



Assesment of Etiologic Factors in Children With Attention Deficit Hyperactivity Disorder: Serum Levels of Boron and Selenium

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ABSTRACT

Objective: We aimed to determine the role of trace elements; selenium and boron levels in children and adolescents who have Attention Deficit Hyperactivity Disorder (ADHD).

Material-Method: The study group consisted of 30 children who were diagnosed as ADHD according to DSM-IV criteria and was compared with 20 healthy children who did not have ADHD. The study and control groups were given to fill out a questionnaire which consists of 30 questions for screening socio-demographic data, age, gender, prenatal, natal and postnatal trauma history, having any toxic-metabolic condition or infection, familial history of ADHD and psychiatric disorders. Turgay's DSM-IV-Based Child and Adolescent Behavioral Disorders Screening and Rating Scale (T-DSM-IV-S), Conners' Teacher Rating Scale, Conners' Parent Rating Scale, Kiddie schedule for affective disorders and schizophrenia-present and lifetime version (K-SADS-PL), and Wechsler Intelligence Scale for Children-Revised (WISC-R) were used to diagnose ADHD. Serum selenium and boron levels were measured with the atomic absorption spectrophotometry.

Result: All the scores of scales rating the ADHD symptoms of the children in the study group were significantly higher than in the control group. A statistically significant decrease in the serum selenium and boron levels was detected in children with ADHD.

Conclusion: One of the important mechanisms in ADHD etiology is brain damage. Deficiency in the level of selenium and boron entering into the structure of the antioxidant enzyme system can lead to ADHD and other psychiatric disorders by causing damage to the brain tissue related to free radicals.

Key Words: Attention deficit hyperactivity disorder, etiologic factors, selenium, boron, trace element.

INTRODUCTION

Attention deficit hyperactivity disorder (ADHD) is one of the most commonly diagnosed psychiatric disorders of childhood. It is characterized by difficulty in maintaining attention developmentally, hyperactivity and behavioral and cognitive impulsivity.¹ ADHD commonly coexists with other psychiatric and social problems. Its frequency is 5% to 10% in children and adolescents, and 4% in adults.²

The DSM-IV diagnostic criteria of ADHD, prevalence is reported as 2% - 12%.³ The relative frequency of ADHD is two fold high in school children compared with adults.^{4,5} ADHD is frequent in boys and the male/female ratio is 6:1 to 9:1.⁶

Although there are several studies to determine the pathogenesis the etiology of ADHD has not clearly been identified yet. However, genetic, biological (neuroanatomic and neurochemical) and peripheral factors are considered as causative factors in ADHD etiology but the interactions between these factors have not been explained yet. Currently ADHD is considered as a hereditary disorder and a cause of some alterations in structure and function of the central nervous system.

The trace element selenium contributes to the stability of neurons for glutathione peroxide activity.^{7,8} Boron is also considered to play role in neuronal membrane stability and neuronal metabolism.⁹ Low levels of both serum selenium and boron may lead to regression in psychomotor skills, attention, perception and memory functions.^{7,8,9} However, there are limited studies about the role of these two trace elements in etiology of ADHD. Considering that both selenium and boron have protective effects on structural and functional properties of neurons, we aimed to investigate the levels of these elements in childhood associated with the occurrence of the ADHD.

METHODS

Participants and Procedure: Patients who were admitted to outpatients' clinics of Child and Adolescent Psychiatry Department and diagnosed as ADHD according to DSM-IV criteria, between September 2007 and April 2008 were included in the study. Outpatients who were admitted to Family Medicine, Pediatrics, Child and Adolescent Psychiatry and who were not diagnosed as ADHD were chosen as the control group. Followed by the given information about the study the consent was taken from their families. Institutional review board of Erciyes University Faculty of Medicine approves the study procedure.

The inclusion criteria were children aged 6-12 years, with an intelligence quotient (IQ) higher than 80, and those who were not using any drug and not suffering from

any neurological, endocrine or metabolic disorder other than ADHD.

The study and control groups were given questionnaires to obtain information regarding age, gender, prenatal, natal and postnatal trauma history, and the information was also checked from their patient files. Also the participants were asked whether they had any existing toxic-metabolic condition or infection, familial history of ADHD and psychiatric disorders.

It is not usual to ingest trace elements in overdose and environmental exposure to certain trace elements may be the cause of overuse.¹⁰ Since selenium fortified egg is the only source of the extra selenium from food in our region, families were asked that if they had used selenium-fortified eggs in the diet of their children.

Turgay's DSM-IV-Based Child and Adolescent Behavioral Disorders Screening and Rating Scale (T-DSM-IV-S), Conners' Teacher Rating Scale, Conners' Parent Rating Scale, Kiddie schedule for affective disorders and schizophrenia-present and lifetime version (K-SADS-PL), and Wechsler Intelligence Scale for Children-Revised (WISC-R) were used to diagnose ADHD as described elsewhere.¹¹

Blood Samples: Thyroid, renal, liver function and complete blood count tests were done to show if the study group has any endocrine, metabolic disorder or anemia or not. a. A 5 cc venous blood sample were drawn and transferred to heparinized tubes from study and control groups. Samples were centrifuged at 4000 rpm for 15 minutes and separated plasma were then stored at -20°C. The boron and selenium elements were tested with an Agilent 750 series model with inductive matched plasma mass spectrometer by calibration method. The sample and calibration solutions was divided by the internal standards and obtained results were noted as an analytical signal. The signals obtained were placed on calibration line and derivations were counted with a software.^{12,13}

Statistical evaluation: SPSS (Statistical Package for Social Sciences) 15.0 software was used in statistical analysis. Descriptive characteristics were calculated as mean and standard deviation ($\bar{x} \pm sd$), median, minimum and maximum [*median (min-max)*]. Independent samples *t* and Mann-Whitney U test was used to compare parametric and non-parametric variables.

RESULTS

The 30 children with ADHD and 20 healthy children (control group) were included in the study. There were 3 girls (10%) and 27 boys (90%) in the study group and 8 girls (40%) and 12 boys (60%) in the control groups

(gender difference was significant, $p < 0.05$). The mean age of children and adolescents with ADHD was 8.63 ± 1.97 and 8.75 ± 1.65 in controls. The mean ages of mothers were 34 ± 4.63 and 34 ± 5.13 , and fathers were 37 ± 5.53 and 38 ± 4.68 respectively in children with ADHD and controls.

The mean WISC-R scale score for performance, verbal and total were 102.60 ± 14.29 , 101.76 ± 12.62 , and 102.40 ± 10.87 respectively in ADHD group. In controls, the corresponding WISC-R scale scores were 112.45 ± 13.34 , 107.80 ± 14.87 , and 110.80 ± 13.00 .

The Conners' Parent Rating Scale's behavioral, learning, and impulsivity, hyperactivity scores were significantly high in ADHD group ($p < 0.001$). The Conners' Teachers Rating Scale's inattention, hyperactivity, and behavior problems scores were about two times higher in the ADHD group ($p < 0.001$). Serum selenium and boron levels were significantly lower in the ADHD group (Table 1).

Table 1: Serum selenium and boron levels of study groups			
	ADHD $\bar{x} \pm sd$ Median(min-max)	Control $\bar{x} \pm sd$ Median (min-max)	p^*
Serum selenium level	84.70 ± 18.50 86.5(56-125)	100.52 ± 27.94 96 (56-191)	0.028
Serum boron level	57.70 ± 34.85 56(16-157)	84.95 ± 49.20 71.5(45-241)	0.017

*Mann-Whitney U test

DISCUSSION

There is limited information about the association between ADHD and trace elements; selenium and boron. Low serum selenium and boron levels are reported to cause regression in psychomotor skills, attention, perception and functions of memory.^{7,8,9} This study aimed to determine whether there are low serum selenium and boron levels in children with ADHD compared with controls. Gender predominance in ADHD prevalence is reported as 6:1 to 9:1 in favor of boys.^{1,6} Corresponding gender predominance (boys vs girls) in our study was 9:1.

Willmore and Rubin first reported the role of selenium for brain functions. It was also proposed that selenium induction with Fe^{2+} improved EEG abnormalities.¹⁴ Low selenium level may cause reduction in brain functions, loss of neurons, predisposition to trauma and other neurodegenerative conditions.¹⁵ Selenium deficiency increases lipid peroxidation together with decrease glutathione peroxidase activity, which leads into membrane injury and loss of neuronal cell.¹⁶ Seafood, meat, garlic and grain crops are the sources of selenium in our location and selenium-fortified egg is the only source of extra selenium. We may consider that dietary deficiency in

selenium may be related with ADHD since even in similar selenium containing soil its bioavailability by plants (grains and e.t.c.) may vary significantly.¹⁷

Schweizer et al. showed that the hippocampal cell death in rats leads selenium deficit since selenium deficit has a neuron protective characteristic.¹⁵ The rapidly developing brain is more vulnerable to nutrient deficiency especially protein, energy, certain fats, iron, zinc, copper, iodine, vitamin A, and selenium. Additional nutrients and/or nutritional deficiency may have impact on brain and behavior development in fetal development.¹⁸ Additionally Durá Travé et al. showed that decrease in total calorie intake with other nutrient and minerals would lead low selenium intake.¹⁹

In 1996, boron element was classified among 'potential basic elements for human health' by World Health Organization (WHO).²⁰ Even though boron is not considered as a significant nutrient in human diet, some human and animal studies show that it may also have a significant role in cellular membrane function, the metabolism of mineral and hormones and enzymes used in metabolic reactions.²¹ Low boron intake is also considered as a cause of regression in psychomotor skills and decline in attention, perception and duties related to memory within mental processes.²² We could not explain subsequent boron deficiency with selenium since boron containing nutrients are used frequently even in diet of people who are in low socioeconomic level. Similar with selenium, boron bioavailability by plants may alter boron intake as a nutrient.

There are four commonly used psychometric tests to diagnose ADHD; T-DSM-IV-S, Conners' Teacher Rating Scale, Conners' Parent Rating Scale, K-SADS-PL, and WISC-R. The WISC-R performance scores of our study group were significantly lower than the controls, which is compatible with the literature.^{23,24} However in T-DSM-IV scale, Conners' rating scale and its sub-tests there was a significant difference between the ADHD and control group. Since a qualified child psychiatrist did these tests, we may conclude that diagnosis of ADHD is reliable. The small sample size can be stated as the major limitation of this study but results indicate that there may be a probable association of selenium and boron deficiency in ADHD and this initial finding may contribute future clinical practice and research for ADHD.

In conclusion ADHD is a relatively prevalent disorder in childhood and adolescence. Although the brain damage in ADHD etiology is well known deficiency of trace elements has not been studied yet. Considering the results with the limitations in our study design one may conclude that our results may contribute as an initial useful

information about ADHD etiology that selenium and boron deficiency may be an etiological factor.

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