Original article

A Study on potential role of Zinc in Attention Deficit Hyperactivity Disorder

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Abstract

Introduction: Attention Deficit Hyperactivity Disorder (ADHD) is a neurocognitive condition characterized by developmentally inappropriate gross motor over activity, inattention and impulsivity. Dietary deficiencies of various trace elements including zinc are implicated in the pathogenesis of ADHD. Zinc is a cofactor for metabolism of many neurotransmitters and fatty acids. It also regulates dopamine metabolism which is involved in the pathogenesis of ADHD. The aim of the study is to compare the serum levels of zinc in ADHD children and control group so that therapeutic zinc supplementation can be beneficial for ADHD children.

Material and methods: Thirty boys in the age group 6-11 years diagnosed as Attention Deficit Hyperactivity Disorder according to DSM IV criteria were enrolled in the study and controls were thirty age, sex and BMI matched healthy children. Serum zinc levels were estimated by colorimetric method. The data was analyzed using Student t test.

Result: The mean serum zinc levels in ADHD children was 88.4 ± 29.55 µg/dl and controls was 107.27 ± 28.13 µg/dl (p = 0.01). The serum zinc levels were significantly decreased in ADHD children when compared to control group.

Conclusion: The significant decrease of serum zinc levels in ADHD children as compared to control group suggests the contribution of zinc in the pathogenesis of ADHD. Hence appropriate zinc supplementation in ADHD children can improve the symptoms of this neuropsychiatric disorder.

KEYWORDS: Attention Deficit Hyperactivity Disorder, Zinc.

Introduction:

Attention Deficit Hyperactivity Disorder (ADHD) is one of the most common childhood neurobehavioral disorder that can continue through adolescence and adulthood. It is characterized by inattention, increased distractibility and difficulty sustaining attention, poor impulse control, decreased self-inhibitory capacity and motor restlessness inappropriate for that particular age [1]. They have poor school performance due to difficulty in focusing their attention efficiently and easy distractibility [2,3]. There is no single causal factor in the etiology of ADHD. Genetic and environmental factors interact during fetal and postnatal development leading to ADHD.

Researchers have recently focused on nutritional issues to understand mental health problems. Evidences for the role of micronutrients in mental health has come from studies focusing on role of zinc in ADHD[4]. Both animal and human studies show relationship between low serum zinc concentration and symptoms of ADHD suggesting improvement of symptoms with zinc supplementation. The prevalence of zinc deficiency in ADHD children is about 26% as opposed to 3.3% prevalence in the normal children[5]. Zinc from meat sources have higher bioavailability than vegetarian sources due to presence of aminoacids which enhance zinc absorption. ADHD children in general have specific liking to vegetarian foods rather than non-vegetarian foods and this may be another reason for their zinc deficiency.

Zinc contributes to behavioral aspects such as focusing attention and reducing aggressiveness through regulatory effects on certain brain neurotransmitters. It is a cofactor for metabolism of several neurotransmitters such as dopamine which is involved in the pathogenesis of ADHD indirectly[6] Dopamine transporter (DAT1) which is involved in the degradation of dopamine has an endogenous high affinity zinc binding site. Zinc interacts with the binding site and acts as a non-competitive blocker preventing dopamine binding to the transporter. This leads to increase in the availability of extracellular dopamine by decreasing its degradation[7]. The micronutrient is also essential for the production and modulation of melatonin which regulates dopamine function[8]. It has been postulated that parasympathomimetic stimulants used in the treatment of ADHD act partly through its effect on melatonin. Zinc is essential for the conversion of dietary pyridoxine to its active form, pyridoxal phosphate which is necessary for conversion of tryptophan to serotonin. As studies show implication of both dopamine and serotonin neurotransmitters in ADHD, zinc supplementation in zinc deficient ADHD children can improve the levels of deficient neurotransmitters thus improving ADHD symptoms of impulsivity[9].

Aim and Objectives

The aim of the study is to evaluate the serum zinc levels in ADHD children and compare with age and sex matched controls. The present study is undertaken with the objective of improving the symptoms of ADHD with therapeutic zinc supplementation as an adjunct, thus enhancing the quality of life in such children.

Materials and methods

The cross sectional study was conducted in the Institute of Physiology and Experimental Medicine, Madras Medical College after receiving approval from the Institutional Ethical Committee, Madras Medical College, Chennai. Thirty male children aged between 6-11 years diagnosed as ADHD according to Diagnostic and Statistic Manual of Mental disorders, 4th edition (DSM-IV) criteria and getting treatment from the Child Guidance Clinic, Institute of Child Health, Egmore, Chennai-600 008 were selected to participate in the study. Thirty age and sex matched apparently healthy children were selected as controls.

Assessment was done using Parent Rating Scale and Vanderbilt ADHD Diagnostic Teacher Rating Scale. IQ Assessment was carried out using the Malin's Intelligence scale for Indian Children (MISIC). Only children with IQ equal to or greater than 90 were selected for the study. Children with Autism, Pervasive developmental Disorder**,** Perinatal hypoxia, Developmental delay, Epilepsy, CNS infection, Demyelinating disorders, chronic medical illness, Malabsorption syndrome, General malnutrition and other psychiatric disorders were excluded from the study. Informed verbal and written consent was obtained from parents of the participant children.Detailed history was collected from the parents of both controls and ADHD children. This includes information regarding birth complications such as preterm delivery, perinatal hypoxia and family history of ADHD and other psychiatric and neurological disorders. Regular anthropometric measurements (height and weight) were recorded in both groups. BMI was calculated using the formula weight in kg/height in cm^2 and compared between normal healthy children of same age and sex. Vitals (Pulse, BP, Respiratory rate and temperature) were measured. General and systemic examination including cardiovascular system, Respiratory system and Central Nervous system were done for the

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participants of the study. Under strict aseptic precautions, blood samples were collected by means of venepuncture from the antecubital vein and the separated serum was stored in deep freezer at -20^{0}C. Serum zinc levels were assayed by colorimetric method in the Department of Biochemistry, Institute of Child Health, Egmore, Chennai.

PRINCIPLE

Zinc in an alkaline medium reacts with Nitro-PAPS to form a purple colored complex. Intensity of the color complex formed is directly proportional to the amount of Zinc present in the sample.

Zinc + Nitro-PAPS ====== Purple Colored Complex in Alkaline medium

Normal reference values: 80 – 170 micrograms / dl

Contents of the kit: 75 ml of the kit contains 60 ml of Buffer Reagent (L1), 15 ml of Color Reagent(L2) and Zinc Standard(200 micrograms/dl).

PROCEDURE

The working reagent was obtained by pouring the color Reagent into the bottle containing Buffer Reagent which is stable for 2 weeks when stored at 2-8^{0}C. Pipetting was done into clean dry test tubes labeled as Blank (B), Standard(S) and Test (T). 1 ml of working reagent and 0.05 ml of distilled water were added to test tube B, 1 ml of working reagent and 0.05 ml of zinc standard were added to test tube S and I ml of working reagent and 0.05 ml of serum sample were added to test tube T. The contents were mixed well and incubated at room temperature (25^{0}C) for 5 minutes. The absorbance of standard (Abs. S) & test sample (Abs. T) were measured against the Blank within 20 minutes.

CALCULATION

Zinc in micrograms / dl = Abs. T / Abs. S X 200

Statistical analysis was done using the software Statistical Package for Social Sciences (SPSS) version 21. Students t test was carried out to compare the means of variables between ADHD children and control group.

Observation and Results:

The study population consists of 30 ADHD children and 30 control subjects with same gender distribution in the age group of 6-11 years. The mean age of control children was 7.67±1.47 years and the mean age for ADHD group was 7.66±1.52 years, both within the range of 6 to 11 years. The mean height of control and ADHD children was 123.18±7.5 and 124.7±8.06 respectively. The mean weight for control children was 23.37±4.15 kg while that of ADHD group was 24.38±4.33 kg. The average BMI for control and ADHD children was 15.27±0.82 and 15.56±0.90 respectively. Thus there was no significant difference between the control and ADHD group in terms of height, weight and BMI making the two groups well comparable. The mean serum zinc levels in ADHD was 88.4 ± 29.5 µg/dl and controls was107.27 ± 28.13 µg/dl. The mean level of zinc was significantly lower in ADHD children when compared with control group.

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Table 1: Comparison of parameters (Mean ±SD) between control and ADHD children

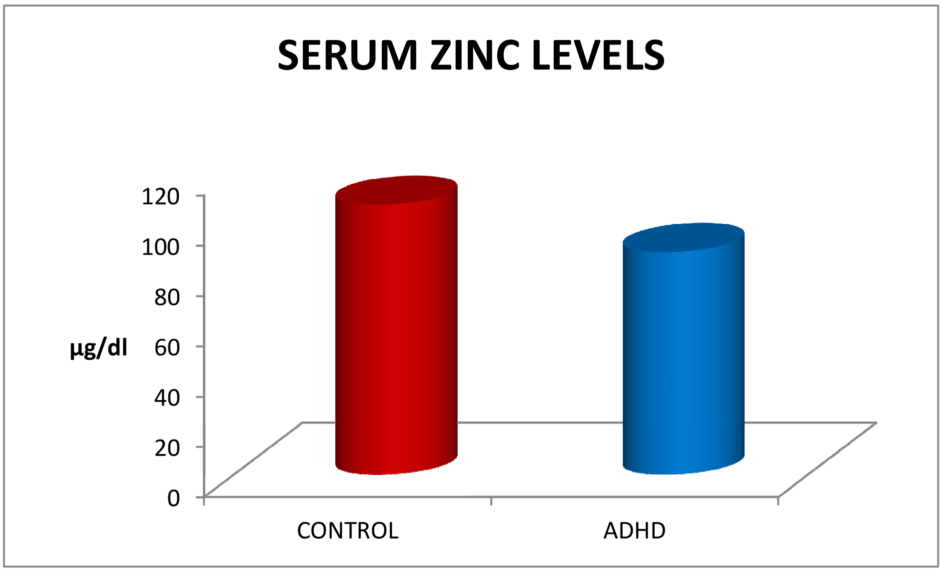
Sl. No	Variables	Control group	ADHD children	p value
1.	Age (years)	7.67 ± 1.47	7.66 ± 1.52	0.97
2.	Weight (kg)	23.37 ± 4.15	24.38 ± 4.33	0.36
3.	Height (cms)	123.18 ± 7.5	124.7 ± 8.06	0.45
4.	BMI	15.27 ± 0.82	15.56 ± 0.90	0.19

Table 2: Serum Zinc levels between control group and ADHD children.

GROUPS	SERUM ZINC LEVELS (µg/dl)	T VALUE	P VALUE
Control group	107.27 ± 28.13	2.53	0.01
ADHD Children	88.4 ± 29.55		

p value : 0.01 (significant)

Figure 1. Comparison of Serum zinc levels between normal and ADHD children



Discussion:

In the present study, t*he serum zinc level is* significantly lower in ADHD children with the mean value of 88.4 ± 29.55µg/dl when compared to the control group with mean value of 107.27 ± 28.13µg/dl. The finding suggests zinc as one of the possible nutritional etiology in ADHD. Zinc acts as building blocks of neuronal membranes as it is involved in the metabolism of PUFAs which constitute important components of neuronal membranes. It also acts as a cofactor for metabolism of several neurotransmitters such as dopamine involved in the pathogenesis of ADHD. So zinc supplementation can benefit ADHD children by correcting the altered neurotransmission and provide improvement in

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ADHD symptoms.

The results are in line with data from previous studies of Kozielec et al[10] and Toren et al .[11] Kozielec et al [10] observed that serum zinc levels were significantly lower in ADHD children ($p < 0.001$) when compared to controls. Toren et al [11] had reported significantly lower serum zinc levels in a group of 39 boys and 4 girls with ADHD in the age group of 6-16 years compared to 28 age matched controls.

Starobrat-Hermelin et al [12] reported iron, copper, magnesium and calcium deficiencies in addition to zinc deficiency by analyzing serum, red blood cells and hair of ADHD children. Bekaroglu et al[13] recorded low mean serum zinc levels in ADHD children (60.6 ± 9.9µg/dl) when compared to controls(105.8 ± 13.2µg/dl). Oner et al [14] suggests that patients with lower zinc levels are at enhanced risk of hyperactivity. Salehi et al [15] acknowledged that zinc supplementation can be used as an adjunct which significantly improved the symptoms of ADHD. Arnold et al [16] reviewed published evidences for the role of zinc in ADHD and concluded that many children with ADHD have lower serum zinc levels than normal controls. Azza El- Bakry et al [17] has observed zinc deficiency in children with ADHD. Bettger et al [18] has shown that zinc is essential for maintaining the neuronal structure as it is essential for the metabolism of PUFA which are the building blocks of neuronal membranes by acting as a cofactor for the enzyme delta-6-desaturase.

Conclusion

The study clearly depicts that zinc deficiency is prevalent among ADHD children strengthening the previous studies which had established an inverse relationship between serum zinc levels and hyperactivity. Hence it becomes essential to utilize the findings of the present study to make timely intervention with zinc supplementation as an adjunct in ADHD children to reduce morbidity.

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