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Trace Elements in Children Suffering from Idiopathic Nephrotic Syndrome

İdyopatik Nefrotik Sendromlu Çocuklarda Eser Element Düzeyleri

Sebahat Tulpar[1], Zubeyde Gunduz[1], Ugur Sahin[2], M. Hakan Poyrazoglu[1], Ismail Dursun[1], Ruhan Dusunsel[1], Funda Bastug[1]

[1]Department of Pediatric Nephrology, Erciyes University Faculty of Medicine, Kayseri, Turkey
[2]Department of Chemistry, Erciyes University Faculty of Arts and Sciences, Kayseri, Turkey

Abstract

Objective: Trace elements play a significant role in several metabolic processes and often circulate in the blood binding to protein. The purpose of this study was to determine the status of selenium, zinc, and boron in idiopathic nephrotic syndrome patients in active and remission phases.

Materials and Methods: Fourteen patients and fourteen healthy age-matched controls were included in the study. The selenium, zinc and boron level in plasma and urine were measured by the inductively coupled plasma mass spectrometry.

Results: The plasma levels of zinc and selenium were significantly lower in both active and remission patients (for all p=0.0001). The plasma boron level was significantly lower only in patients in active phase (p=0.0002 vs control). The concentrations of urinary boron and selenium were significantly higher during active phase compared with remission (p=0.0003 and 0.0001, respectively).

Conclusion: Supplementation with zinc, selenium and boron may be justified in patients suffering with this disease.

Key Words: Boron, children, nephrotic syndrome, selenium, zinc

Özet

Amaç: Eser elementler birçok metabolik süreçte yer alır ve sıklıkla proteine bağlanarak dolaşırlar. Bu çalışmada nefrotik sendromlu hastaların aktivasyon ve remisyon dönemlerinde selenyum, çinko ve bor durumlarının araştırılması amaçlanmıştır.

Gereç ve Yöntem: Ondört hasta ve 14 sağlıklı, benzer yaşta kontrol grubu çalışmaya alındı. Plazma ve idrarda selenyum, çinko ve bor düzeyleri indükleyici çiftleşmiş plazma kitle spektrometri yöntemi ile ölçüldü.

Bulgular: Plazma çinko ve selenyum düzeyleri hem aktivasyon hem de remisyon döneminde anlamlı olarak düşük bulundu (hepsi için p=0,0001). Plazma bor düzeyi sadece aktivasyon döneminde anlamlı olarak düşüktü (p=0,0002, kontrol ile karşılaştırıldığında). İdrar bor ve selenyum düzeyleri aktivasyon döneminde remisyon dönemine kıyasla anlamlı olarak yüksekti (p=0,0003 ve 0,0001, sırasıyla).

Sonuç: Nefrotik sendromlu hastaların çinko, selenyum ve bor açısından desteklenmesi gerekebilir.

Anahtar Kelimeler: Bor, çinko, çocuklar, nefrotik sendrom, selenyum

Introduction

Trace elements play a significant role in several metabolic processes and often circulate in the blood binding to protein. Their deficiency can adversely affect children who are in the process of growth and development [1]. Zinc is known to be an essential element and is involved the structure of about 120 enzymes such as DNA polymerase, reverse transcriptase and RNA polymerase [2]. Selenium is also an essential element and also has an important role in gene transcription, antioxidant system, thyroid hormone metabolism and immune system [1, 3]. Boron, which is another trace element, influences the hormones functioning energy and mineral metabolism, including thyroid hormone, vitamin D and insulin. It has been shown that boron has beneficial effects on bone health, immune system and some cancers. In addition, boron has favorable effects on brain functions. It is thought that boron is necessary for membrane integrity and cell function [4, 5].

Idiopathic nephrotic syndrome (INS) is one of the most common renal diseases in the pediatric age group and it is characterized by hypoalbuminemia, hyperlipidemia and proteinuria [6]. There are few studies investigating the level of trace elements in the nephrotic NS during childhood and the results of these studies are somewhat contradictory in terms of some trace elements [7-9]. To our knowledge, there is no study investigating the level of boron in the NS patients. The aim of this study was to investigate the status of trace element selenium, zinc, and boron of INS patients in active and remission phase.

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Correspondence to: Sebahat Tulpar, Department of Pediatric Nephrology, Erciyes University Faculty of Medicine, Kayseri, Turkey
Phone: +90 442 232 53 60 e-mail: stulpar76@yahoo.com

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Materials and Methods

The study was approved by the ethics committee of the Erciyes University, and informed consent was obtained from all families before study entry. The research conformed to all the ethical requirements of the Helsinki declaration.

This prospective study was conducted between January 2007 and March 2008. Children with NS without renal failure or systemic disease were included in the study. Fourteen patients with INS suffering from their initial episode or during a relapse, with a mean age of 8.5±4.9 10 males and 4 females were included in the study. The control group was consisted of 14 age-matched (8 males, 6 females) healthy children.

Blood and urine samples were taken from children with NS both in active phase of NS and remission. Only blood samples were taken from healthy children. The samples from patients in active phase were obtained before starting steroid. Active NS was defined as serum albumin concentration below 2.5 g/dL and urinary protein excretion above 40 mg/m^2 per hour with high cholesterol levels. Remission was defined as no proteinuria using the colorimetric qualitative test and a urinary protein/creatinine ratio of <0.2 on a random urine sample. Blood samples were collected from the venous vein. After centrifugation plasma samples were stored at -80°C, while urine samples were stored at -26°C until analysis.

The plasma and urine levels of boron, zinc and selenium were measured by inductively coupled plasma mass spectrometry (Agilent 7500a; Agilent Technologies, Stockport, UK). Results were expressed as µg/L.

Statistical analysis

Statistical analysis was performed using the Version 15.0 of Statistical Package for the Social Sciences (SPSS) for Windows. Determinations of distributional normality were tested by using the Shapiro–Wilk test. Data are presented as mean±SD. For trace elements in plasma, different between groups were determined using the Student's *t* test or paired samples *t* test. For trace elements in urine, differences between paired samples in remission and active phase were determined using paired samples t-test. The comparisons of proportions were performed with the χ^2-test. All tests were considered as statistically significant if p values were <0.05.

Results

There were no statistical differences between both groups regarding gender distribution (p=0.2).

Plasma boron, zinc and selenium levels of the NS group in active phase were significantly lower than in the control group (p=0.0003, p=0.0001 and p=0.0001, respectively). Plasma zinc and selenium levels had not returned to normal levels during the remission. There was no statistical difference between INS group in remission and control group in terms of boron levels (117±32 vs 136±41µg/L, p=0.2). Plasma boron and selenium levels were markedly decreased during active phase compared to remission (73.6±37.4 vs 117.2±32.2, p=0.002 and 39.9±7.3 vs 54.8±4.5, p=0.001, respectively) (Figure 1).

The concentrations of urinary boron and selenium were significantly higher during active phase compared to remission (1658±264 vs 1106±331 µg/L, p=0.0003 and 20.9±5 vs 8.6±2.6 µg/L, p=0.0001, respectively). No statistically significant difference was noted between urinary zinc of NS patients in remission and in active phase (133±107 vs 191±143 µg/L, p=0.2) (Figure 2).

Discussion

In this study, we evaluated the status of boron, selenium and zinc in children with INS. We demonstrated in active phase of INS, plasma boron and selenium concentrations were different from remission period.

Plasma boron level of the NS group in active phase was found to be lower than in remission period and in control group. According to our knowledge this is the first study to examine the status of boron in NS. An experimental recent study reported that boron deficiency causes an increase in the level of homocysteine [10]. In another experimental study, podocyte injury was observed in rats with hyperhomocysteinemia [11]. Hyperhomocysteinemia is known to be a risk factor for venous thromboembolism [12]. In a study conducted on adults, homocysteine levels were found higher in patients with NS [13]. Thromboembolism, especially venous thromboembolism, is an important complication in nephrotic children. It is believed that incidence of thromboembolism has been associated with severe hypoalbuminemia and proteinuria in NS [6]. Hunt et al. [14] demonstrated that supplementation of boron temporarily decreased albuminuria in rat model of diabetes mellitus. Perhaps boron supplementation may reduce albuminuria and thromboembolic complications in NS.

Selenium is an important constituent of glutathione peroxidase enzyme and its deficiency resulting in a marked decline in glutathione peroxidase activity of many tissues, which leads to increased oxidative stress [15]. We found that plasma selenium levels were low in NS patients during both active and remission phase and plasma selenium level had a tendency to return to normal in remission, this is in good agreement with the results of selenium published by Mishra et al. [9]. Additionally, we found that plasma zinc level was lower in the NS group in active and remission phase, which is in good agreement with the results published by Reimold [16] and Perrone et al. [7], but not with those of Mishra et al. [9], who observed no difference between NS and control groups in terms of plasma zinc level. Furthermore, in an experimental study, low serum

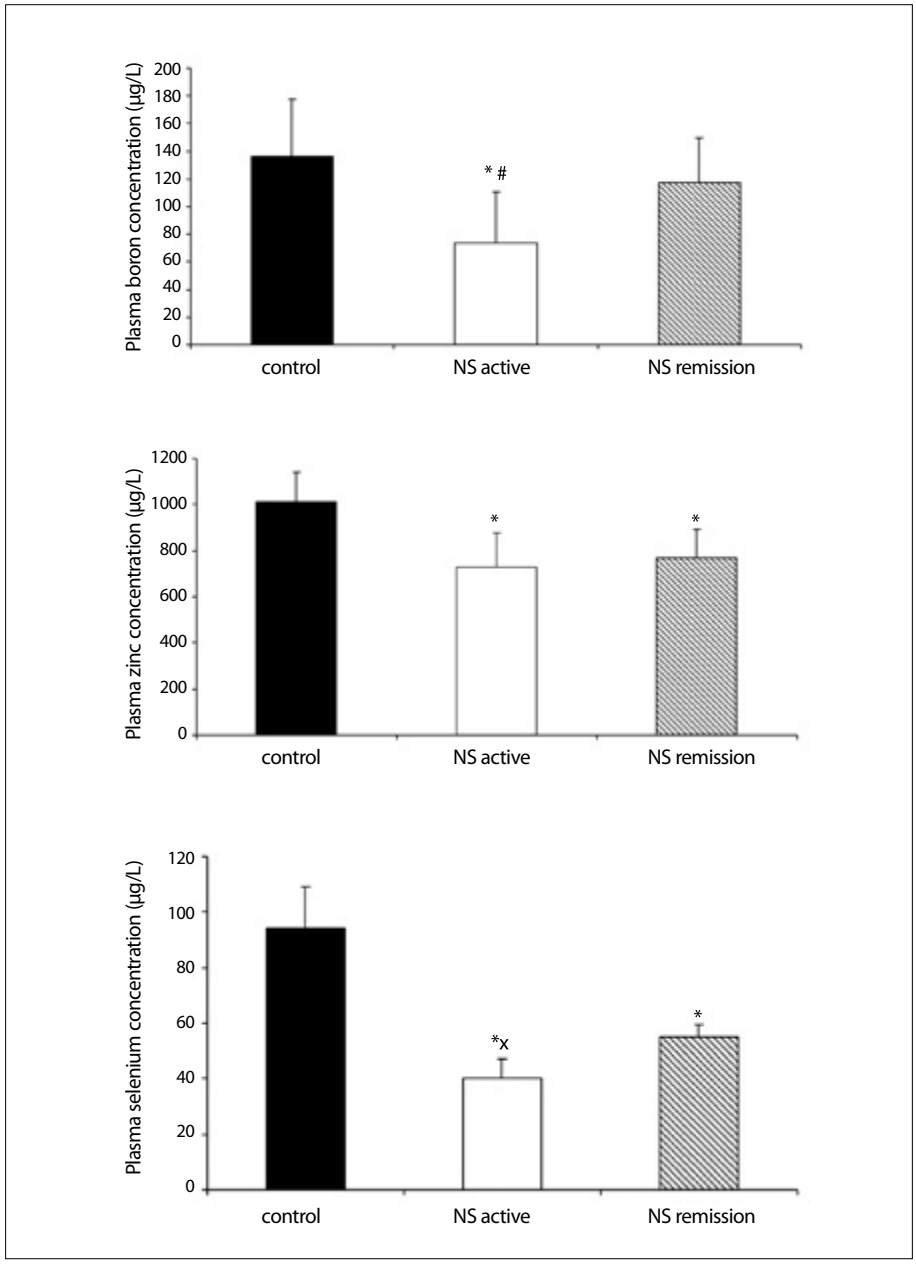

Figure 1. *Trace elements concentrations of groups in plasma. Results are presented as means±SD.*
**p<0.001 versus control*
#p<0.01 versus patients in remission
xp<0.001 versus patients in remission

v and high urinary zinc excretion were observed in nephrotic rats [17]. There are studies reporting an impaired oxidant-antioxidant balance in children with NS [8, 9, 18]. Fujieda et al. [19] observed that the decrease of glutathione peroxidase activity, pronounced proteinuria, and glycosuria occurred in rats fed selenium-deficient diet. Recently, it has been observed that alone or combined supplementation of selenium and zinc in diabetic rats improved antioxidant status and decreased lipid peroxidation both in the liver and kidney tissues [20]. Furthermore, it was observed that supplementation of zinc-reduced relapses in children with NS [21].

In our study, urinary excretions of selenium and boron were higher in active period compared to remission phase. Furthermore, plasma concentrations of these trace elements

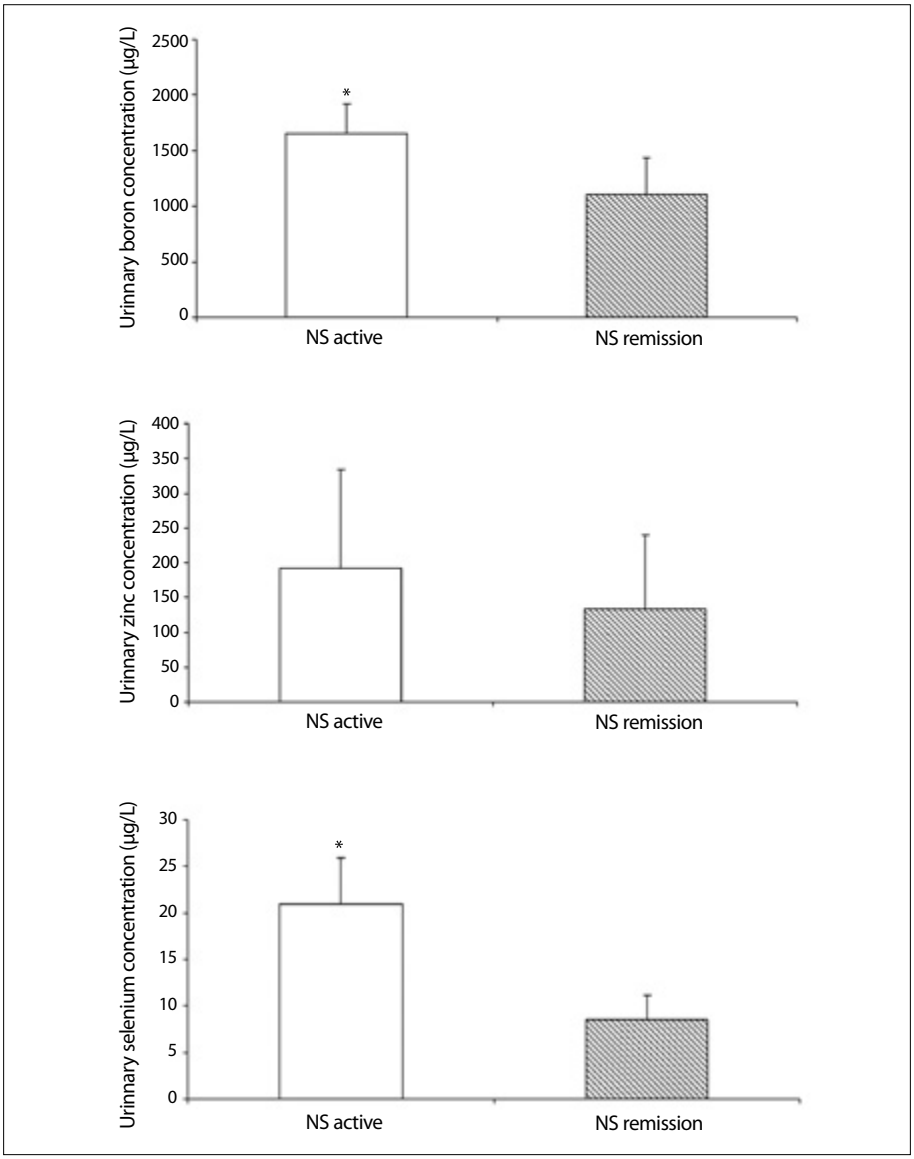

Figure 2. *Trace elements concentrations of groups in urine. Results are presented as means±SD.*
**p<0.001 versus patients in remission*

were lower in active phase than in remission period. According to our study findings, it can be speculated that one of the causes of decreased systemic selenium and boron levels is the increased renal excretion of these elements.

The current study had some limitations. First, the number of patients and controls was small. Furthermore, we did not measure the urinary levels of trace elements in controls.

In conclusion, our data show that the plasma levels of boron, selenium and zinc in children with NS lower than in healthy children. In light of these results, the supplementation of these trace elements may be considered in patients with NS. Further studies with larger numbers of patients are warranted to assess the beneficial effects of these trace elements supplementation in this patient group.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Erciyes University.

Informed Consent: Written informed consent was obtained from parents of the patients who participated in this study.

Peer-review: Externally peer-reviewed.

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