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Evaluation of serum boron levels and lipid profile in pregnancies with or without gestational diabetes

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Abstract

Aims: Animal research has demonstrated that boron has effects on triglycerides and glucose and may act as a metabolic regulator in several enzymatic systems. Gestational diabetes mellitus (GDM) is a prevalent obstetrical complication and the lack of data on maternal status of boron in normal/diabetic pregnancies, prompted us to undertake this study.
Methods: Maternal blood samples were collected during screening and diagnosis of GDM at 24–28 weeks. Serum lipids (total cholesterol, high-density cholesterol, low density cholesterol, triglycerides, lipoprotein-a, apolipoprotein-A-I and apolipoprotein-B) and boron levels were determined. Fifteen non-GDM and 19 GDM women constituted the study population.
Results: The mean age was 30.1±5 years. The median boron levels were 15.2 μg/L (0.0152 ppm; range, 8.4–25.4 μg/L). When GDM and non-GDM cases were compared for age, gravidity, parity, lipid profiles and serum boron levels, no significant differences were found (P>0.05). No correlation was found between lipids and boron levels.
Conclusion: This preliminary study contributes to the limited information about the metabolic aspects of boron. Considering the evidence that boron acts as a regulator of energy substrate utilization, the effect of dietary boron on glucose metabolism deserves further research.

Keywords: Boron; gestational diabetes mellitus; lipids, lipoprotein; trace elements.

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Introduction

There is a paucity of data concerning maternal and fetal outcome associated with trace elements, such as copper, iron, and zinc, and data on boron are lacking. Boron is a trace element known to be essential for plants and animals. Nutritional amounts of boron are beneficial for humans. The concentrations of boron in human tissues are very low. Daily intake of boron by humans depends on the dietary intake mainly from fruits and vegetables [16]. The biochemical and physiological functions of boron in humans is not yet clearly defined. There are a limited number of studies evaluating boron in humans.

Some studies in animals have demonstrated that boron has effects on energy substrates like triglycerides and glucose [3, 7], and may act as a metabolic regulator in several enzymatic systems [8]. Considerable evidence indicates that glucose responds to physiologic supplements of dietary boron, especially during concomitant vitamin D_3 deficiency [8]. In animals with vitamin D_3 deficiency, dietary boron decreased the abnormally elevated plasma glucose concentrations by 29% as compared to 6% in the control group without vitamin D_3 deficiency [6]. Ongoing research in animals suggests an interaction between dietary boron and vitamin D_3, that modifies energy substrate utilization [8]. Moreover, boron modulates hepatic glycolysis and a lipid lowering action of this molecule has also been reported [8]. The lack of data on the maternal status of boron in normal and diabetic pregnancies prompted us to undertake this study. This study is the first in the literature evaluating serum boron levels and lipid profile in pregnancies with or without gestational diabetes mellitus (GDM).

Materials and methods

The study was approved by the research Ethics Committee of the university. All participants gave informed consent before enrollment to the study and all were carrying singleton gestations. The study population consisted of patients who were admitted to a university clinic for routine antenatal follow-up. Participants who completed prenatal care and delivered a live term infant after 36 weeks, were included in the study (n=34). The exclusion criteria were pregestational diabetes mellitus, pre-eclampsia or gestational/chronic hypertension (systolic blood pressure >140 mm Hg and diastolic blood pressure >90 mm Hg), fetal congenital anomaly, multiple pregnancies, smoking and alcohol consumption.

The age, prepregnancy weight, gravidity, and parity were noted at admission. In all cases, blood samples for serum boron levels and the lipid profile were collected in the morning after overnight fasting for at least 12 h. Blood sampling was performed during screening and diagnosis of GDM at 24–28 weeks of gestation. A glucose challenge

test (50 g in all women) was performed at 24–28 weeks of gestation in all participants [18]. Screen positive (plasma glucose ≥140 mg/dL) women further underwent a 100 g glucose tolerance test (GTT). Screen negative (plasma glucose <140 mg/dL in 50 g) results or one abnormal plasma glucose level in 100 g GTT, were considered as a non-GDM pregnancy. If two of four plasma glucose levels were abnormal in 100 g GTT (≥105, 190, 165 and 145 mg/dL) then a diagnosis of GDM was made [18].

Maternal blood samples were collected from antecubital veins into a non-heparinized tube. Samples were immediately centrifuged, and serum was separated and frozen at –80°C until it was assayed. Serum boron levels were measured from thawed serum samples. Concentrated nitric acid (5 mL) was added to the containers holding the sample and the cap was tightened. The container was then loaded into a 12-position carousel and placed into a microwave oven. The samples were heated with 600 W of power for about half of a 12.5 min program (6 min). The samples were allowed to cool to room temperature, and 0.75 mL of 30% hydrogen peroxide was added. The containers were recapped and heated again as before. The samples were removed from the oven, allowed to cool, filtered through Whatman 541 filter paper, and diluted with 15 mL of deionized water. Blank, method blank, and quality control samples were also treated in the same manner. The analytical instrument used for analysis of standards and samples was an Inductively Coupled Plasma – Mass Spectrometer (ICP-MS, 7500 cx, Agilent Technologies, Inc., Bellevue, WA, USA). The intra assay and inter assay coefficients of variation are 1.66% and 3.26%, respectively, for boron analyses by ICP-MS. Serum lipids (total cholesterol [Total-C], high-density cholesterol [HDL-C], low density cholesterol [LDL-C], triglycerides [TG], lipoprotein a [Lpa], apolipoprotein-A-I [apo-A-I] and apolipoprotein-B [apo-B]) were determined. The serum levels of lipids were determined with enzymatic colorimetric assays (Roche Diagnostic, Mannheim, Germany). Gestational age at birth and birth weight of the neonates were obtained from medical records.

Statistical analyses

Data analysis was performed using SPSS for Windows, version 11.5 (SPSS Inc., Chicago, IL, USA). Whether the distributions of continuous variables were normal or not was determined by the Shapiro-Wilk test. Data were shown as mean±standard deviation (SD) or median (range) where applicable. The means were compared using the Student's *t*-test; otherwise, the Mann-Whitney *U*-test was applied for comparisons of the median values. Nominal data were analyzed by the χ^2 or Fisher's exact test. Degrees of association between continuous variables were calculated by Spearman's rank correlation analyses. A P-value <0.05 was considered statistically significant.

Results

Fifteen participants who were screened were negative for GDM and 19 cases were diagnosed with GDM. The mean age was 30.1±5 years. The median (range) of gravidity and parity of the study population were 2 (1–9) and 0 (0–4), respectively. The mean gestational age at serum sampling was 25.3±1.6 weeks. The mean birth weight and gestational age at birth were 3480±305 g and 38±1 weeks, respectively. Maternal and fetal parameters of the patients are shown in Table 1. The mean serum boron levels were 15.5±4.2 µg/L (16.3±4.3 µg/L in non-GDM and 14.9±4.1 µg/L in the GDM group).

The mean values for the lipid profile of the women were as follows (Table 2): total-C=236±38 mg/dL; HDL-C=70±17 mg/dL; LDL-C=137±37 mg/dL; and TG=200±64 mg/dL. The median values (range) were 0.3 g/L (0.1–1.8 g/L) for Lp(a); 2.2 g/L (1.6 g/L–2.9 g/L) for apo-A-I; 1.0 g/L (0.7 g/L–1.6 g/L) for apo-B. apo-A-I/HDL cholesterol was calculated in both groups. Mean apo-A-I/HDL cholesterol in the non-GDM and GDM groups was 0.0300±0.0054 and 0.0318±0.00526, respectively. There were no statistically significant differences between the baseline characteristics (age, gravidity, parity), lipid profiles and serum boron levels in GDM and non-GDM cases (Table 1, P>0.05). Also, apo-A-I/HDL cholesterol did not differ between the two groups (P=0.293). The results of Spearman's rank correlation analysis showed no correlation between lipid profile parameters and serum boron levels in the whole group.

Discussion

Boron is poorly investigated in human tissues and body fluids. The data in the literature does not provide an adequate basis for formulating baseline concentrations of boron. Therefore, results from selected studies are available for information only. The reported reference values for boron from earlier investigations using colorimetry are unreliable, due to analytical problems of sampling and contamination [9]. The progress in analytical chemistry of trace element measurement in clinical specimens helped to resolve this problem. The technique used in this study, ICP-MS, gives reliable data for ultra-trace concentrations. In recent studies, the median of normal boron

Table 1 Maternal and fetal parameters of the patients.

Parameter	GDM group (n=19)	Non-GDM group (n=15)	P
Maternal age (years) mean±SD	30.3±5.4	30.0±4.7	NS
Maternal weight (kg) mean±SD	65.7±9.1	64.5±9.3	NS
Gravidity median (range)	2 (1–4)	2 (1–9)	NS
Parity median (range)	0 (0–2)	1 (0–4)	NS
Gestational age at serum sampling (weeks) mean±SD	25.6±1.9	24.8±1.0	NS
Gestational age at birth (weeks) mean±SD	38.3±1.7	39.3±0.8	NS
Birth weight mean±SD	3374.7±276.3	3614.2±296.2	<0.05

GDM=gestational diabetes mellitus, SD=standard deviation, NS=not significant.

Table 2 Lipid profile of the patients.

Parameter	GDM group (n=19)	Non-GDM group (n=15)	P
Total-C (mg/dL) mean±SD	239.8±39.7	232.2±36.7	NS
HDL-C (mg/dL) mean±SD	67.5±13.7	75.3±20.3	NS
LDL-C (mg/dL) mean±SD	138.9±42.1	135.6±31.0	NS
TG (mg/dL) mean±SD	207.9±66.8	191.1±60.7	NS
Lp(a) (g/L) median (min–max)	0.39 (0.08–1.21)	0.27 (0.01–1.83)	NS
Apo-A-I (g/L) median (min–max)	2.05 (1.6–2.6)	2.26 (1.8–2.9)	NS
Apo-B (g/L) median (min–max)	1.01 (0.7–1.5)	0.95 (0.7–1.6)	NS

Apo-A-I=apolipoprotein-A-I, Apo-B=apolipoprotein-b, GDM=gestational diabetes mellitus, HDL-C=high-density cholesterol, LDL-C=low density cholesterol, Lp(a)=lipoprotein a, NS=not significant, SD=standard deviation, Total-C=total cholesterol, TG=triglycerides.

levels was reported as 0.022 ppm (range=0.008–0.048 ppm) in blood serum samples of 50 humans [1]. In our study, the median serum boron levels of the participants were 15.2 μg/L (0.0152 ppm, range=8.4–25.4 μg/L), which is within the previously reported normal range. Others [21] reported the mean level of boron in serum as 0.022 ppm±0.005 in normal humans. Like many other trace elements, the concentrations of boron in tissues and body fluids are influenced by dietary availability or environmental factors. Therefore, as previously suggested by Iyengar and Woittiez [9], the median values of boron seem to be a better indicator of the central tendency than the mean.

Among the factors known to influence serum levels of different trace elements like age, sex, living environment and diet, pregnancy, also, is a common condition that might alter the normal values. This study is the first in the literature reporting data for the concentrations of boron in serum samples of pregnant women. Although the serum boron levels of pregnant women in this study are within the normal range when compared with previous data reporting serum values of non-pregnant individuals, further studies evaluating serum boron levels in pregnancy are required to evaluate the influence of pregnancy on blood boron levels. Furthermore, it has been postulated that boron participates in the hydroxylation process, or extends the half life of steroid hormones through its affinity for hydroxyl groups [15]. Whether there is a specificity of action of boron on steroid hormones (progesterone and estrogens) that gradually increase throughout the pregnancy, awaits further research.

Forbes et al. [4] determined boron levels in several tissues of one individual, and found that bone tends to have a higher level of boron, while fat, muscle, heart, lung, and intestine show lower amounts of the element. The reported different concentrations of this element in these tissues might be due to diverse effects of boron. However, there are only limited studies in animals about the metabolic role of boron.

Although a larger sample size would allow a more optimal statistical analysis, our study did not find any significant difference between GDM and non-GDM groups. Despite the fact that this study was carried out in a small population, the data is unique for evaluating the metabolic aspects of pregnancy and serum boron levels. This preliminary data does not allow us to draw strong conclusions, but will add to understanding of the metabolic aspects of boron during pregnancy. Further studies are needed to determine any difference in serum boron levels in these patients.

Vitamin D_3 influences energy substrate utilization as well as mineral metabolism. Vitamin D_3 is essential for insulin secretion [10, 17], and the effect of vitamin D_3 on glycolysis was shown in animal studies [8]. In addition, treatment of patients with chronic renal failure, impaired glucose tolerance and hyperlipoproteinemia, using a synthetic analogue of vitamin D_3, has reduced fasting blood-glucose levels and serum triglycerides [13]. In pregnancy, the role vitamin D plays in development and glycemic control of GDM needs future randomized trials, but recent studies showed that women with GDM had a 2.66-fold increased risk of 25-hydroxy vitamin D_3 deficiency (<15 ng/mL) compared with the control group [19]. These findings were supported by a retrospective, cross-sectional study which found that lower 25(OH)D levels were independently associated with poorer glycemic control in GDM [12]. If further data supports the importance of vitamin D_3 in GDM, then boron levels in pregnancy may receive more attention, as boron affects some aspect of vitamin D_3 metabolism [8]. We hypothesize that the effects of boron on vitamin D_3 and energy substrate metabolism may play a role in the development of GDM in pregnancy. Although serum vitamin D_3 levels were not measured in our study, all the participants received 500 IU vitamin D_3 supplementation, and serum boron levels did not differ between GDM and non-GDM pregnancies.

The effect of boron on plasma lipids is another aspect necessitating research. The only available data regarding this subject is from animal studies. According to present findings, boron containing hypolipidemic agents administered to rats, reduce cholesterol, triacylglycerol and LDL-C levels, and elevate HDL-C after 2 weeks [5]. Additionally, the lipid-lowering action of boron was further observed in a study performed in rats [14]. The probable favorable effects of boron levels on plasma lipids in humans are yet to be evaluated. This is the first study designed to evaluate the association between serum boron levels and lipids in pregnant women.

During early pregnancy, an accumulation of maternal fat occurs followed by increased adipose tissue lipolysis and subsequent hyperlipidemia, which mainly corresponds to increased triglycerides in all circulating lipoproteins. In

normal pregnancies, plasma cholesterol levels increase, but the elevation of plasma triglycerides is more profound. The results of lipid profiles in the cases in this study are very similar to lipid levels reported in previous studies [2]. In our study, consistent with the previous data, [20], no significant differences in the lipid levels of GDM and non-GDM groups were observed. On the contrary, Koukkou et al. [11] reported higher triglyceride and lower LDL cholesterol levels in GDM, but no difference in HDL cholesterol, TC, apo-A-I, and apo-B. The role that boron might play in the metabolism of lipids is based on the hypothesis that this element stimulates the hydroxylation-related processes of the cholesterol nucleus [15]. Although no correlation between boron levels and lipid parameters was found in this study, further studies with a larger number of cases and different patient populations will help to clarify this issue.

This preliminary study will contribute to the limited information about the metabolic aspects of boron. Considering the evidence that boron acts as a regulator of energy substrate utilization, the effect of dietary boron on glucose metabolism deserves further research.

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