, and cross-sectional.

Diagnostic methods included the study of parameters of the carbohydrate-lipid spectrum of blood with the determination of basal glycemia, triglyceridemia, total cholesterol, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol. Immunoreactive insulin and leptin were determined by enzyme immunoassay using reagents from Diagnostic System Laboratories (USA). The catalase activity was determined by the amount of hydrogen peroxide decomposed under the influence of catalase (M.A. Korolyuk), peroxidase activity was determined by the method of photometric registration of a decrease in the concentration of indigo carmine (T. Popov, L. Neykovskaya, 1971). The study of the levels of metals (Cu, Zn, Cr) in blood serum was performed by atomic absorption spectroscopy on an Analyst 400 device (Perkin Elmer, USA).

The obesity phenotype was determined by the visceral adiposity index (VAI), an indicator of "visceral adipose tissue function" and insulin sensitivity. VAI is not used for diagnosing complications of obesity or concomitant pathology but indicates an assessment of the cardiometabolic risk (predisposition) for patients with obesity. The resulting indicator is assessed depending on gender and age group [19, 20]. The VAI indicator was calculated according to the equation:

$$VAI = WC / 36.58 + 1.89 \times BMI \times TG/ /0.81 \times 1.52 / HDL,$$

where VAI — visceral adiposity index; WC — waist circumference; BMI — body mass index; TG — triglycerides; HDL — high-density lipoproteins.

For healthy patients, VAI = 1. Criteria for cardiometabolic risk were taken as VAI values of 2.52 for women younger than 30 years; 2.23 for women aged 30–42 years old; and 1.92 for women aged 42–45 years old [21].

The severity of obesity was determined following BMI classification (World Health Organization, 1997) [14].

The equation determined BMI:

$BMI = m/h^2$, where m — body weight (kg); h — height (m).

The insulin resistance index (HOMA-IR, homeostasis model assessment of insulin resistance) was calculated by the equation:

$$\text{HOMA-IR} = \text{insulin } (\mu U/ml) \times \times \text{ plasma glucose } (mmol/l) / 22.5.$$

Statistical analysis of the study was performed using the statistical software package Statistica 10.0 for Windows (StatSoft Inc.). The distribution of a characteristic of the sample was performed according to the Shapiro–Wilk test. When distributed correctly, the data are presented as $M \pm \sigma$ (mean ± standard deviation). The correct distribution was typical for micronutrient indicators in groups with varying severity of obesity (Table 1). In skewed distributions, the data were presented as a median (*Me*) (noted in all groups of indicators with distribution by obesity type, Table 2). For this reason, the statistical significance of the relationship between the values of the concentration indicators of Zn, Cr, and Cu with some anthropometric (BMI, waist circumference/hip circumference) and biochemical indicators and enzymes was assessed using Spearman's nonparametric R-test (since in this case, the distribution may not necessarily be normal). Differences were considered significant at a p-value lower than 0.05.

The study was approved by the ethics committee of the Kazan State Medical Academy, a branch of the Russian Medical Academy of Continuing Professional Education of the Ministry of Health of Russia, on 09/08/2016 (protocol No. 2-09).

Results. The data obtained were analyzed according to three groups of indicators: the state of carbohydrate metabolism, the state of fat metabolism, the tissue activity of enzyme systems, and the blood micronutrient composition.

The comparison of data obtained in patients with different types of obesity revealed that obesity is associated with indicators of carbohydrate-fat metabolism and micronutrient status. At the same time, significant metabolic changes were noted in the group of patients with ECO-AT, including an increase in glucose level and triglycerides with a reduced level of high-density lipoprotein cholesterol and an increased level of low-density lipoprotein cholesterol (Table 2). In addition, in the group of patients with ECO-AT, higher insulin and leptin levels were detected compared with the control group and with patients in the ECO-GT group. And, accordingly, similar changes were identified in HOMA-IR.

Table 1. Metabolic parameters of patients depending on the type of obesity (Me).

Indicator	ECO-AT (*n* = 116)	ECO-GT (*n* = 172)	Control (*n* = 38)	p_{1-2}	p_{1-3}	p_{2-3}
Indicators characterizing the carbohydrate metabolism						
Fasting glycemia. mmol/l	5.33 [5.05; 5.81]	5.14 [4.72; 5.61]	4.44 [3.59; 5.50]	>0.05	<0.01	<0.05
Insulin. mIU/L	25.2 [17.83; 35.15]	21.9 [17.61; 28.80]	8.4 [4.58; 9.35]	<0.05	<0.01	<0.01
Leptin. ng/ml	75.45 [50.30; 97.45]	68.03 [45.50; 85.88]	27.3 [18.73; 31.58]	<0.05	<0.01	<0.01
HOMA. c.u.	6.35 [4.10; 8.45]	5.1 [4.71; 5.64]	1.8 [1.52; 2.05]	<0.05	<0.01	<0.01
Indicators characterizing the lipid metabolism						
Triglycerides. mmol/l	1.80 [1.07; 2.75]	1.54 [1.41; 2.03]	1.12 [0.96; 1.28]	<0.01	<0.05	≤0.01
Total cholesterol. mmol/l	3.99 [3.49; 4.66]	5.40 [4.42; 6.22]	4.95 [3.84; 5.08]	>0.05	0.005	<0.05
High-density lipoprotein cholesterol. mmol/l	1.15 [0.75; 1.39]	1.44 [1.32; 1.77]	1.67 [1.51; 1.79]	<0.01	<0.01	<0.01
Low-density lipoprotein cholesterol. mmol/l	4.47 [3.75; 5.09]	3.77 [3.11; 4.07]	2.9 [2.32; 3.01]	>0.05	<0.01	<0.01
Indicators characterizing the condition of enzyme systems						
Catalase. µkat/L	873 136.0 [555 484; 1 151 181]	742 800.0 [566 100; 1 078 456]	960 972.2 [761 436; 1 242 124]	<0.05	<0.05	<0.01
Peroxidase. µmol/l	101.18 [53.0; 164.2]	101.12 [87.9; 200.0]	113.03 [69.5; 148.3]	>0.05	<0.05	<0.05
Micronutrients						
Zinc. mg/l	0.801 [0.596; 1.144]	0.876 [0.704; 0.983]	0.981 [0.721; 1.176]	<0.05	<0.01	<0.01
Chromium. mg/l	0.015 [0.012; 0.022]	0.020 [0.009; 0.080]	0.034 [0.019; 0.042]	>0.05	<0.01	>0.05
Copper. mg/l	1.21 [0.97; 1.33]	1.18 [0.78; 1.40]	0.986 [0.89; 1.26]	>0.05	<0.01	<0.01

Note: the inversion criterion was used for statistical analysis — $p < 0.05$; $p < 0.01$; differences were considered significant at $p < 0.05$; p_{1-2} — differences between the ECO-AT and ECO-GT groups; p_{1-3} — differences between patients with ECO-AT and a group of healthy people; p_{2-3} — differences between patients with ECO-GT and the healthy group. ECO-AT — android type exogenous-constitutional obesity; ECO-GT — gynoid type exogenous-constitutional obesity; HOMA-IR (homeostasis model assessment of insulin resistance) — insulin resistance index.

A lower concentration of Cr and Zn in the blood serum was detected in female patients with obesity compared with controls ($p < 0.01$), and in the ECO-AT group, the Zn concentration was significantly lower than in the ECO-GT group ($p < 0.05$), with a tendency toward a decrease in the Cr concentration. In addition, in patients with obesity, a higher concentration of Cu was recorded compared with the control group, primarily in the ECO-AT group ($p < 0.01$; Table 1). Despite the relative homogeneity of the group, we assessed the correlation between the studied micronutrients with age, type of obesity, and BMI (Table 3).

There was a high correlation in the level of Cu with the type of obesity ($r = 0.98$) and the proportion of body fat ($r = 0.74$), the levels of glycemia ($r = 0.85$), insulin ($r = 0.75$), and leptin ($r = 0.74$). An equally significant relationship was noted between the Cu level index and the levels of the major indicators of lipid metabolism, namely the levels of triglycerides ($r = 0.97$) and cholesterol ($r = 0.88$), and the activity of enzyme systems (Table 3).

An analysis was also performed with the distribution of patients into groups according to the degree of obesity, namely 116 patients with the degree I, 112 patients with degree II, and 60 patients with degree III. However, according to this criterion (the number of patients with different degrees of obesity), the distribution in the groups was unbalanced. The distribution of patients according

Table 2. Correlation relationship of micronutrients with morphological criteria of obesity, carbohydrate and fat metabolism indicators, and enzyme activity according to Spearman's coefficient

Indicator	Zinc	Chromium	Copper
Age	0.61	0.53	0.75
Body mass index	0.62	0.54	0.75
Waist circumference/hip circumference	1.00	0.63	0.98
Fat content	0.60	0.48	0.74
Glycemia	0.74	0.58	0.85
Insulin	0.62	0.56	0.75
Leptin	0.59	0.54	0.74
Triglycerides	0.90	0.66	0.97
Cholesterol	0.77	0.60	0.88
Catalase	0.57	0.54	0.72
Peroxidase	0.59	0.49	0.73

Note: the Chaddock scale is used to assess the strength of the correlation relationship: weak — from 0.1 to 0.3; moderate — from 0.3 to 0.5; noticeable — from 0.5 to 0.7; high — from 0.7 to 0.9; very high (strong) — from 0.9 to 1.0.

to the degree of obesity resulted in the ECO-AT group included 39 (33.6%) patients with the degree I obesity, 42 (36.2%) patients with degree II obesity, and 35 (30.2%) patients with degree III obesity. The group of patients with ECO-GT included 77 patients (44.7%, $p < 0.05$) with degree I obesity, 70 patients (40.8%, $p < 0.05$) with degree II obesity, and 25 patients (14.5%, $p < 0.05$) with degree III. For this reason, the analysis of the relationship between the severity of obesity and the indicators under study was also performed, considering the degree and the type of obesity (Table 1). It was noted that with an increase in the degree of obesity, the level of Cu in the blood serum was also increased. Furthermore, in groups with different types of obesity, the Cu concentration was significantly higher than in healthy people ($p < 0.01$; Table 1). In patients with ECO-AT, a progressive decrease in Zn values was registered (Table 1). However, we noted the opposite phenomenon in patients with ECO-GT. The level of Zn increased with an increase in obesity severity. The Cu levels in patients with obesity in both groups were raised, and, starting from the degree II obesity, it was significantly higher than in the control group. Cr levels were significantly reduced in all patients with obesity regardless of type and degree of obesity (Table 1).

Discussion. In our study, we analyzed the content of micronutrients and uncovered the differences in the values of Cu, Zn, and Cr in female patients with different types and severity of obesity. Almost all indicators revealed a correlation, which confirmed the early manifestation of a disruption of the micronutrient composition of the blood in patients with obesity. It is still debatable whether the imbalance of micronutrients leads to insulin resistance and oxidative stress or is a consequence of these processes. Nevertheless, we identified a noticeable relationship between the indices of insulin and leptin with the levels of Zn and Cr. The relationship of insulin and leptin with the level of Cu was also found to be high. In addition, there was a high correlation between the indicators of Zn and Cu and the level of glycemia. Thus, our study illustrates the importance of determining micronutrients in early diagnostics and predicting insulin resistance and metabolic syndrome development, which undoubtedly requires further study.

The indicators of metabolic processes also were found to be dependent on the degree of obesity. As the degree of obesity increased, deterioration in the indicators of carbohydrate-fat metabolism was found to increase the average values of the concentration of glucose, triglycerides, high-density lipoprotein cholesterol, and low-density lipoprotein. The insulin and leptin levels increased progressively, and with obesity of degrees II and III, the type of obesity already had a minimum significance in improving these indicators. The levels of Zn, Cu, and Cr in the ECO-AT and ECO-GT groups (all degrees of obesity) differed significantly from those in the group of healthy women ($p < 0.01$).

We expected to establish a correlation between some micronutrients, and the values of laboratory parameters characterizing the state of carbohydrate and fat metabolism as several scientific publications from various authors have indicated the effect of deficiency of certain micronutrients such as Cr, Zn, Cu in the development of metabolic syndrome [6–9]. Some studies noted that carbohydrate metabolism disorder could be predicted according to the micronutrient composition in the body. For example, high iron (Fe) levels in the blood correlate with hyperglycemia and type 2 diabetes mellitus. High levels of magnesium (Mg), calcium (Ca), and Zn are associated with the development of metabolic syndrome [1–6]. Furthermore, many studies have recommended Ca and Zn intake to normalize carbohydrate metabolism disorders [7, 8].

Our study showed that patients with obesity had reduced Zn level, which was more pronounced in patients with ECO-AT. Zn deficiency progressed with an increase in the degree of obesity, as it was 0.85 ± 0.007 mg/l with degree II (0.98 ± 0.008 mg/l in the control group), and 0.77 ± 0.006 mg/l with degree III. Given the high correlation of Zn levels with the type of obesity in patients of this group

Table 3. Metabolic parameters of patients depending on the degree of obesity (M ± σ)

Degree of obesity	Obesity type		Healthy group (control) (n = 38)	p_1	p_2	p_3
	ECO-AT (n = 116)	ECO-GT (n = 172)				
Zinc. mg/l						
I	0.92±0.12	0.94±0.20	0.98±0.09	0.335	0.003	0.22
II	0.85±0.15	1.02±0.11		0.0001	0.038	0.026
III	0.77±0.29	1.19±0.31		0.0001	0.0001	0.0001
Copper. mg/l						
I	1.11±0.32	1.06±0.39	0.99±0.13	0.252	0.026	0.276
II	1.19±0.19	1.18±0.26		4	0.0001	0.0001
III	1.28±0.15	1.20±0.14		0.0001	0.0001	0.0001
Chromium. mg/l						
I	0.022±0.004	0.024±0.003	0.34±0.005	0.0001	0.0001	0.0001
II	0.018±0.003	0.019±0.002		0.0001	0.0001	0.0001
III	0.018±0.005	0.018±0.004		1.00	0.0001	0.0001

Note: the inversion criterion was used for statistical analysis; $p < 0.05$; $p < 0.01$; p_1 — differences between patients with ECO-AT and ECO-GT; p_2 — differences between patients with ECO-AT and the group of healthy people; p_3 — differences between patients with ECO-GT and the group of healthy people; ECO-AT — android type exogenous-constitutional obesity; ECO-GT — gynoid type exogenous-constitutional obesity.

(according to the criterion of waist circumference/hip circumference; r = 1.0), the levels of glycemia (r = 0.74), triglycerides (r = 0.90), and total cholesterol (r = 0.77), further research should be aimed at a more detailed study on the effect of a progressive decrease in Zn levels on the risk of formation of other components of the metabolic syndrome. Moreover, in the group of patients with ECO-GT, a reduction in Zn level was recorded, however to a much lesser extent than in patients with ECO-AT. And with an increase in the degree of obesity, on the contrary, there was a tendency to a rise in the level of Zn, possibly a compensatory one, since it is Zn that is part of more than 80 enzyme systems regulating the synthesis and breakdown of carbohydrates, fats, and proteins [11, 13]. Notably, this indicates better preservation of the metabolic regulation mechanisms in patients with ECO-GT.

A decrease in Cr levels was registered in patients of both study groups (ECO-AT and ECO-GT), and it was very significant compared with the control. This indicates reduced intolerance to glucose and impaired permeability of cell membranes, dyslipidemia, and a decrease in antioxidant protection [8, 9]. Moreover, the Cr level turned out to be in the correlation dependence of the average strength on the indicators of carbohydrate and lipid metabolism and the indicators characterizing enzyme activity (catalase, peroxidase). The fact that we were unable to identify dependence on the type or severity of obesity confirmed the significant influence of oxidative stress on the disease progression. Therefore, it is hardly possible to reckon an effective treatment without eliminating this factor. Patients with obesity had a higher blood level of Cu compared with the control, and the maximum values were in patients with ECO-AT degree III.

The data obtained enabled us to identify a correlation between the level of the trace elements under study and the development and progression of the metabolic syndrome, particularly with a deficiency of Zn and Cr and an excess of Cu. The identified associations of these disorders with the type and severity of obesity will permit us to determine the trend of further research on the optimization of treatment management. Such studies must consider the micronutrient deficiency in patients with various types and degrees of obesity and the use of means of equalizing the micronutrient balance to achieve the maximum clinical effect.

Since our study was observational, and the sample was large enough, the female patients had some differences in the therapy received, and the changes with time of the indicators could turn out to be depending on this fact, but since the article presented discusses issues that are more related to primary diagnostics (at the time of the follow-up initiation) and prognostication based on these data, the survey results were presented in full. All deviations from bias were within the limit (±SD). Further studies will be required to evaluate the efficiency of obesity treatment with the inclusion of micronutrient correction.

CONCLUSIONS

1. The study revealed an increase in the concentration of Cu in patients with obesity, especially in the group with the abdominal type of exogenous-constitutional obesity in case of obesity above degree II. A reduction in Zn and Cr levels has been detected, which progressed with the increase in obesity.

2. Increased Cu and decreased Cr and Zn concentrations are unfavorable signs in patients with obesity. This is indicative of profound disorders of metabolic processes and the development of the metabolic syndrome.

Author contributions. T.V.N. performed the study design, obtained and analyzed the data, wrote the manuscript, approved the final version, and agreed to be responsible for all aspects of the work; I.A.K. conceived and designed the study, performed the data analysis, wrote the manuscript, approved the final version, and agreed to be responsible for all aspects of the work.

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