European Review for Medical and Pharmacological Sciences 2013; 17: 2396-2400

The evaluation of selected serum mineral concentrations and their association with insulin resistance in obese adolescents

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Abstract. – BACKGROUND: In obesity, elevated insulin resistance is observed, which may be associated with disturbances in mineral status in the body. The few studies concerning the status of minerals and their relationships with insulin resistance and body composition in adolescent populations have brought inconclusive results.

AIM: of this study is, thus, to assess serum mineral concentration in obese adolescents, and to evaluate their potential association with insulin resistance.

SUBJECTS AND METHODS: Seventy-eight obese adolescents and 20 healthy volunteers aged 12-18 years were recruited for the study. Selected anthropometrical measurements and levels of iron, zinc, copper, calcium, and magnesium were assessed in serum. Insulin resistance in the participants was evaluated according to the homeostatic model of assessment for insulin resistance (HOMA-IR) protocol. Levels of iron, zinc, copper, calcium, and magnesium were assessed in serum.

RESULTS: Obese subjects had significantly higher HOMA-IR indices than the control group. Compared to healthy subjects, the serum concentration of zinc, calcium, and magnesium was significantly lower in obese subjects. A significant inverse relation was found between HOMA-IR and zinc levels in serum.

CONCLUSIONS: Obese adolescents have a poorer mineral status (especially zinc) than adolescents of normal weight, which can contribute to insulin resistance.

Key Words:
Obesity, Insulin, Minerals, Adolescents

Introduction

Excess body mass is increasingly common among children and teenagers all over the world[1,2]. Overweight and obese adolescents are at risk of serious health consequences, including diabetes mellitus and cardiovascular diseases[3]. It is well-documented that excessive body fat is associated with insulin resistance, elevated blood pressure, and inflammation[4]. It is suggested that excessive body fat is also associated with micronutrient deficiencies[5]. Some studies, including our own, indicate a relationship associating obesity with comorbidities and mineral status disorders[6-8]. Animal-model and human studies have reported that low zinc intake and low zinc levels in serum are associated with an increased prevalence of obesity and diabetes[5-7]. It is known that zinc is involved in regulating insulin and leptin[9]. Calcium deficiency may also increase the risk of obesity, especially as calcium helps to regulate thermogenesis and lipogenesis in the body[7,9]. In obese individuals, disorders of serum iron, zinc, copper, calcium, and magnesium concentration have been reported, and relationships have been observed between these disorders and glucose and lipid serum levels[7,8].

However, there is a lack of data concerning the status of minerals and their relationships with insulin resistance and body composition in adolescent populations with obesity. Therefore, the aims of our study were thus to measure the con-

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centration of selected minerals in a cohort of obese adolescents and to evaluate their potential association with insulin resistance level.

Materials and Methods

Study Patients

The study protocol was approved by the Local Ethics Committee (approval number 384/08). Informed consent was obtained from all subjects.

The study was conducted on 78 obese adolescents (42 girls and 36 boys, mean age 14.5±1.8) and 20 normal-weight adolescents of comparable age. To participle in this study, adolescents must have been between 12 and 18 years old, either obese (in the study group) or with normal weight (in the control group), apparently healthy, and not on any medication. One additional inclusion criterion was stable body weight (less than 3 kg of self-reported change during the previous 3 months). The exclusion criteria were a history of use of any dietary supplements or dietary or physical activity interventions within the 3 months prior to the study, a history of infection in the month before the study, smoking, and any other condition that, in the opinion of the investigator, would make participation not in the best interest of the subject, or could prevent, limit, or confound the protocol-specified efficacy assessments.

Anthropometric Measurements

Anthropometric measurements were conducted with the subjects wearing light clothing and no shoes. Weight was measured to the nearest 0.1 kg, and height to the nearest 0.5 cm. The BMI was calculated as weight divided by height squared (kg/m^2). Obesity was defined as having a body mass index (BMI) ≥ the 95th percentile for the age and gender. Additionally, the percent of body fat (%FAT) was determined by impedance analysis using a Bodystat analyzer (1500 MDD; Bodystat, Isle of Man).

Biochemical Measurements

All participants had blood collected from a forearm vein. Blood samples were collected after an overnight fast and following 30 minutes in the supine position. Serum samples were stored at -20°C for no longer than 2-3 days.

The iron, copper, zinc, calcium, and magnesium serum contents were determined by the flame atomic absorption spectrometry method (AAS-3 spectrometer, Carl Zeiss, Germany with deuterium background correction). In order to determine the concentrations of the serum minerals, the samples were diluted (v/v 1:1) as follows: for iron, zinc and copper analyses, 0.01% Triton X-100 (Merck, Darmstadt, Germany) was used; while for the magnesium and calcium analysis, aqueous solutions consisting of 0.01% Triton X-100 (Merck) and 0.05% lanthanum chloride (Merck) were used. The iron, copper, zinc, calcium, and magnesium content in serum were determined at the following wavelengths: 248.3 nm (iron), 324.8 nm (copper), 213.9 nm (zinc), 422.7 nm (calcium), and 285.2 nm (magnesium).

The accuracy of the method was verified with certified reference material (HUM ASY CONTROL 2), and amounted to 95%, 99%, 96%, 99%, and 101% for Ca, Mg, Fe, Zn, and Cu, respectively.

Fasting glucose levels were determined by the routine enzymatic method. Plasma insulin was determined by immunoradiometric assay (DIAsource Immunoassays S.A., Nivelles, Belgium). The accuracy and precision of the techniques used to assay glucose and insulin were validated.

Insulin resistance in the participants was evaluated according to the homeostasis model assessment, using the insulin resistance (HOMA-IR) protocol:

HOMA-IR index = [fasting insulin (mU/l) × fasting glucose (mmol/l)]/22.5

Statistical Analysis

Data are shown as means ± SD. All calculations and statistics were performed using STATISTICA 6.0 software (StatSoft, Inc.). Comparisons between groups were carried out using the Mann-Whitney U test. Simple associations between variables were calculated as the Spearman coefficient of correlation. A p value of < 0.05 was regarded as significant.

Results

The characteristics of the 78 adolescents with obesity and the 20 healthy volunteers are shown in Table I. Obese subjects had significantly higher serum glucose and insulin concentrations, as shown in Table II. The levels of the HOMA-IR index significantly exceeded those observed in the control group.

Compared with the control group, the serum concentrations of Zn, Ca, and Mg were signifi-

Table I. Characteristics of the participants.

	Obese	Normal-weight control	*p*
N	78	20	
Gender (female/male)	42/36	11/9	NS
Age (years)	14.5±1.8	15.2±1.7	NS
BMI (kg/m^2)	31.1±5.6	20.9±1.4	$p < 0.001$
Body fat (%)	30.4±7.3	21.6±1.7	$p < 0.001$

BMI: body mass index; NS: not significant; N: number of subjects; *p*: significance level.

cantly lower than in obese subjects. There were no differences in the levels of Cu and Fe between the groups (Table III).

A strong inverse relation was documented between serum Zn concentration on one hand, and insulin concentration and HOMA-IR index on the other (see Table IV). Correlation between other minerals and insulin resistance and between BMI value and % of fat and minerals were not found. In the control group, no significant correlations were observed.

Discussion

The association of obesity with insulin resistance has been recognized in studies for decades[1,3,10]. In the present study, we found significant insulin resistance in obese adolescents, as represented by increased HOMA-IR indices, serum insulin, and glucose concentrations. In other studies, it has been observed that excess body fat, especially visceral fat, contributes to decreased insulin sensitivity in tissues[10].

In this study, the connection between obesity, fat content, and insulin resistance was confirmed in a coherent group of adolescents. We also found association between obesity and poor mineral status and its possible connection with insulin resistance in obese adolescents. The relationship between poor zinc status on one hand, and hyperinsulinemia and insulin resistance on the other in obese young people has also been observed in other studies[11,12]. It is known that zinc plays a major role in the synthesis and action of insulin. Zinc is a component of many enzymes, and is involved in the synthesis, storage, and release of insulin. Many experimental and clinical studies have documented the fact that zinc deficiency may create a predisposition to glucose intolerance and insulin resistance[13]. In this study, lower zinc concentration was found in the serum of the obese individuals than in the control. The low status of zinc may be caused by the low intake and urinary loss of this element in obese young people[15].

In this study, markedly lower serum calcium concentration was found among the obese adolescents than in the control group. In several studies, a lower intake of calcium and vitamin D has been demonstrated in obese children and adolescents than in nonobese children and adolescents[14,16]. Low dietary intake of calcium and vitamin D may decrease the serum calcium level of obese people. Low serum concentrations of calcium in obese adolescents may be connected with low vitamin D status. The interaction between vitamin D and calcium is well known. A deficit of the active vitamin D metabolite, 1,25-dihydroxyvitamin D (1,25(OH)(2)D), decreases absorption of calcium and disturbs calcium circulation in the body[17]. The results of some studies have shown that vitamin D deficiency is common among obese adolescents. Garanty-Bogacka et al[18] found that low vitamin D status is an independent predictor of insulin resistance. Vitamin

Table II. Glucose and insulin serum concentration and insulin resistance level in the studied groups.

	Obese	Normal-weight control	*p*
N	78	20	
Glucose (mmol/L)	5.0±0.3	4.7±0.3	$p = 0.01$
Insulin (μUI/mL)	16.8±6.9	8.0±1.8	$p < 0.001$
HOMA-IR index	3.7±1.4	1.7±0.4	$p < 0.001$

HOMA-IR: homeostasis model assessment-insulin resistance; N: number of subjects; *p*: significance level.

Table III. Serum concentration of minerals in the studied groups.

	Obese	Normal-weight control	*p*
N	78	20	
Fe (μmol/L)	20.6±4.5	20.1±3.4	NS
Zn (μmol/L)	11.9±2.5	16.0±3.0	$p < 0.001$
Cu (μmol/L)	15.7±2.8	17.0±3.1	NS
Ca (mmol/L)	2.2±0.1	2.4±0.1	$p < 0.05$
Mg (mmol/L)	0.8±0.1	0.9±0.1	$p < 0.05$

NS: not significant; N: number of subjects; *p*: significance level.

D deficiency has been shown to affect insulin secretion. It has been proposed that the potential role of vitamin D deficiency in insulin resistance is associated with inherited gene polymorphisms involving immunoregulatory function and other molecular actions for maintaining glucose homeostasis and mediating insulin sensitivity in the presence of low calcium status and obesity[19]. A limitation of this study is that we did not have available measurements for vitamin D to analyze its correlations with insulin resistance.

Lower magnesium status in obese children and adolescents was demonstrated in both our study and in others. Some authors found negative correlations between magnesium deficiency on one hand, and body mass index and insulin resistance on the other[20,21]. Magnesium plays a major role in regulating insulin effect and insulin-mediated glucose uptake in the body; a deficit of this element disturbs carbohydrate metabolism. In this study, we did not find a significant association connecting magnesium to body mass index or to insulin resistance index, although it was observed that low levels of magnesium in serum were related to high HOMA-IR index in obese adolescents.

Our study suggests some criticisms, for example we did not analyse the dietary intake (energy, minerals and vitamins) of the subjects. Moreover, other markers of mineral status for example transferrin concentration in serum, urinary ca:creatinin ratio or minerals concentration in urine were not assessed.

Table IV. Significant correlation between minerals and parameters in the obese.

	R	*p*
Zn-serum insulin	-0.52	< 0.001
Zn-HOMA-IR	-0.50	< 0.001

R: Spearman coefficient; HOMA-IR: homeostasis model assessment-insulin resistance;
p: significance level.

Conclusions

In this study it was found poorer zinc, calcium and magnesium status in obese subjects as compared to adolescences with normal weight. It was also found that low zinc status is associated with insulin resistance in obese adolescents. Increase of zinc, calcium, and magnesium intake in obese teenagers should be considered.

Acknowledgements

The research was supported by grants from the Polish Ministry of Science and Higher Education (0287/B/P01/2008/35).

Conflict of interest

The Authors declare that they have no conflict of interests.

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