Original Research Article

A prospective study of serum zinc levels in children presenting with simple febrile seizures

Sowjan M.[1]

[1]Dr. Sowjan M., Assistant Professor, Department of Pediatrics, Karpagavinayaga Institute of Medical Sciences, Padalam, Chennai, India.

Corresponding Author: Dr. Sowjan M., Assistant Professor, Department of Pediatrics, Karpagavinayaga Institute of Medical Sciences, Padalam, Chennai, India.

Abstract

Aim: To estimate the levels of serum zinc in children with simple febrile seizures and to compare serum zinc levels between children with febrile seizures and febrile children without seizures. **Materials and Methods:** A prospective case control study was done on 100 children for a period of one year from June 2018 to January 2019, admitted in Karpaga Vinayaga Institute of Medical Sciences, Padalam, Chennai, who satisfied the inclusion and exclusion criteria. Of these 50 children were diagnosed to have febrile convulsions. The other 50 were febrile children without seizures. Serum zinc levels were measured in all 100 children. **Results:** Mean Serum zinc levels in children with febrile seizures were 58.4 micrograms/dl and mean serum zinc levels in control group was 94.1 micrograms/dl (p=0.0001). Serum zinc levels were significantly low in children who had febrile seizures of prolonged duration (p=0.0001). **Conclusion:** These findings revealed that there is correlation between serum zinc and simple febrile seizures. Serum zinc level was significantly lower in children with simple febrile seizures in comparison with febrile children without seizure.

Key words: Simple febrile seizures, Serum zinc, Convulsions

Introduction

Febrile convulsion is one of the most common causes of hospitalization of children in pediatric ward in INDIA. The international league against epilepsy (2009) defines a "febrile seizures as a seizure occurring in childhood between 6 months and 6 years of age associated with a fever more than 38°c (rectal temperature) not caused by an infection of the central nervous system, with previous neonatal seizures or a previous unprovoked seizures and not meeting criteria for other acute symptomatic seizures"[1]. Febrile convulsions tend to occur in families, although the exact mode of inheritance is not known and varies between families. Febrile convulsion susceptibility trait is inherited by autosomal dominant pattern with reduced penetrance.

The risk of another child having febrile convulsions is one in five withone affected sibling and one in three if both parents and a previous child had febrile convulsions. The seizure incidence in off spring of individuals with ahistory of febrile convulsion was 10% [2]. The pathogenesis of this condition is still unknown. However, several theories, such as genetic basis, reduction of serum as well as cerebrospinal fluid (CSF) zinc and magnesium level and low Gamma-aminobutyric acid (GABA) have been proposed [3,4]. Low CSF GABA values have been reported in association with several seizure disorders, including febrile convulsion.

Zinc is known to play a control role in the immune system, and zinc- deficient persons experience increased susceptibility to a variety of pathogens.

Zinc also functions as an antioxidant and can stabilize membranes. Zinc modulates the affinity of neurotrans-mitters such as glutamate to their receptors and facilitates the inhibitory effect of calcium on Nmethyl-D-aspartate receptors and thus prevents the excitatory neuronal discharge [5].

Materials and Methods

Type of Study: We carried out a prospective case-control study in a tertiary care hospital to reveal the relationship between lowserum concentration of zinc and febrile convulsion.

Manuscript received: 25th February 2019
Reviewed: 4th March 2019
Author Corrected: 10th March 2019
Accepted for Publication: 14th March 2019

Study Setting: A comparative study was done on 100 children for one year period from July 2108 to January 2019, admitted in Karpaga Vinayaga Institute of Medical Sciences.

Inclusion Criteria: Of these 50 children were diagnosed to have febrile convulsions. The other 50 were febrile children without seizures were taken as control. The controls were age and sex matched. Serum zinc levels were measured in all 100 subjects using calorimetric methods.

Exclusion Criteria: Children on zinc supplementation, diarrheal disease, seizure disorder, malnutrition and on chronic drug intake were excluded from the study.

Statistical Consideration: Data was analyzed using mean, standard deviation Pearson chi square test and SPSS version 15 and p value <0.05 was taken as significant.

Ethical Considerations: The study was approved by institutional ethical committee. Informed consent was obtained from the subject's parents or guardians.

Sampling Methods: A detailed history was obtained including age, sex, socioeconomic status, duration of fever before onset of seizures, duration of seizures, consanguinity, family history of epilepsy, family history of febrile seizures and consanguinity. Complete physical examination of the child was performed with weight, height, head circumference and mid arm circumference to emphasise that there is no evidence of malnutrition.

Sampling Methods: All children were subjected to the following investigation: Hemoglobin and total leukocyte count which was done by auto analyzer. C-reactive protein (CRP) done by nephelometry method and serum zinc done by calorimetric method.

Zinc status in children with febrile seizures were compared with different variables such as age, sex, socioeconomic status, duration of fever before seizures, duration of seizures, consanguinity, family history of epilepsy, family history of febrile seizures and consanguinity, zinc levels in febrile children without seizures. Normal range of serum zinc levels were taken as 70 to 150 micrograms/dl.

Results

The mean serum zinc levels in children with simple febrile seizures 58.40 micrograms/dl and in children with fever without seizures was 94.18 micrograms/dl. The difference was statistically significant (p<0.001). The clinical characteristics of serum zinc levels of cases and controls are shown in table. Majority of the cases were between 1 to 2 years (44%). Infants were 42%. Very few children were between 2 to 3 years (10%) and between 3 to 4 years (4%).

Table-1:Demographic assessment of groups.

Gender	Cases		Controls	
	No.	%	No.	%
Male	33	66	26	52
Female	17	34	24	48
Total	**50**	**100**	**50**	**100**

Table-2: Serum Zinc Levels among Cases and Controls

Serum zinc	Cases		Controls	
	No.	%	NO.	%
Normal	19	38	45	90
Low	31	62	5	10
Total	**50**	**100**	**50**	**100**

Discussion

Febrile seizure is a commonly occurring problem in young children. Although its pathogenesis is debatable, studies have revealed that the genetic factors, family background, immunologic disorders, iron deficiency and zinc deficiency may play a significant role in febrile convulsions. The infection state exhibits non-specific host responses, including immune responses such as changes in the concentrations of certain plasma

proteins, cytokines (tumor necrosis factor, interleukin-1and inter leukin-6) and interferon which may result in reduction of serum zinc level. Hypozincemia has been suggested as a possible change during the rising phase of body temperature in febrile patients. It is generally believed that febrile seizure is an age dependent response of the immature brain to fever.

This postulation is supported by the fact that most (80-85%) febrile seizures occur between 6 months and 2 years of age, with the peak incidence at 18 months [6,7]. Age of presentation in our study is, majority of children (82%) were between 6 months to 2 years. Males have consistently emerged as having a higher frequency of febrile seizures (male to female ratio, 1.1:1 to 2:1)[8].

However, some large studies have shown no significant gender difference. In our study majority were males (66%). Frequency of low serum zinc level was found in 62% children with febrile seizures in this study, which is comparable with several international studies in children with febrile seizure.

Several studies support the idea that low zinc levels increase seizure susceptibility.Altering dietary zinc intake can alter seizure susceptibility in a genetic mouse model of epilepsy, with low zin being increased susceptibility and high zinc being protective [9]. A similar study done by Ganesh R et al [10] which falls under same geographical area as our study which compared serum zinc levels in 38 cases of simple febrile seizure with 38 age matched controls also showed that Indian children with febrile seizure had low serum zinclevels with statistically significant results ($p<.001$).

Salehiomran et al in 2013 in north Iran published a case control study of 50 children with febrile seizures and 50 children with fever without seizures which is same as our study also showed that mean serum zinc levels were significantly lower in children with febrile seizures [11].

Heydarian et al in 2010 also reported that the serum level of zinc was significantly lower in children with simple febrile seizure compared to febrile children without seizure [12]. On the other hand, in one report by Cho et al. from Korea in Pusan Hospital, there was no significant difference between serum zinc level of children with febrile seizure and that of control group.

This difference with our result may be due to their small sample size (study was performed on 11 patients in each group) [13]. However Garty BZ et al findings were against the hypothesis that low serum zinc level is a risk factor for febrile seizures.We think that this may be due to delayed CSF sampling after the febrile illness in their study [14]. This finding of a variety of zinc related clinical disorders revealed the importance of zinc in human nutrition [15]. Zinc is second to iron as the most abundant trace element in the body. More than 300 zinc enzymes occur in all six categories of enzyme system [15].

Severe zinc deficiency is known to affect mental health, with varying degrees of confusion and depression being consistent with zinc enzymes have important role in brain development and function [15].

Zinc can suppress some excitatory mechanisms in CNS. It can directly elevate the threshold of the seizure level by inhibiting N-methyl-D-aspartate (NMDA) receptors or through improving calcium inhibitory function [16,17]. In conclusion, our study results showed that children with febrile seizures had significantly lower serum zinc levels than those with fever without seizure.

It is important to answer these questions that how zinc level plays role in the pathophysiology of febrile seizure and whether zinc supplementation could be effective in preventing febrile seizures.

More and larger studies are required to answer these questions and also comparative study between serum and CSF zinc levels can be some what helpful. One limitation of our study is it was done in small number of patients.

More prospectively designed, multi center studies involving larger sample sizes are needed to answer these questions.

Conclusion

In conclusion In our study serum zinc levels were low in children with simple febrile seizures in comparison with febrile children without seizures. So children with low serum zinc levels are more prone to get febrile seizures than children with normal serum zinc levels. This study adds that not only iron deficiency is a risk factor for simple febrile seizures but low serum zinc levels is also a risk factor for developing simple febrile seizures

What this study adds to Existing Knowledge- Hypozincenemia is one of the risk factor for simple febrile seizures

Recommendations

1. Zinc supplementation in children with simple febrile seizures may reduce further episodes

2. Children in zinc deficient areas should be supplemented with zinc to prevent simple febrile seizures

3. Study has to be done in larger population with multi centre involvement.

4. Zinc levels have to be monitored in all children with seizures disorders.

Funding: Nil, **Conflict of interest:** None initiated,
Perission from IRB: Yes

References

1. Kleigman RM, Stanton BF, Schor NF, St. Geme JW, Bherman RE. Nelson textbook of paediatrics, 19 ed. Philadelphia, PA: saunders; 2011.

2. Doose H, Maurer A. Seizure risk in offspring of individuals with a history of febrile convulsions. Eur J Pediatr. 1997 Jun;156(6):476-81.

3. Mollah MA, Dey PR, Tarafdar SA, et al. Zinc in CSF of patients with febrile convulsion. Indian J Pediatr. 2002 Oct; 69 (10):859-61.

4. OP Mishra, Deepak Singhal, Ram S Upadhyay, Rajniti Prasad And DivyaAtri. Cerebrospinal fluid zinc, magnesium, copper and gamma-aminobutyric acid levels in febrile seizures. journal of pediatric neurology 2007; 5(1): 39-44.

5. Peters S, Koh J, Choi DW. Zinc selectively blocks the action of N-methyl-D-aspartate on cortical neurons. Science. 1987 May 1;236(4801):589-93.

6. Graves RC, Oehler K, Tingle LE. Febrile seizures: risks, evaluation, and prognosis. Am Fam Physician. 2012 Jan 15;85(2):149-53.

7. Patterson JL, Carapetian SA, Hageman JR, et al. Febrile seizures. Pediatr Ann. 2013 Dec;42(12):249-54. doi: 10.3928/00904481-20131122-09.

8. Stafstrom CE. The incidence and prevalence of febrile seizures.In: Baram TZ, ShinnarS, editors. Febrile seizures. San Diego: Academic Press; 2002. pp. 1–25.

9. Fukahori M, Itoh M. Effects of dietary zinc status on seizure susceptibility and hippocampal zinc content in the El (epilepsy) mouse. Brain Res. 1990 Oct 8;529 (1-2): 16-22.

10. Ganesh R, Janakiraman L. serum zinc levels in children with simple febrile seizures. clinical paediatrics 2008; 47(2):164-166.

11. Salehiomran MR, Mahzari M. Zinc status in febrile seizure: a case-control study. Iran J Child Neurol. 2013 Fall; 7 (4):20-3.

12. Heydarian F, Ashrafzadeh F, Ghasemian A. Serum zinc level in patient with simple febrile seizure. Iran J Child Neurol 2010; 4(2):41-43.

13. Cho WJ, Son BH, Kim SW. Levels of Sodium and Zinc concentration in febrile convulsion. Korean Child Neural Soc 1999; 7(2): 214-219.

14. Garty BZ, Olomucki R, Lerman-Sagie T, et al. Cerebrospinal fluid zinc concentrations in febrile convulsions. Arch Dis Child. 1995 Oct;73(4):338-41.

15. Burtis carl A, Ashwood Edwhard R, Brun David E. Tietz fundamentals of clinical chemistry, 6th ed. Philadelphia: saunders; 2005.505-507

16. Smart TG, Hosie AM, Miller PS. Zn2+ ions: modulators of excitatory and inhibitory synaptic activity. Neuroscientist. 2004Oct;10(5):432-42. DOI:10. 1177/1073858404263463

17. Mollah MA, Rakshit SC, Anwar KS, et al. Zinc concentration in serum and cerebrospinal fluid simultaneously decrease in children with febrile seizure: findings from a prospective study in Bangladesh. Acta Paediatr. 2008 Dec; 97 (12): 1707-11. doi: 10. 1111/j. 1651-2227.2008.01001.x.Epub 2008 Sep 15.

……..

How to cite this article?

Sowjan M. A prospective study of serum zinc levels in children presenting with simple febrile seizures. Int J Pediatr Res. 2019;6(03):118-121.doi:10.17511/ijpr.2019.i03.03

……