

Original Research Article

Estimation of serum zinc levels in children with febrile convulsions

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ABSTRACT

Background: Febrile seizures are the most common form of convulsion in children with the aged between 6 months to 6 years. Different studies have shown that reduction of zinc leads to the incidence of febrile seizures in children. This study was conducted with the goal of examination of the zinc level in the patients with Febrile Seizures.

Methods: This cross sectional study was conducted on 50 children in two equal groups of children with febrile seizures, febrile children without seizures. 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.

Results: 31 males (47.2%) and 19 female children (52.8%) with the average age of 27.23 ± 15.3 months were examined. The two groups had no significant difference in terms of age and sex. The average of zinc level in the patients with Febrile Seizures was $57.4 \mu\text{g/dL}$ and it was $116 \mu\text{g/dL}$ in the febrile children without FS there was a significant difference between the two groups in terms of the zinc level ($P=0.01$).

Conclusions: The low serum zinc level in the group of patients with Febrile Seizures compared with children without febrile seizures indicate the existence of a relationship between the serum zinc level and development of FS in children aged between 6 months and 6 years.

Keywords: Children, Febrile seizures, Zinc

INTRODUCTION

Febrile seizures are impetuous transition in the behavioural activity with limited time and results from the aberrant electrical activity of the brain.¹ They are common in the age group of children and one of the prevailing forms in children are febrile seizures which occur in 2% - 5% of children aged between 6months 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 pleasant surmise; however, due to the increase in recrudescence of such convulsions and the risk of epilepsy in the future, they are considered as grievous malady.⁴ Some studies

have divulged that the genetic factors, family backgrounds, iron deficiency, immunologic disorders and zinc deficiency may portray in febrile seizure. Zinc is a pre-eminent factor in growth, development and normal brain function and it is also a principal compound for different enzymes such as DNA and RNA Polymerases.⁵⁻¹⁴

Etiology of febrile seizures has not been entirely determined yet. Risk factors are being stated by different studies conducted⁵⁻¹⁴

- Central nervous system infection (meningitis, encephalitis)
- Electrolyte imbalance

- Hereditary metabolic disorder
- Structural CNS complications
- Positive family history of febrile seizures
- Alcohol consumption and smoking by mother during pregnancy
- Maternal complication in pregnancy
- Prematurity
- Complication during childbirth
- Recent vaccination

Febrile seizures occur because the electrical system of the brain is not capable enough to withstand against the accent of body temperature. It is due to their co-enzyme activity and repercussion of ion channels and receptors.¹⁵ Studies have shown that iron, zinc, magnesium, selenium and copper are consequentially eminent in febrile seizures.¹⁶ Zinc is one of the crucial materials that plays the major part in management and deterrance of neurological diseases.¹⁷ The top-drawer of zinc is hippocampus.^{18,19} Zinc is an important factor for growth, evolution and normal functions of the brain and a significant co-factor for DNA and RNA Polymerase enzymes.²⁰ Zinc regulates the activity of Glutamic Acid and the rate-limiting enzyme in the synthesis of Gamma-Amino Butyric Acid (GABA) which is an inhibitory neurotransmitter.²¹ 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.²²

According to the importance of febrile seizures, possible factors involved in them including zinc deficiency and limited number of studies happened to explore, this study was conducted with the goal of evaluation of serum zinc level in children with febrile convulsions and comparison with the serum zinc level of children who are febrile without convulsions.

METHODS

In this cross sectional study, 25 children afflicted with their first febrile seizure (case group) were compared with 25 febrile children without seizures (control group) based on serum zinc levels in Yenepoya Medical College Hospital, Mangalore, India. Ethics committee of our institution approved the study protocol before the initiation of study enrollment. After giving a brief and clear explanation of main topics of the experiment, a written agreement was signed by each parent. Both groups were matched for age, sex, weight, height and head circumferences. Children were selected sequentially.

Inclusion criteria

- age between 6 months to 6 years in both groups
- presence of standard criteria for febrile seizures in case group
- occurrence of febrile seizure for the first time.

Exclusion criteria

- children who had consumed zinc over the past month;
- mental or brain retardation and signs of genetic syndrome;
- history of chronic disease and infections of the central nervous system;
- long-time drug use and;
- patients with malnutrition and failure to thrive (FTT).

Using propylene acid-washed tubes, 3 ml of peripheral blood was collected for each patient during the first 24 hours after admission to the hospital, while the seizure episode was controlled. Following proper labeling, the samples were centrifuged under aseptic condition. All samples were tested in duplicate while the instruments were calibrated using recommended protocol. The normal range for zinc using the above technique was 70-120 µg/dl. Data were analyzed with statistical and t test methods. Statistical significance was accepted for a p value of <0.05.

RESULTS

Of a total 25 children afflicted with febrile seizure (case group), 15 (57.7%) were male and 10 (42.3%) were female. Among the control group, there was 16 males (59.9%) and 9 females (40.4%). The minimum and maximum ages in both groups were 7 months and 5.5 years, respectively. The mean age in case group was 27.23±15.3 and in control group 26.46±12.61 months. There was no significant difference in sex and age between the two groups (p >0.05).

Table 1: Anthropometry, gender distribution of the subjects under this study.

Total number of cases	25
Total number of controls	25
Age distribution in cases	15-males (57.7%) 10-females (42.3%)
Age distribution in controls	16-males (59.9%) 9-females (40.4%)
Mean age in cases	27.33±15.30 months
Mean age in controls	26.46±12.61 months
Mean weight in case group	10.62 +/- 2.61 kgs
Mean weight in control group	11.02±2.58 kgs
Mean height in case group	82.4±10.91 cms
Mean height in control group	84.5±12.36 cms
Mean head circumference in case group	47.4±2.52 cms
Mean head circumference in control group	47.29±2.56 cms

The mean weight in case and control group was 10.62±2.61 and 11.02±2.58 kg, respectively. The mean height in case group was 82.4±10.91 and in control group 84.5±12.36 cm. The mean head circumference in case

group was 47.4±2.52 and in control group 47.29±2.56 cm. There was no significant difference between two groups regarding weight, height and head circumference (p > 0.05) (Table 1).

Table 2: Serum zinc levels in cases and controls observed in this study.

Groups	Serum zinc level		
	Minimum value	Maximum value	Mean zinc level
Cases	30.6 ug/dL	84.2 ug/dl	57.4±18 ug/dL
Controls	68.4 ug/dL	126.6 ug/dL	97.5±16 ug/dL

The minimum and maximum serum levels of zinc in case group were 30.6 and 84.2 µg/dl, respectively, with average level of 57.4±18. µg/dl. The similar values for zinc in control group were 68.4 and 126.6 µg /dl, respectively, with average level of 97.5±16 µg /dl (Table 2).

Table 3: Comparison of serum zinc levels among children with febrile seizures and febrile children with no seizures in this study.

Serum zinc level	Febrile children (Case group)		Febrile children with no seizures (Control group)	
<70	21	84%	2	8%
>70	4	16%	23	92%
Total	25	100%	25	100%

A significant statistical difference was observed between the two groups regarding the average level of serum zinc (p = 0.0001). 21 (84%) of children in case group and 2 (9%) in control group were found to have hypozincaemia compared with normal values (70-120 µg/dl). There was a significant difference between two groups regarding the hypozincaemia (p <0.05) (Table 3).

DISCUSSION

The results of this study conceal that the mean serum zinc level in children wretched with febrile seizure is lower than in control group and the discordance is significant. Febrile seizure is the prevalent type of seizure in children as 3-4% of all children apprehend such a condition during their life.⁷ Limited numbers of studies have been conducted regarding the role of zinc in eventuating febrile seizures. Certain number of studies have proved its role play in seizures. The average level of serum zinc in children suffered with febrile seizure was less than control group and were statistically significant.^{10-12,23-25} Hamed and Abdellah conducted a study and reported that the trace elements such as zinc have major role in pathogenesis of seizures.²³ The reason for reduction of serum zinc level in patients afflicted with febrile seizure is not clear. It is believed that the release of Tumor Necrosis Factor (TNF) and Interleukin (IL) during fever

or tissue injury may result in diminution of serum zinc level.^{11,26}

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 (IL) 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. Thus, proving the pathogenesis of hypozincemia on febrile convulsions results from the altered GABA functioning. 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.^{21,27}

Some authors have reported that the serum zinc level in children with febrile seizure is lower than in control group and concluded that this trace element may have a role in febrile seizure. A study conducted by Srinivasa and Manjunath on children with febrile seizures reported that they have serum zinc level lower than the normal range.¹⁶ Similarly, in another study 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.²⁸ A similar study was performed on 30 children with febrile seizures and 30 healthy children reported marked hypozincemia in children with febrile seizures as compared to healthy children, thus proving the hypothesis that zinc has an important role in pathogenesis of febrile seizures.²⁹ Izumi et al, stated that the hypozincemia during fever activate the NMDA receptor, one of the associate of Glutamate classification of receptors, which may execute a salient role in the indoctrinating of epileptic discharge during febrile seizures.³⁰

Although our study also insinuate that the reduction in serum zinc level occurs during febrile seizure, regardless, we are not assure that this is involved in epileptic discharge. The role of zinc in nervous system function has been broadly analyzed in literature.^{31,32} Brain holds an abundant value of zinc, precisely in hippocampus region. 5-15% of zinc is condensed as vesicle zinc in Glutamatergic synapses.³¹ Zinc acts as a neurotransmitter and improves the communicating and locomotive function, and also maturation of neurological system.¹⁴ Zinc deficiency depreciates the hippocampal zinc and steers to seizure release.³²

Regarding the findings of the studies carried out by

different researchers, observable rampancy of febrile seizures; the uncertainty of recurrent seizures, epilepsy and brain mutilation; and also, the essential role of zinc in central nervous system. The controversy is to what level the zinc executes a role in the patho-physiology of febrile seizures and how much the prophylactic prescription of zinc could be adequate of preclusion febrile seizure.^{14,31-33}

CONCLUSION

The verdict of this study that the serum zinc level in children oppressed with their febrile seizure is lower than in febrile children without seizures and the discordance is statistically significant. More studies are required to inscribe these queries and 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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