Magnesium, zinc and copper estimation in children with attention deficit hyperactivity disorder (ADHD)

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Abstract  Background: Attention deficit hyperactivity disorder (ADHD) is a common neurodevelopmental disorder. Evidence for dietary/nutritional treatments for (ADHD) varies widely, however recommended daily allowance of minerals and essential fatty acids is an ADHD-specific intervention.

Aim of the work: To estimate magnesium, zinc and copper levels in the sera and hair of children with ADHD and compare them to normal children and also to correlate these levels with the disease symptoms.

Methods: This case–control study was conducted on 20 patients with ADHD and 20 age and sex matched healthy controls. All subjects were subjected to psychiatric evaluation according to DSMIV-R, magnesium, zinc and copper estimation in serum and hair follicles. ADHD children were further assessed by the Stanford Binnet intelligence scale for children, Conners’ parent rating scale, and Wisconsin’s card sorting test.

Results: Magnesium, zinc and copper deficiencies were found in 13 (65%), 14 (60%) and 12 (70%) of ADHD children respectively. Magnesium and zinc deficiencies were found to be correlated with hyperactivity, inattention and impulsivity. However, this correlation was not found in the copper deficient ADHD cases.

Conclusion: Children with ADHD have lower levels of zinc, copper and magnesium compared to both laboratory reference ranges and to normal controls in both hair and serum. These deficiencies are correlated with the core symptoms of ADHD.

1. Introduction

ADHD is a chronic debilitating psychiatric illness that often co-occurs with other common psychiatric problems. Although empirical evidence supports pharmacological and behavioral treatments, side effects and concerns regarding safety and fears

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about their long-term use contribute to families searching for alternative methods for treating the symptoms of ADHD [1].

According to Wilson [2]; calcium, magnesium and zinc are deficient on the tissue mineral analyses of many ADHD children. Supplementation with these minerals alone may occasionally end the hyperkinetic behavior.

Zinc deficiency has an important role in the pathogenesis of ADHD [3]. Zinc is an important cofactor for metabolism relevant to neurotransmitters, prostaglandins, and melatonin, and indirectly affects dopamine metabolism [4]. It mediates the release of neurotransmitters like gamma amino butyric acid [GABA] and glutamate. This indicates that it may be a key modulator of neuronal excitability [5]. Also, zinc is an important cofactor for more than 300 other nutrients. So, zinc deficiency may create functional deficiency of these other nutrients [6]. These functions have been shown to be affected by moderate zinc deficiencies in humans [7]. Several data suggest that zinc deficiency may be more concentrated in the ADHD population [7]. It, also, seems likely that zinc supplementation in zinc-deficient ADHD patients improves the binding status of the dopamine transporter [8].

Magnesium deficiency is typified by a number of reductions in cognitive ability and processing, and in particular a reduced attention span along with increased aggression, fatigue and lack of concentration [9]. Other common symptoms of magnesium lack include becoming easily irritated, nervousness, fatigue and mood swings [10]. Given the nature of these symptoms and the significant amount of overlap that they share with ADHD, this has led many experts involved in the treatment and care of ADHD to hypothesize that children who suffer from the condition also have magnesium deficiency as well [11]. Moreover, magnesium helps in generating ATP and energy [11], disposing brain ammonia, which is related to inattention [12] and converting essential fatty acids into DHA (docosahexaenoic acid), which is related to proper function and structure of brain cells [12]. It has an antioxidant effect, where it can decrease the oxidative stress related to pathophysiology of ADHD [13]. Moreover, magnesium can improve sleep disturbance seen in ADHD [14] which may adversely affect the attention.

Copper is an essential factor for both development and function of the central nervous system [15]. It acts as a cofactor for several key enzymes, most notably dopamine B-hydroxylase which catalyzes the conversion of dopamine to norepinephrine [16]. Copper is needed in trace amounts, but excess is toxic. Excess copper increases lipid peroxidation and depletes glutathione reserves, which makes the organism more vulnerable to oxidative challenges [15]. Zinc to copper ratio is abnormally low in individuals with disorders associated with hyperactivity. Low zinc may be associated with ADHD [16] and has been directly related to low Cu/Zn Superoxide dismutase (SOD) concentration. Hurt et al. [17] showed that a decreased serum Cu/Zn SOD may be also associated with high copper in children with ADHD.

This paper was done to examine the hypothesis that there are trace element deficiencies in Egyptian patients with ADHD and that these deficiencies may lead to worsening of the disease symptoms.

2. Subjects and methods

This case-control study was conducted on 20 patients with ADHD and 20 age and sex matched healthy controls.

2.1. Participants

We evaluated 50 children (age range 6–16 years) chosen randomly from our Child and Adolescence Psychiatry Clinic, Children Hospital, Ain Shams University who had a diagnosis of ADHD. Twenty patients were found eligible to be included in the study. Patients were considered eligible for the study if they fulfilled criteria of ADHD according to DSMIV-R, had an age range between 6–16 years and an IQ above 70. Ineligibility for the study included presence of other medical conditions such as significant anemia, chronic illness, hearing or vision impairment or medications side effects which may result in hyperactivity and/or impaired sleep rhythm.

Twenty healthy children gathered from the outpatient clinic were included in the study as controls. These children were visiting the outpatient clinic suffering from minor acute illness (common cold, pharyngitis, etc...). Psychiatric assessment was done for all control participants to exclude ADHD and other developmental conditions. This study was approved by the Ethics Committee of Ain Shams University and written consents were obtained from parents. The work has been carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

2.2. Methodology

Each patient in this study was subjected to the following: full detailed medical history; including presence of organic or psychological diseases, perinatal and developmental history, family history of similar cases, and the history of previous treatment which was received and Clinical Examination including; physical examination and neurological examination. Psychometric evaluation was performed by a trained psychologist for both cases and controls.

- Diagnostic and Statistical Manual, fourth edition-Revised (DSM-R IV) criteria [18] to confirm the diagnosis of ADHD in cases and to exclude concomitant psychiatric disease.
- Conners’ parent rating scale [19] Items were scored on 14 subscales but in our study we used only the hyperactivity, inattention, oppositional and impulsivity scores.
- Wisconsin’s card sorting test (WCST) [20] is a neuropsychological test of “set-shifting”, i.e. the ability to display flexibility in the face of changing schedules of reinforcement. It’s a measure of executive function.
- Stanford-Binet Intelligence scale [21] shows that the intelligence quotient or IQ is simply the ratio of mental age (MA) to chronological age (CA) multiplied by 100: IQ = MA/CA × 100.

2.3. Laboratory investigations

- Serum magnesium, zinc and copper levels were assayed by auto analyzer and compared to the reference value for normal children [22].
- Hair magnesium, zinc and copper [23] these samples were collected from cases and controls by single cutting from the occipital region. The hair was cut to lengths of about
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