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Serum Zinc Level in Children With Febrile Convulsion

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Abstract

Background: Febrile seizures (FS) are the most common form of convulsion in children with the aged between 6 months to 5 years. Different studies have shown that reduction of zinc leads to the incidence of FS in children.
Objectives: This study was conducted with the goal of examination of the zinc level in the patients with FS.
Patients and Methods: This case-control study was conducted on 90 children in three equal groups of children with febrile seizures, febrile children without febrile seizures (FS) and healthy children. In order to examine the zinc level blood samples were taken of all subjects and the zinc level of these patients was determined. The data was analyzed using the SPSS-16 statistical software and by descriptive statistical tests and ANOVA.
Results: Forty three male (47.2%) and 47 female children (52.8%) with the average age of 2.43 ± 1.23 years were examined. The three groups had no significant difference in terms of age and sex. The average of zinc level in the patients with FS was 56.8 ± 52.7 μg/dL and it was 96.1 ± 53.4 μg/dL in the febrile children without FS and 108 ± 28 μg/dL in the healthy control group. According to ANOVA test, there was a significant difference between the three groups in terms of the zinc level ($P = 0.01$).
Conclusions: The low serum zinc level in the group of patients with FS compared with two other groups can indicate the existence of a relationship between the serum zinc level and development of FS in children aged between 6 months and 5 years.

Keywords: Febrile Seizures, Zinc, Children

1. Background

Convulsion is sudden change in the dynamic or behavioral activity with limited time and results from the abnormal electrical activity of the brain [1]. Convulsions are common in the age group of children and one of the most common forms of convulsion in children are febrile seizures which occur in 2% - 5% of children aged between 6 months and 5 years [2, 3]. Based on the definition of American academy of pediatrics (AAP), febrile seizures occur in the absence of central nervous system infection, metabolic disorders and history of febrile seizures [3]. Febrile seizures usually have a good prognosis; however, due to the increase in recurrence of such convulsions and the risk of epilepsy in the future, they are considered as serious conditions [4]. Etiology of febrile seizures has not been precisely determined yet. Some of the conditions involved in the etiology of febrile seizures include the family history of febrile seizures and alcohol and cigarette consumption by the mother during pregnancy [5, 6]. The mother's diseases during pregnancy, prematurity, complications during childbirth and recent vaccination are among other risk factors of febrile seizures [7, 8]. Febrile seizures occur because the electrical system of the brain has not been adequately evolved so as to struggle against the stress of body temperature increase [9].

It is often said that due to their coenzyme activity and impact on ion channels and receptors, some elements have an important role in febrile seizures. Studies have shown that iron, zinc, magnesium, selenium and copper are highly effective in febrile seizures [10]. Zinc is one of the essential minerals that plays the main role in treatment and prevention of neurological diseases [11]. The highest zinc concentration has been found in hippocampus [12, 13]. Zinc is an important factor for growth, evolution and normal function of the brain and a significant cofactor for DNA and RNA polymerase enzymes [14]. Zinc regulates the activity of glutamic acid and the rate-limiting enzyme in the synthesis of gamma-aminobutyric acid (GABA) which is an inhibitory neurotransmitter [15]. This element also facilitates the inhibitory effect of calcium on N-methyl-D-aspartate receptors (NMDA) and by these effects prevents the stimulation of neuronal discharge [16]. High concen-

tration zinc exists in the synaptic vesicles of glutamatergic neurons including the hippocampal mossy fiber which can be synaptically released during neural activity as in convulsion [17]. According to the important role of zinc in the nervous system, studies have shown that lack of zinc might have a role in pathogenesis of febrile seizures. In a study that Srinivasa and Manjunath conducted on 100 children with febrile seizures, the results showed that 62% of these children had a serum zinc level lower than the normal range [10]. In a study that was carried out by Modarresi et al. with the goal of comparison of zinc in the three groups of children with febrile seizures, children with fever and healthy children, the research findings showed that the zinc level among patients with febrile seizures was significantly lower than the other two groups [18].

2. Objectives

According to the importance of febrile seizures and possible factors involved in them including lack of zinc, this study was conducted with the goal of examination of the serum zinc level in children with FS and comparison with the serum zinc level of two groups of children with febrile without seizures and healthy children.

3. Patients and Methods

This case-control study was performed on 90 children in three equal groups of children with febrile seizures, febrile children without febrile seizures (FS) [admitted to the pediatric emergency department of Ali ibn Abi Talib Hospital in Zahedan city in Iran] and healthy children. After gaining permission from the research council of the faculty of medicine of University of Medical Siences of Zahedan and obtaining informed consent from legal guardians of the children based on inclusion in the study, data collection was conducted. All the children aged between 6 months and 5 years whom had suffered from convulsion for the first time following fever and no simulating disease other than fever was assumed for their convulsion, were included in this study. The study exclusion criteria included: 1, children who had consumed zinc over the past month; 2, mental or brain retardation and signs of genetic syndrome; 3, history of chronic disease and infections of the central nervous system; 4, long-time drug use and; 5, patients with malnutrition and failure to thrive (FTT) were excluded from the study. Thirty children with febrile seizures and 30 children with febrile and without seizures; and 30 healthy children that were similar in terms of sex and age and had no other underlying disease and had the features for inclusion in this plan, were selected. After admitting the children to the pediatric emergency department and taking remedial measures to control and treat the seizures, 3 mL blood sample was taken of each of the three group children and was immediately sent to the hospital lab for examination of the serum zinc level. In the lab, after centrifugation and separation of plasma, the sample was preserved at a temperature of -70°C and was subsequently measured by the atomic absorption spectrophotometer of the flame type made by Spain by the method of atomic absorption of the serum zinc level. The data was analyzed using descriptive statistics and ANOVA test and SPSS-16 statistical software. $P \leq 0.05$ was considered as significant.

4. Results

Among the 90 children that were included in this study, 43 children (47.7%) were male and 47 children (52.3%) were female. In the group of febrile seizures 16 children were male (53.3%) and 14 children (46.7%) were female. In the group of febrile without seizures 13 children were male (43.3%) and 17 children were female (56.7%), and in the healthy children 14 children were male (46.7%) and 16 children (53.3%) were female. There was no significant difference between the three groups in terms of sex (Table 1). All the subjects under study were aged between 6 months and 5 years. The mean $\pm$ SD of age of the subjects under study was 2.40 $\pm$ 1.32 years. In the group of febrile seizures the mean $\pm$ SD of age was 2.26 $\pm$ 1.30 years and in the group of febrile children without seizures the mean $\pm$ SD of age was 2.54 $\pm$ 1.36 and in the healthy group it was 2.48 $\pm$ 1.05 years; and there was so significant difference between the two groups in terms of age.

In terms of serum zinc level based on the measurements conducted the zinc level in the children with febrile seizures was between 4 and 160 μg/dL with the mean and standard deviation of 56.8 $\pm$ 52.7 μg/dL. In the febrile group without seizures the serum zinc level was between 33 and 1077 μg/dL with the mean $\pm$ SD of 96.1 $\pm$ 53.4 μg/dL, and in the healthy children the serum zinc level was between 76 and 150 μg/dL with the mean $\pm$ SD of 108.1 $\pm$ 28.1 μg/dL. According to the ANOVA test there was a significant difference between the three groups in terms of the zinc level (P = 0.001) and the results showed that the serum zinc level in the patients with FS was extremely lower than in children only with fever and healthy children (Table 2).

5. Discussion

According the results of this study, the zinc level in the patients with febrile seizures was lower than children

Table 1. Gender Distribution of the Subjects Under Study[a,b]

	Children With Febrile Seizures	Children With Febrile Without Seizures	Healthy Children
Male	16 (53.3)	13 (43.3)	14 (46.7)
Female	14 (46.7)	17 (56.7.7)	16 (53.3)
Total	30 (100)	30 (100)	30 (100)

[a] Values are expressed as No. (%).
[b] P = 0.732

Table 2. Level of Zinc in the Two Groups of Children With Febrile Seizures and the Control Group[a]

Group Values	Mean ± SD
Children With Febrile Seizures	56.86 ± 52.78
Children With Febrile Without Seizures	96.14 ± 53.46
Healthy Children	108.1 ± 28.14

[a] P = 0.001

only with fever and healthy children. Many similar studies have been undertaken so far regarding the level of different elements in blood and its relationship with the incidence of febrile seizures. For instance it has been stated that there is a relationship between a reduction in the level of iron, zinc, selenium and magnesium and pathogenesis of febrile seizures. Similar studies have been conducted on the zinc level and incidence of febrile seizures. In a study that Akbayram et al. conducted on 48 children with febrile seizures and 55 healthy children with the goal of examination of the level of different elements in patients with febrile seizures, the results showed that the zinc level in the patients with febrile seizures is lower than the normal group [19]. In this study as in our study the zinc level in the group of febrile seizures was lower than the control group and the results of this study were aligned with our study.

A study was carried out by Lee and Kim which was aimed at comparison of the zinc level in the patients with febrile seizures and those with seizures without fever (nonfebrile seizures). This study was performed on 288 children. This results of this study indicated that the zinc level in the patients with febrile seizures was 60.5 ± 12.7 μg/dL and 68.9 ± 14.5 μg/dL in the patients with nonfebrile seizures; and statistically speaking, the zinc level in children with febrile seizures was significantly lower than in children with nonfebrile seizures [20]. This study was conducted to investigate the zinc level between the patients with febrile seizures and the patients with nonfebrile seizures which is different from our study in terms of the control group; yet the results of this study showed that the zinc level in the group of febrile seizures is lower than in other types of seizures. In the present study, the average zinc level in the group of children with febrile seizures was 56.8 μg/dL which is slightly lower than the similar group of the study above; but in general, the results of these two studies are in line with each other. In another study was conducted by Amiri et al. examination of different elements in the blood of the patients with febrile seizures was done. Amiri et al. study was performed on 30 children with febrile seizures and 30 healthy children. The zinc level in the patients with febrile seizures was 44.92 ± 10.93 μg/dL and in healthy children it was 62.98 ± 9.80 μg/dL. The results of that study showed that zinc has an important role in pathogenesis of febrile seizures [21]. That study has examined several elements in the blood of patients with febrile seizures and one of these elements is zinc the level of which in patients with febrile seizures was lower than that of the control group; and the results of this study are aligned with our recent study. The reason for reduction of the serum zinc level in the patients with febrile seizures is not known. Nevertheless, severe fever and infection might be effective in development of such conditions. It is believed that release of tumor necrosis factor (TNF) and interleukin in fever and tissue damage might lead to a reduction in the serum zinc level. The studies show that zinc regulates the activity of glutamic acid and the rate-limiting enzyme in the synthesis of GABA which is an inhibitory neurotransmitter and that the low level of GABA in the brain brings some seizure disorders including febrile seizures. As a result, it can be say that the pathogenesis of zinc reduction on febrile seizures results from a disorder in the GABA performance. On the other hand, zinc facilitates the inhibitory effect of calcium on N-methyl-D-aspartate receptors and with these effects prevents the stimulation of neuronal discharge; thus, reduction in the zinc level is a stimulus for neuronal discharge. Zinc is also effective in the function of 300 enzymes, the function of the immune system and the fetal brain development [15, 16]; therefore, by a reduction in the zinc level various complications will be developed in the body as the seizures.

The findings obtained from this study showed that there is a significant relationship between reduction of serum zinc level and febrile seizures. More studies must be conducted in order to confirm the findings obtained from this study and in case the results of the future studies are aligned with this study, the zinc supplements can be used in to treat the febrile seizures.

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Footnotes

Authors' Contribution: Study design, Ali Khajeh, Zohreh Safdari; data collection and analysis, Ghasem Miri-Aliabad, Maryam Keikha, Zohreh Safdari, Hassan Askari; manuscript preparation, Hassan Askari, Afshin Fayyazi.

Conflict of Interest: The authors declare that they have no conflict of interests.

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