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Trace Elements in Obese Turkish Children

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Abstract The quality of the diet of obese children is poor. Eating habits may alter micronutrient status in obese patients. In this study, we determined the serum levels of selenium, zinc, vanadium, molybdenum, iron, copper, beryllium, boron, chromium, manganese, cobalt, silver, barium, aluminum, nickel, cadmium, mercury, and lead in obese Turkish children. Thirty-four obese and 33 healthy control subjects were enrolled in the study. Serum vanadium and cobalt levels of obese children were significantly lower than those of the control group (0.244±0.0179 vs. 0.261±0.012 μg/l, $p<0.001$, and 0.14±0.13 vs. 0.24±0.15 μg/l, $p=0.011$, respectively). There was no significant difference between groups regarding the other serum trace element levels. In conclusion, there may be alterations in the serum levels of trace elements in obese children and these alterations may have a role in the pathogenesis of obesity.

Keywords Trace elements · Obesity · Children

Introduction

In the past 20 years, the prevalence of overweight and obesity has been increasing in children in developed countries [1]. Obese children are fed by diet including high carbohydrate and high fat [2]. This eating habit may alter micronutrient status in obese patients. [2]. Humans obtain trace elements from their daily diet and the serum concentrations of some trace elements are

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related to dietary intake of individuals [3, 4]. It has been shown that the serum zinc level is low in obese subjects because the dietary intake is insufficient [4]. Another trace element, iron, has also been found to be low in obese subjects; however, the etiology of the hypoferremia in obesity has remained uncertain [5]. It has been reported that some trace elements, especially chromium and vanadium, have a relationship with insulin resistance [6, 7]. In the pediatric age group, there are few studies which have shown a relationship between obesity and trace elements. In this study, we determined the serum levels of 18 trace elements in obese Turkish children.

Materials and Methods

This prospective observational study was conducted in the Department of Pediatric Endocrinology of Gulhane Military Medical Academy. All participants were recruited among patients who had been referred to the institution for evaluation of obesity. All patients were living in urban areas.

The participants underwent detailed physical examination, including evaluation for syndromes and endocrine diseases, and laboratory evaluation, including thyroid function testing and determination of diurnal variation of cortisol. Children with Prader–Willi and Laurence–Moon Biedl syndromes and those having obesity due to endocrine causes (Cushing's syndrome and hypothyroidism) were excluded. None of the subjects was on medication or had a history or evidence of metabolic, cardiovascular, respiratory, or hepatic disease. Patients receiving vitamin and/or mineral supplementation were excluded. Standing height (cm) was measured to the nearest 0.1 cm with a Harpenden fixed stadiometer (Holtain, Crosswell, UK), and body weight (kg) was determined on a SECA balance scale (Seca Vogel & Halke, Hamburg, Germany) to the nearest 0.1 kg, while the subjects were wearing a light T-shirt and shorts. Obesity was defined according to the body mass index (BMI) (>97th percentile) using the definition of the International Task Force of Obesity in Childhood and population-specific data [8, 9].

Blood samples were drawn using metal-free and stainless steel needles into appropriately coated tubes (Becton Dickinson Laboratories, Franklin Lakes, NJ, USA) for measurement of serum levels of selenium (Se), zinc (Zn), vanadium (V), molybdenum (Mo), iron (Fe), copper (Cu), beryllium (Be), boron (B), chromium (Cr), manganese (Mn), cobalt (Co), silver (Ag), barium (Ba), aluminum (Al), nickel (Ni), cadmium (Cd), mercury (Hg), and lead (Pb) in obese and control subjects. The tubes were centrifuged at 2,000×g for 10 min and the samples were tested for trace elements using Agilent 7500cx inductively coupled plasma-mass spectrometry (ICP-MS; Agilent Technologies, USA). The instrumental operating conditions for ICP-MS are presented in Table 1.

Fasting serum glucose, serum triglycerides (TG), total cholesterol (TC), and high-density lipoprotein cholesterol (HDL-C) levels were measured enzymatically using an autoanalyzer (Olympus 2700; Olympus Medical Systems Corp., Tokyo, Japan). The LDL-cholesterol (LDL-C) level was calculated using the Friedewald equation. Plasma insulin was measured by the electrochemiluminescence immunoassay method using an automated immunoassay analyzer (E170; Roche, Hitachi, Osaka, Japan). Glucose measurements were carried out with the photometric hexokinase method using an Advia 1800 chemistry analyzer (Siemens Healthcare Diagnostics, Deerfield, IL, USA). The children were carefully instructed to fast for a period of at least 12–14 h. The homeostasis model assessment of insulin resistance (HOMA-IR) index (fasting insulin×fasting glucose/22.5) was used for the determination of insulin resistance [10]. Insulin resistance criteria included a HOMA-IR >2.5 for prepubertal children and a HOMA-IR >4.0 for adolescents [11].

Table 1 Instrumental operating conditions for ICP-MS

Spectrometer	Mass
Integration time	3/point=9/mass for Hg
RF power (W)	1,500
Plasma gas flow rate (l/min)	(Argon) 15
Auxiliary gas flow rate (l/min)	0.90
Carrier gas flow rate (l/min)	1.06
Sampling depth (mm)	7.1
Acquisition mode	Spectrum
Number of replicates	3
Cone	Nickel

Statistics

All statistics were performed using SPSS 15.0 for Windows (SPSS, Inc., Chicago, IL, USA). A Student's *t*-test was used for comparisons of the two groups and Pearson's correlation tests were performed for correlations between parameters. Linear regression analysis was used to determine the effects of age, gender, BMI, HOMA-IR, and pubertal stage on trace elements, which are statistically different between groups.

Results

Thirty-four consecutive obese children (18 females and 16 males) with a mean age of 10.59±2.90 years, and 33 healthy control subjects (18 females and 15 males) with a mean age of 10.71±2.07 years were enrolled in the study. Obese children did not differ significantly from normal-weight children with respect to age, gender, and pubertal stage.

The rates of insulin resistance in obese and control groups were 52% (18/34) and 0.6% (2/33), respectively. The HOMA-IR values, fasting insulin levels, and serum TG levels of obese patients were higher compared to controls, whereas the serum HDL-C levels were found to be lower. Although the levels of serum Be, V, Cr, Fe, Zn, Co, Mo, Se, Ni, and B were lower in obese children, a significant difference was detected only for the V and Co levels. According to the levels of toxic trace elements, such as Hg, Pb, Al, and Ag, there was no significant difference between the groups. The laboratory values of both groups are presented in Table 2.

There was a negative correlation between serum Co levels and HOMA-IR, while the serum Ba, Pb, and Cd levels were positively correlated with the HOMA-IR values (Table 3).

According to the linear regression analysis, a negative linear correlation was found between BMI and V serum level ($r=-0.416$, $p=0.001$), whereas age, gender, HOMA-IR, and pubertal stage had no effect on serum V levels (Table 4). Moreover, there was a negative linear correlation between Co serum level and HOMA-IR, and BMI ($r=-0.330$, $p=0.007$ and $r=-0.302$, $p=0.013$, respectively). Age, gender, and pubertal stage had no effect on serum Co serum levels (Table 4).

Table 2 Comparison of laboratory values between groups

	Obese	Control	*p*
Insulin (U/l)	17.81±9.26	6.48±2.93	<0.001
Glucose[a]	90.23±9.84	86.36±8.59	0.092
HOMA-IR	4.04±2.21	1.41±0.69	<0.001
Cholesterol[a]	165.58±32.91	156.66±26.85	0.229
Triglycerides[a]	118.14±51.39	76.21±34.21	<0.001
HDL[a]	46.70±9.42	56.69±22.10	0.018
LDL[a]	89.32±34.35	84.84±19.95	0.518
AST	24.24±4.35	25.70±7.33	0.331
ALT	22.39±11.70	17.38±5.30	0.033
Hg (μg/l)	0.09±0.55	0.12±0.66	0.299
Pb (μg/dl)	4.44±7.87	4.19±7.37	0.898
Ba (μg/l)	3.32±5.18	2.21±0.85	0.242
Al (μg/l)	10.08±12.48	9.72±11.16	0.904
Ag (μg/l)	0.77±0.09	0.85±0.08	0.718
Be (μg/l)	0.067±0.09	0.086±0.12	0.487
B (μg/l)	1.14±2.09	1.36±1.72	0.640
V (μg/l)	0.244±0.0179	0.261±0.012	<0.001
Cr (μg/l)	13.59±2.47	13.84±1.61	0.624
Mn (μg/l)	0.72±1.51	0.55±0.41	0.530
Fe (μg/dl)	41.50±16.74	49.41±24.75	0.131
Ni (μg/l)	0.78±0.68	1.17±0.65	0.051
Co (μg/l)	0.14±0.13	0.24±0.15	0.011
Cu (μg/l)	987.11±183.83	962.01±248.59	0.641
Zn (μg/dl)	67.45±18.42	74.45±18.42	0.186
Se (μg/l)	111.01±38.24	122.10±36.67	0.234
Mo (μg/l)	0.68±0.38	0.73±0.23	0.549
Cd (μg/l)	0.041±0.050	0.039±0.023	0.831

[a] Values are expressed in mg/dl

Discussion

The eating habits are different between overweight and normal-weight children [12]. It has been reported that the quality of the diet of obese children is poor [2, 13]. In obese adolescents 56.6%, 30.5%, and 13.0% of energy was derived from carbohydrates, fats, and proteins, respectively [2]. Washi and Ageib [2] have also reported that, compared with the dietary reference intake, carbohydrate and fat intakes were higher, and calcium, iron, and zinc intakes were lower in obese children [2]. We thought that the eating habits of obese children may also alter the serum levels of other trace elements. In the current study, the alterations in serum levels of trace element were demonstrated in obese Turkish children.

It was reported that the prevalence of Fe deficiency in those who were overweight or obese was higher than normal-weight children and adults [5, 14]. In a cross-sectional, exploratory study, Menzi et al. [5] suggested that differences in the intake of heme and non-heme Fe, or intake of dietary factors known to have an effect on Fe absorption, were not

Table 3 Correlation of trace elements with HOMA-IR

	HOMA-IR	
	r	*p*
Be	−0.175	0.171
B	0.015	0.907
Al	0.138	0.276
Ba	0.339	0.007
V	−0.126	0.323
Cr	0.110	0.388
Mn	0.142	0.265
Fe	−0.064	0.618
Ni	−0.191	0.130
Co	−0.314	0.012
Cu	0.065	0.609
Zn	0.041	0.752
Se	−0.216	0.087
Mo	−0.142	0.263
Pb	0.376	0.003
Ag	−0.097	0.448
Cd	0.274	0.029
Hg	−0.144	0.259

r correlation coefficient, *p* significance

associated with lower serum Fe concentrations in obese adults [5]. On the other hand, Moayeri et al. [14] reported that the increased prevalence of Fe deficiency in adolescence mostly occurred in female adolescents. The reasons of Fe deficiency in female adolescents were explained by earlier pubertal onset or menarche [14].

Zn is an essential trace element in many biochemical reactions and for protein production [14]. Insulin action and insulin receptor tyrosine kinase (IRTK) activity may be stimulated by Zn [15–17]. There are different results in terms of serum Zn levels in obese children and adults. Marreiro et al. [18] reported that Zn concentrations in plasma and erythrocytes were significantly lower in the obese group, and they also reported that Zn

Table 4 Linear regression tests results

	V		Co		Ba		Pb		Cd	
	r	*p*	*r*	*p*	*r*	*p*	*r*	*p*	*r*	*p*
Age	−0.016	0.455	−0.061	0.328	−0.210	0.062	0.020	0.442	0.152	0.132
Gender	−0.132	0.165	−0.189	0.084	−0.160	0.122	−0.100	0.223	0.035	0.400
BMI	−0.416	0.001	−0.302	0.013	0.118	0.195	0.006	0.483	0.048	0.363
HOMA-IR	−0.075	0.291	−0.330	0.007	0.439	<0.001	0.412	0.001	0.287	0.016
Pubertal stage	0.053	0.350	−0.067	0.314	0.242	0.037	0.178	0.097	−0.041	0.383

r correlation coefficient, *p* significance

supplementation might improve insulin resistance in women [19]. In contrast, Weisstaub et al. [20] reported that the serum Zn levels in preschool children were not associated with body weight. In our study, we found that serum levels of Fe and Zn tended to be lower in obese children; however, the difference was statistically insignificant. This may be explained by the low number of subjects enrolled in the study and the high prevalence of Fe deficiency in Turkish children.

V is a trace element having several functions in biochemical and physiological processes [21]. It has been reported that V complexes may stimulate glucose uptake, glycogen synthesis, and lipogenesis, and suppress lipolysis and gluconeogenesis [22–25]. Insulin acts via insulin receptor substrates-1 and -2 in cells, and insulin action is terminated by tyrosine phosphatase. V may inhibit tyrosine phosphatase [23], and thus has an insulin-like effect in vivo [26] and may improve hyperinsulinism, hypercholesterolemia, and hypertension [27]. Hyperinsulinism is common in childhood obesity. In the current study, we found that serum V levels were significantly lower in the obese group. Although the serum V levels were not correlated with insulin resistance parameters, we considered that V replacement might have a beneficial effect on obese children, especially in the case of hyperinsulinism. However, further studies should be performed to support this hypothesis.

It has been shown that suboptimal dietary intake of Cr(III) is a major contributing factor for type 2 diabetes mellitus and cardiovascular diseases [28]. Cr has beneficial effects on obesity and insulin resistance [29]. However, Wang and Cefalu [30] have reported that a consistent significant and beneficial effect of chromium may not be observed. They have also reported that recent data fail to demonstrate significant improvement in carbohydrate metabolism in individuals with metabolic syndrome, impaired glucose tolerance, or consistently in individuals with type 2 diabetes [30]. Wang and Cefalu suggest that patient selection may be an important factor in determining clinical response, as it was concluded that a clinical response to chromium may be more likely in insulin-resistant individuals with type 2 diabetes who have more elevated fasting glucose and hemoglobin A (1c) levels [30]. In the current study, Cr was not correlated with HOMA-IR, and there was no statistically significant difference between obese and control groups.

We found a correlation between HOMA-IR and Co levels in this study. Previously, Vasudevan and McNeill [31] and Nomura et al. [32] have reported that that chronic cobalt treatment decreases plasma glucose levels in STZ-diabetic rats and improves tolerance to glucose. Different mechanisms have been suggested in this beneficial effect of Co on glucose metabolism. Vasudevan and McNeill [31] suggested that Co has an insulinomimetic effect like vanadium. Nomura at al. [32] have demonstrated that cobalt treatment may improve glycogen depot via suppressing glucagon signaling. Our results have suggested that Co may also have an effect on human glucose metabolism. Despite these beneficial effects of Co, it has not been forgotten that it may be toxic for human in ionic form.

Ni may alter glucose homeostasis by affecting insulin secretion [33, 34]. In the study of Aguilar et al. [35] serum levels of Ni were high in adults with type 2 diabetes mellitus. On the other hand, in the present study, there was a statistically insignificant difference between two groups with respect to serum Ni levels and no correlation was observed between HOMA-IR and serum Ni levels.

In conclusion, there may be alterations in the serum levels of trace elements in obese children. These alterations may also play a role in the pathogenesis of obesity. We suggest that a high-quality diet and trace element supplementation would have beneficial effects on insulin resistance and obesity in children.

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