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Relationship Not Found Between Blood and Urine Concentrations and Body Mass Index in Humans With Apparently Adequate Boron Status

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Abstract The impact of boron on the development of obesity remains controversial in the analysis of experimental and clinical data. The objective of this study was to investigate the relationship between blood and urine boron concentrations and obesity in normal, overweight, obese, and morbidly obese subjects in different age groups. A total of 105 subjects were categorized into 12 groups based on body mass index and three different age levels: as young adult (18 to 34 years old), adult (35 to 54 years old), and older adult (greater than 55 years old). Age, gender, body mass index, and blood and urine boron concentrations were recorded for each subject. There were 50 women and 55 men, with a mean age of 44.63 ± 17.9 years. Blood and urine boron concentrations were similar among the groups (p = 0.510 and p = 0.228, respectively). However, a positive correlation between age and blood boron concentration (p = 0.001) was detected in contrast to the presence of a negative correlation between age and urine boron concentration (p = 0.027). Multiple linear regression analysis showed that there was no significant relationship between gender, age, and quantitative values of body mass index for each subject, and blood and urine boron concentrations. Although the relationship between boron and obesity has not been confirmed, changes of blood and urine boron concentrations with age may have some physiologic sequences to cause obesity.

Keywords Obesity · Morbid · Body mass index · Boron · Adults · Age

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Introduction

Boron is an element which is consumed from natural substances like water, vegetables, and fruits. It is known to have an effect on bone metabolism, coagulation systems, and physiologic effects of steroid hormones and pro-inflammatory cytokines [1–3]. In studies on humans and animals, it has been shown that boron consumption with supra nutritional amounts leads to weight loss due to short- and long-term metabolic effects of boron. In addition, the high catabolic rate caused by the increase in thermogenesis and lipolysis was thought to be important as the underlying pathophysiological mechanism [4–6].

In another study which was performed on healthy obese and non-obese people, it was determined that there was an inverse relationship between blood boron concentration (BBC) and body mass index (BMI) [7]. Although this study was the first human study showing the inverse relationship between obesity and boron, age of the individuals seemed to be the parameter affecting the results. In previous studies, it has also been shown that age is an important issue in terms of physiology and metabolic effects of boron [2, 8, 9]. With regard to physiology, absorption, and metabolism of boron, more reliable conclusions can be made by using both BBC and urine boron concentration (UBC) [7]. As an indicator of boron exposure or intake, UBC can be regarded as the ideal sample for screening purposes due to the fact that almost all ingested boron is excreted in urine within 24 h [2]. Therefore, age-controlled prospective studies with use of both BBC and UBC are needed.

This study aimed to investigate the possible interaction between BMI, BBC, and UBC of individuals in different age groups.

Materials and Methods

A prospective observational study approved by the local Ethical Committee of Clinical Trials was conducted. All subjects gave informed consent for inclusion into the study.

The cases were categorized into four groups based on their BMI which was calculated by dividing weight in kilograms by the square of height in meters: BMI 18.5 to 24.9 kg/m^2 as normal; BMI 25.0 to 29.9 kg/m^2 as overweight; BMI 30.0 to 39.9 kg/m^2 as obese; and >BMI 40.0 kg/m^2 as morbid obese. Additionally, all groups were subdivided into three subgroups based on age grouping as young adult (18 to 34 years old), adult (35 to 54 years old), and older adult (greater than 55 years old), yielding a total of 12 groups.

A total number of 120 subjects with 10 in each group from January 2014 to December 2014 were planned and enrolled consecutively from a list of general surgery and bariatric surgery outpatient clinics to minimize the effect of age on the results of the study. Patients receiving vitamin and/or mineral supplementation, and who had history of chronic metabolic, cardiovascular, respiratory, or hepatic diseases were excluded. Therefore, 105 subjects were included into the study (Table 1).

Demographic data including age, gender, and BMI was recorded for each subject. Blood samples were taken and centrifuged for 10 min at 3000 rpm. Blood boron testing was performed using Thermo Scientific X Series 2 ICP-MS (power, 1460 W; nebulizer gas, 1.06 l/min; cooling gas, 13 l/min; auxiliary gas, 0.7 l/min). Ammonia (0.07 mM), 0.01 mM EDTA, 0.07 % Triton X-100 *v*/*v*, and 1.5 % butane-1-ol *v*/*v* solutions were used to have 1/20 diluted samples. Urine samples taken as the first urine of the day were diluted to 1/15 by using solution of HNO_3 1 %. Calibration solutions were prepared in doses of 2, 20, 200, and 2000 parts per billion (ppb). Abbreviations of ppb and parts per million (ppm) were used for BBC and UBC, respectively. Mean values of three measurements for each blood and urine sample were recorded as BBC and UBC, respectively.

Table 1 Distribution of the subjects based on the age grouping

Age groups	Groups based on BMI			
	Normal	Overweight	Obese	Morbid obese
<35 years	14	8	7	3
35–54 years	10	12	10	8
>55 years	6	11	10	6

Statistical Analysis

All statistics were performed using SPSS 20.0 for Windows (SPSS, Inc., Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviation (SD). Categorical variables were expressed as frequencies and evaluated by the chi-square test. The Pearson chi-square test was used for comparison of gender distribution among the groups. One-way analysis of variance (ANOVA) and Kruskal-Wallis test were used to compare the differences in age, BBC, and UBC between the groups based on BMI, respectively. Pearson's correlation tests were performed for correlations between these variables. Multiple linear regression analysis was used to determine the effect of BBC and UBC, age, and gender on BMI. The differences were considered statistically significant if the *p* value was equal to or less than 0.05.

Results

The study group included 105 subjects consisting of 50 women and 55 men, with a mean age of 44.63 ± 17.9 years. The mean BBC and UBC of the all individuals were 70.7 ± 78.8 ppb and 0.93 ± 0.6 ppm, respectively. Demographic features, BBC, and UBC are given in Table 2.

Distribution of the age pattern among the groups were similar ($p = 0.133$, ANOVA). However, there was a heterogeneous gender pattern between the groups resulting in a significant difference ($p = 0.018$, Pearson chi-square). There were more male subjects in the overweight group contrary to the presence of more female subjects in the morbid obese group. BBC and UBC were similar among the groups ($p = 0.510$ for BBC and $p = 0.228$ for UBC, Kruskal-Wallis for both).

There was a significant correlation between age and BBC ($p = 0.001$) (Table 3). While age was increasing, BBC was also increasing significantly. However, a negative correlation was detected between age and UBC ($p = 0.027$).

Multiple linear regression analysis (Table 4) used the BMI as the dependent variable, and gender, BBC, UBC, and age as independent variables. None of the independent variables was significantly associated with variability in BMI ($p > 0.05$).

Discussion

It has been thought that there may be a relationship between the levels of trace elements and obesity. Although an adequate boron status based on serum boron levels was detected in obese and control groups, serum vanadium and cobalt levels

Table 2 Demographic data, BBC, and UBC of the subjects

Groups	*N*	BMI	Age	Gender (M/F)	BBC[a]	UBC[b]
Normal	30	22.7 ± 1.75	38.4 ± 16.5	15/15	56.1 ± 50.6	0.9 ± 0.6
Overweight	31	26.9 ± 1.13	45.418.1	22/9	83.4 ± 95.5	0.9 ± 0.5
Obese	27	34.2 ± 2.92	48.0 ± 18.2	14/13	82.9 ± 98.2	1.2 ± 0.8
Morbid obese	17	43.7 ± 5.74	48.9 ± 16.7	4/13	54.0 ± 45.5	0.7 ± 0.3
p			0.133	0.018	0.510	0.228

[a] Parts per billion (ppb)

[b] Parts per million (ppm)

were significantly lower in obese children. Therefore, it is thought that alterations in the serum levels of trace elements may have a role in the pathogenesis of obesity [10].

Although a negative significant relationship between BMI and BBC has been previously shown by the same authors, the present study has not proved this relationship after controlling the age parameter. This appeared to be a factor influencing the results in the previous study [7]. Therefore, future studies are still needed to clarify the possible relationship between trace elements and obesity, although it is proved to be a difficult issue.

Although there has been conflicting results with regard to the effect of boron on weight loss in animals, it has been speculated that low dose oral boric acid supplementation causes serious weight loss in mice [4]. In Aysan's study, it was thought that higher catabolism of macronutrients with unknown mechanisms produced the body's weight-reducing effect of boron. In the subsequent experiment by the same author, it was shown that oral boric acid intake caused over-expression of thermogenic proteins via uncoupling protein pathways in the adipose and skeletal muscle tissues [6]. The result was accelerated lipolysis and body weight loss. Therefore, it can be thought that supra nutritional consumption of boron causes some pathological changes resulting in body weight loss. But, it is believed that translation of this association to clinical studies still needs to be supported by future studies.

The subjects in this study were categorized according to their BMI as normal, overweight, obese, and morbid obese. All groups were similar in terms of gender in contrast to the previous study in which age has been regarded as an uncontrolled parameter [7]. Beside the presence of more male and female subjects in the overweight and the morbid obese groups, respectively, there was no difference in BBC and UBC for all groups. Therefore, the hypothesis in which there is a negative association between boron and obesity has not been confirmed.

It is generally accepted that the assessment of boron intake is difficult because there is no national database for boron amounts in foods, drinking water, and personal care products [11]. The subjects who were included in the study were all provided from the most crowded city of Turkey. There are no reports investigating boron deficiency of the people living in all cities of our country until now. Therefore, it could not be possible to show any relationship between the results of our study and boron deficiency status. However, an adequate boron status was seen in all individuals attending to the present study according to BBC over 0.5 ppb as an indicator of adequacy [2, 12]. In the present study, the data with regard to the usual adult human dietary consumption of boron was also lacking. It is generally accepted to use mineral excretion data calculated as the percentage of mineral intakes because of fluctuations of energy intakes adjusted with body weight [2]. However, it is difficult to control and measure the amount of

Table 3 Pearson correlation analysis between parameters

		Age	UBC	BBC	BMI
Age	Pearson correlation coefficient	1	−0.216[a]	0.306[b]	0.194[a]
	2-tailed significance		0.027	0.001	0.047
UBL	Pearson correlation coefficient	−0.216[a]	1	0.018	0.025
	2-tailed significance	0.027		0.859	0.798
BBC	Pearson correlation coefficient	0.306[b]	0.018	1	−0.029
	2-tailed significance	0.001	0.859		0.770
BMC	Pearson correlation coefficient	0.194[a]	0.025	−0.029	1
	2-tailed significance	0.047	0.798	0.770	

[a] Significant at the 0.05 level (two-tailed)

[b] Significant at the 0.01 level (two-tailed)

Table 4 Multiple regression analysis of BMI (dependent variable) on gender, BBC, UBC, and age as independent variables

Model	*R* square	*F*	*p*
1	0.079	2.135	0.082

dietary intake of such elements. It is generally known that foods of plant origin, due to high water solubility of boron, are usually rich sources in contrast to meat and fish [11, 13]. In previous studies, it has been shown that boron intake increased significantly in cases of consumption of some specific foods such as apples, grapes, tomatoes, avocado, and broccoli [2, 11]. Thus, the daily intake of boron by humans shows great variability based on food groups in the diet [13]. In the present study, food consumption profile of the subjects was not evaluated in addition to the dietary consumption of boron. It has been thought that assessment of these parameters, i.e., food consumption profile and dietary consumption of boron, may contain important challenges to reach an accurate result in our population. If this could be achieved, it is possible to calculate accurate assessment of physiology, absorption, and excretion of boron in each subject and by this way the impact of boron on obesity could be better determined.

Absorption of boron from the gastrointestinal tract and excretion from the urinary tract are nearly 100 % [8, 11]. It has been thought that boron may be under homeostatic control with some biological functions in humans due to obligatory boron loss and relatively small changes in blood boron values during substantial increases in dietary boron supplementations and lack of boron accumulation except in bone [2, 11, 14]. Boron is kept in relatively stable concentrations in plasma when boron is fed in nutritionally adequate amounts. Also, it has been known that supra nutritional boron intakes do not cause significantly proportional increases in plasma concentrations because of increased renal excretion [11]. As a result, tissue and blood boron concentrations are usually kept at a steady state irrespective of other parameters including dietary intake. However, there has been some controversy about sensitivity of BBC as an indicator of dietary boron intake. It has also been known that there was a remarkably narrow range of blood boron concentrations in subjects with unknown dietary histories [2, 14]. The differences in blood boron values among the previous studies were thought to originate from the analysis methods that were used. In Hunt's study including postmenopausal women subjects, there was a 1.5-fold increase in plasma blood boron concentrations beside a 9.0-fold increase in dietary boron [2]. Although it would be expected that daily boron excretion rate is influenced by dietary boron intake and regarded as an indicator of boron intake, it has been shown that there was no correlation between boron excretion, dietary intake, and boron accumulation in humans [2, 11, 13]. In light of this evidence, differences in BBC should not be considered alone to evaluate the possible association between boron and its metabolic consequences. The rate of boron excretion is extremely rapid responding to dietary boron supplementation within 24 h [2]. Therefore, it is more logical to consider the urinary boron concentrations mirroring the boron intake.

The Nutrition and Food Board of the USA considers age as an important factor for the amount of boron intake [15]. In the present study, a significant positive correlation was detected between age and BBC. However, lower concentrations of UBC were detected as age of the subjects was increasing. This difference in UBC may just be caused by the age factor in which the amount of urine excreted varies with age. Therefore, variances in age and gender, hormonal status, boron-deficient status, and dietary boron intake should be considered in evaluation of these conflicting findings [13]. Therefore, this issue remains to be clarified by future experimental studies.

Limitations

First, although we planned to include a total of 120 subjects, it was not possible to obtain this number. In addition, it may be thought that the number of the participants was inadequate to prove the hypothesis. Second, it was not possible to control the distribution of age and gender throughout the study. Age and gender were the uncontrolled parameters possibly affecting the results in the previous and the current study, respectively. Third, the status of boron deficiency, if present, and the concentration of boron intake could not be calculated for the study. Lack of data with regard to menopausal status and hormonal concentrations of the female participants and status of the thyroid function of all subjects might be regarded as the other limitation factors.

Conclusion

Although the relationship between boron and obesity has not been confirmed even after controlling the age parameter, it appears to be a factor influencing the results. Changes of blood and urine boron concentrations with age may have some physiologic sequences to cause obesity. Therefore, future prospective studies are still needed to clarify the physiology, absorption, and excretion of boron in humans with different age groups.

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