



**A STUDY ON ROLE OF ZINC IN FEBRILE SEIZURES IN CHILDREN**

**Dr. Jasashree Choudhury\* and Dr. Sidharth Sraban Routray**

<sup>1</sup>Assoc Prof. Department of Pediatrics. IMS and SUM Hospital, BBSR, India.

<sup>2</sup>Assoc Prof. Department of Anaesthesiology and Critical Care, SCB Medical College, Hospital. Cuttack, Odisha, India.

**\*Author for Correspondence: Dr Jasashree Choudhury**

Assoc Prof. Department of Pediatrics. IMS and SUM Hospital, BBSR, India.

Article Received on 23/11/2015

Article Revised on 14/12/2015

Article Accepted on 03/01/2016

**ABSTRACT**

Background : Febrile seizure is the most common type of Seizure in paediatric age. The objective of the present study was to compare the serum zinc levels in children with febrile seizure in healthy children. **Methods:** A total of 120 infants and children aged between 6 months to 6 years were included. The study comprised of 3 groups – Group A: Children with febrile seizures (40 cases), Group B: Children with only fever, but no seizures (40 cases) and Group C: Healthy children (40 cases). Serum zinc level was measured by colorimetric method and compared among the groups using statistical methods. **Results:** There was no significant difference in sex, age, weight, height and head circumference between the three groups ( $P>0.05$ ). There was no statistically significant difference between the groups regarding temperature at the time admission. Mean serum zinc level was  $40.41 \pm 13.15$   $\mu\text{gm/dl}$ ,  $65.84 \pm 17$   $\mu\text{gm/dl}$  and  $88.00 \pm 18.36$   $\mu\text{gm/dl}$  in Groups A, Group B and Group C respectively. Serum zinc level was significantly lower in Group A compared to Group B and it was significantly lower in group B compared to Group C. **Conclusions :** Serum zinc level was lower in children with simple febrile seizures as compared to children with acute febrile illness and healthy children which were found to be statistically significant.

**KEYWORDS:** Zinc, febrile seizure, children.

**INTRODUCTION**

Febrile Seizure is one of the most common neurological conditions in paediatric age. It is a serious condition due to the recurrence rates which may develop into epileptic attacks. Various factors have been attributed to the pathophysiology of febrile seizures like bacterial and viral infections, susceptibility of the immature brain to temperature, association with interleukins, circulating toxins, trace element deficiency and iron deficiency. Role of trace elements like selenium, magnesium, copper and zinc have been studied in association with febrile seizures. Trace elements play a role by their ability to modulate the neurotransmission by acting on ion channels and their coenzyme activity.<sup>[1-6]</sup>

Zinc is a trace element which plays important role in growth, development and normal brain function. It is also an important cofactor for different enzymes, and is involved in cellular growth and differentiation. It is involved in different steps of cellular growth, enzymatic activity of different organs, proteins and cellular metabolism. In brain, Zinc is present in synaptic vesicles in subgroup of glutaminergic neurons and plays role in release of neurotransmitters. These include both excitatory and inhibiting receptors particularly NMDA (N-methyl-D aspartate) and GABA (gamma aminobutyric acid) receptors respectively.<sup>[7,8]</sup> Zinc has an

inhibitory effect on NMDA receptors which is responsible for excitatory phenomenon after binding with glutamate.<sup>[9,10]</sup> In this study we have studied whether decreased zinc levels plays any role in pathogenesis of febrile seizures.

**METHODS**

This study was a cross sectional study held at Central intensive care unit, SCB Medical College, Hospital. Cuttack and IMS and SUM hospital, BBSR, Odisha during the period Feb 2015 to Nov 2015. A total of 120 infants and children aged between 6 months to 6 years were included. The study comprised of 3 groups. Group A: Children with febrile seizures (40 cases), Group B: Children with only fever, but no seizures (40 cases) and Group C: Healthy children (40 cases). Inclusion criteria: children with simple febrile seizure and acute febrile illness without seizure and normal development. A written informed consent was obtained from parents of all the children after fully explaining the study procedure. Socio-demographic data, seizure details, nature of febrile illness, family history of febrile seizures, temperature at admission, nutritional status and vital signs like heart rate, respiratory rate and blood pressure were measured. The axillary temperature was recorded in all children with mercury thermometer placed in axilla for three minutes. Taking proper aseptic precaution, 2 ml of blood was collected after

venipuncture in morning, within 24 hours of contract of patient in all the 3 groups. All samples were sent for serum zinc estimation.

In the present study serum zinc level less than 65  $\mu\text{g}/\text{dl}$  was taken as cut off for zinc deficiency.<sup>[11]</sup> The three groups included in the study were compared with respect to serum zinc level.

**Table 1 : Baseline characteristics, anthropometric parameters, temperature at admission and mean serum zinc levels in 3 groups.**

Variables	Febrile seizure group (N=40)	Febrile Group (N=40)	Normal children (N=40)
Sex	Male-30(75%)	28(70%)	32 (80%)
	Female -10(25%)	12(30%)	8(20%)
Age (months)	26.16 $\pm$ 17.77	28.96 $\pm$ 16.42	27.66 $\pm$ 18.22
Mean weight(kg)	10.68 $\pm$ 2.52	11.62 $\pm$ 2.80	11.84 $\pm$ 2.24
Mean height (cm)	86.44 $\pm$ 11.58	85.32 $\pm$ 12.45	85.89 $\pm$ 13.10
Mean head circumference (cm)	47.65 $\pm$ 2.48	48.59 $\pm$ 2.34	48.24 $\pm$ 2.89
Mean temperature at admission ( $^{\circ}\text{C}$ )	38.65	38.64	
Mean serum zinc ( $\mu\text{g}/\text{dl}$ )	40.41 $\pm$ 13.15	65.84 $\pm$ 17.0	88.00 $\pm$ 18.36

The mean serum zinc was significantly low in febrile seizure group compared to febrile illness group and normal children ( $p < 0.01$ ). There was no statistically significant difference in the serum zinc level in relation to age and sex between the three groups. 75% of group A and 45% of group B had serum zinc level  $< 65 \mu\text{g}/\text{dl}$ . There was a statistically significant difference in serum zinc between the groups ( $p < 0.001$ ).

## DISCUSSION

In his study Burhanoglu M et al. reported that the average level of serum zinc in children affected with febrile seizure was less than control group.<sup>[12]</sup> Ehsani F et al. carried out study on 32 children with febrile seizure and 58 healthy children and found that the serum zinc level in children with febrile seizure was lower than those in control group.<sup>[13]</sup> Tutuncuoglu S et al. reported that the serum zinc level among children with febrile seizure was considerably lower than those in control group.<sup>[14]</sup> In a study by Hamed SA et al., it was shown that the trace elements such as zinc have crucial role in pathogenesis of seizures.<sup>[15]</sup> The study of Gunduz Z et al. on 102 children with febrile seizures indicated that the serum zinc level in the group affected with febrile seizures was significantly lower than those in control group.<sup>[16]</sup> In a study by Mishra OP et al, it was reported that the serum zinc level in children affected with febrile seizure was lower than those in control group, and the difference was significant.<sup>[17]</sup> In contrast to our study, Kafadar I et al found no significant difference in serum Zinc concentration in children with febrile convulsion and other two control groups. This may be due to the smaller sample size in their study.<sup>[18]</sup>

The reason for reduction of serum zinc level in patients affected with febrile seizure is not very clear. Fever and acute infection may have some roles in developing such

## RESULTS

There was no significant difference regarding sex, age, weight, height, head circumference temperature at admission between the 3 groups.

condition. The release of Tumor Necrosis factor (TNF) and interleukin (IL) during fever or tissue injury may result in reduction of serum zinc level.<sup>[19]</sup> Further studies are needed to identify the cause of this observation. Serum zinc levels are influenced by the time of day, the specific disease, or the presence of other trace elements.<sup>[20]</sup>

## CONCLUSION

This study shows that serum zinc levels are decreased in children with febrile convulsions, thus indicating that zinc deprivation plays significant role in the pathogenesis of febrile convulsions. The role of zinc in febrile convulsions should be investigated by further studies and if the results are reproducible, zinc supplementation can be given in febrile convulsions.

## REFERENCE

1. Millichap JG, Millichap JJ. Role of viral infections in the etiology of febrile seizures. *Pediatr Neurol.*, 2006 Sep; 35(3): 165-72.
2. Holtzman D, ObanaK, Olson J. Hyperthermia-induced seizures in the rat pup: a model for febrile convulsions in children. *Science.*, 1981; 213: 1034-6.
3. Tsai FJ, Hsieh YY, Chang CC, Lin CC, Tsai CH. Polymorphisms for interleukin 1 beta exon 5 and interleukin 1 receptor antagonist in Taiwanese children with febrile convulsions. *Arch Pediatr Adolesc Med.*, 2002; 156: 545-8.
4. Virta M, Hurme M, Helminen M. Increased plasma levels of pro-and anti-inflammatory cytokines in patients with febrile seizures. *Epilepsia.*, 2002; 43: 920-3.
5. Amiri M, Farzin L, Moassessi ME, Sajadi F. Serum trace element levels in febrile convulsion. *Biol Trace Elem res.*, 2010; 135(1): 38-44.

6. Kumar PL, Nair MK, Nair SM, Kails L, Geeth S. Iron deficiency as a risk factor for simple febrile seizures – a case control study. *Indian Pediatr.*, 2011; 49: 17-9.
7. Ebadi M, Wilt S, Ramaley R. The role of zinc and zinc-binding proteins in regulation of glutamic acid decarboxylase in brain. In: Ebadi M, Wilt S, Ramaley R, eds. *Chemical and Biological aspects of Vitamin B6, Catalysis*. 1<sup>st</sup> ed. New York: Alan R Liss., 1984 (Part A): 255-275.
8. Cossart R, Bernard C, Ben-Ari Y. Multiple facets of GABAergic neurons and synapses: multiple fates of GABA signaling in epilepsies. *Trends Neurosci.*, 2005; 28: 108-15.
9. Macdonald RL, Kang JQ. Molecular pathology of genetic epilepsies associated with GABA<sub>A</sub> receptor subunit mutations. *Epilepsy Curr.*, 2009; 9: 18-23.
10. Peters S, Koh J, Choi W. Zinc selectively blocks the action of NMDA on cortical neurons. *Science.*, 1987; 236: 589-93.
11. Report of WHO/UNICEF/IAEA/IZINCG Interagency meeting on Zinc Status Indicators. Executive summary. Recommendations for indicators of population zinc status. *Food Nutr Bull.* 2007; 28: S399-400.
12. Burhanoglu M, Tutuncuoglu S, Tekgul H, Ozgur T. Hypozincaemia in febrile convulsion. *Eur J Pediatr.*, 1996 Jun; 155(6): 498-501.
13. Ehsani F, Vahid-Harandi M, Kany K. Determination of serum zinc in children affected by febrile convulsion and comparison with control group. *J Iranian Medi Sci Univ.*, 2006; 12: 219-76.
14. Tutuncuoglu S, Kutukculer N, Kepe L, Coker C, Berdeli A, Tekgul H. Proinflammatory cytokines, prostaglandins and zinc in febrile convulsions. *Pediatr Int.*, 2001 Jun; 43(3): 235-9.
15. Hamed SA, Abdellah MM. Trace elements and electrolytes homeostasis and their relation to antioxidant enzyme activity in brain hyperexcitability of epileptic patients. *J Pharmacol Sci.*, 2004 Dec; 96(4): 349-59.
16. Gunduz Z, Yavuz I, Koparal M, Kumandas S, Saraymen R. Serum and cerebrospinal fluid zinc levels in children with febrile convulsions. *Acta Paediatr Jpn.*, 1996 Jun; 38(3): 237-41.
17. Mishra OP, Singhal D, Upadhyay RS, Prasad R, Atri D. Cerebrospinal fluid zinc, magnesium, copper and gamma-aminobutyric acid levels in febrile seizures. *J Pediatr Neurol.*, 2007; 5: 39-44.
18. Kafadar I, Akinci AB, Pekun F, Adal E. The role of serum zinc level in febrile convulsion etiology. *J Pediatr Inf.*, 2012; 6: 90-3.
19. Garty BZ, Olomuki R, Lerman-Sagie T, Nitzan M. Cerebrospinal fluid zinc concentrations in febrile convulsions. *Arch Dis Child.*, 1995 Oct; 73(4): 338-41.
20. Maret W, Sandstead HH. Zinc requirements and risks and benefits of zinc supplementation. *J Trace Elem Med Biol.*, 2006; 20: 3-18.