SERUM ZINC LEVEL IN CHILDREN WITH FEBRILE SEIZURE

A. Mahyar*[1], A. A. Pahlavan[2] and A. Varasteh-Nejad[1]

1) Department of Pediatrics, School of Medicine, Qazvin University of Medical Sciences, Qazvin, Iran

2) Department of Microbiology and Clinical Diagnostic Laboratory, Qazvin University of Medical Sciences, Qazvin, Iran

Abstract- Febrile seizure is the most common type of seizure in children and a variety of causes are considered to be responsible for it. There are some reports that zinc may have a role in febrile seizure. The aim of this study was to compare the serum zinc level in children with and without febrile seizure. In this case-control study, 52 children with febrile seizure compared with 52 healthy children based on serum zinc level. Both groups were matched for age, sex, weight, height, and head circumference. The age range of children was 9 months to 5 years. Serum zinc level was measured using flame atomic absorption spectrophotometry. Of 52 children in case group, 30 (57.7%) were male and 22 (42.3%) female and among the control group, there was 31 (59.9%) males and 21 (40.4%) females. The mean age of children in case group was 27.13 ± 15.72 and in control group 28.49 ± 16.5 months. The mean zinc level in case group was 62.84 ± 18.40 μg/dl and in control group 85.70 ± 16.76 ($P < 0.05$). This study revealed that the serum zinc level in children afflicted with their first febrile seizure is lower than in healthy children and the difference is statistically significant. It seems that the zinc deficiency may play a role in febrile seizure.

Acta Medica Iranica 2008; 46(6): 477-480.

Key words: Febrile seizures, zinc, children

INTRODUCTION

Febrile seizure is the most common type of seizure in children as 3-4% of children experience such condition during their lives. This type of seizure is mainly observed in the age range of 9 months to 5 years (1). By definition, children affected with febrile seizure are free of serious diseases such as central nervous system infections (meningitis, encephalitis), electrolyte imbalance, hereditary metabolic disorders, and also neurological and structural brain problems (2). Studies have revealed that the genetic factors (1), family backgrounds (1), iron deficiency (3, 4), immunologic disorders (7) and zinc deficiency (5, 6) may play a role in febrile seizure.

Received: 6 Sep. 2007, Revised: 9 Nov. 2007, Accepted: 19 Jan. 2008

*** Corresponding Author:**
Abolfazl Mahyar, Department of Pediatrics, Qods Children Hospital, Qazvin University of Medical Sciences, Qazvin, Iran
Tel: +98 281 3664934,
Fax: +98 281 3669947
E-mail: Abolfazl473@yahoo.com

Zinc is an important element in growth, development and normal brain function and it is also an important cofactor for different enzymes such as DNA and RNA polymerases. The mechanism by which zinc in involved in cellular growth and differentiation, enzymatic activity of different organs, proteins and cellular metabolism is well known (8, 9). 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 (5, 6).

The aim of this study was to compare the serum zinc level in children with and without febrile seizure.

MATERIALS AND METHODS

In this case-control study, 52 children afflicted with their first febrile seizure (case group) were compared

with 52 healthy children (control group) based on serum zinc levels in Qods Children Hospital, Qazvin (Iran) in 2006. 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. The control group was composed of healthy children who were visited at local health center on a regular basis. Children were selected sequentially. The inclusion criteria were: 1) age between 9 months to 5 years in both groups, 2) the presence of standard criteria for febrile seizures in case group, and 3) occurrence of febrile seizure for the first time.

Using propylene acid-washed tubes, 2 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 at 2,500 rpm under aseptic condition. Serum samples were then removed using acid-washed tips and stored at -20° C.

Later, all samples were transferred to biochemistry department at Iranian Atomic Energy Organization (Tehran). Zinc levels were measured by flame atomic absorption spectrometry (AAS) using a Varian SpectraAA220. 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 of 52 children afflicted with their first attack of febrile seizure (case group), 30 (57.7%) were male and 22 (42.3%) were female. Among the control group, there was 31 males (59.9%) and 21 females (40.4%). The minimum and maximum ages in both groups were 9 months and 5 years, respectively. The mean age in case group was 27.13 ± 15.73 and in control group 28.49 ± 16.51 months. There was no significant difference in sex and age between the two groups ($P > 0.05$).

The mean weight in case and control group was 11.62 ± 2.61 and 12.02 ± 2.58 kg, respectively. The mean height in case group was 81.96 ± 10.91 and in control group 85.62 ± 14.16 cm. The mean head circumference in case group was 48.6 ± 2.44 and in control group 48.19 ± 2.16 cm. There was no significant difference between two groups regarding weight, height and head circumference ($P > 0.05$).

The minimum and maximum serum levels of zinc in case group were 31.5 and 106.5 μg/dl, respectively, with average level of 62.84 ± 18.40 μg/dl. The similar values for zinc in control group were 55 and 127.5μg /dl, respectively, with average level of 85.70 ± 16.76 μg /dl. A significant statistical difference was observed between the two groups regarding the average level of serum zinc ($P = 0.0001$). Thirty seven (53.81%) of children in case group and 10 (9.6%) in control group were found to have hyopozincaemia compared with normal values (70-120 μg/dl) (Table 1). There was a significant difference between two groups regarding the hyopozincaemia ($P < 0.05$).

Table 1. Comparison of serum zinc level in children with first febrile seizure (case group) and healthy children (control group)*

Serum zinc (μg /dl)	Case		Control	
	Number	Percent	Number	Percent
< 70 (Less than normal)	37	58.8	10	9.6
> 70 (Normal)	15	46.2	42	90.4
Total	52	100	52	100

*$P < 0.05$.

DISCUSSION

The results of this study revealed that the mean serum zinc level in children afflicted with febrile seizure is lower than in control group and the difference is significant.

Febrile seizure is the most common type of seizure in children, as 3-4% of all children experience such a condition during their life (1). The exact etiopathogenesis of febrile seizure is unknown. However, a variety of factors are considered to be involved in pathogenesis of febrile seizure such as genetic factors (1), family backgrounds (2), iron deficiency (3, 4), immunologic disorders (7) and zinc deficiency (5, 6).

Limited numbers of studies have been conducted regarding the role of zinc in occurrence of febrile seizures. Burhanoğlu *et al.* reported that the average level of serum zinc in children afflicted with febrile seizure was less than control group (5). Another study carried out on 34 children with febrile seizure and 58 healthy children revealed that the serum zinc level in children with febrile seizure was lower than those in control group and the difference was significant, statistically (6). Tütüncüoğlu *et al.* reported that the serum zinc level among children with febrile seizure was considerably lower than those in control group (7). In a study by Hamed and Abdellah, it was shown that the trace elements such as zinc have crucial role in pathogenesis of seizures (10). The study of Gündüz *et al.* on 102 children with febrile seizures indicated that the serum zinc level in the group afflicted with febrile seizures was significantly lower than those in control group (11). In a very latest study by Mishra *et al.* on 20 children with febrile seizures and 48 children as control group, it was reported that the serum zinc level in children afflicted with febrile seizure was lower than those in control group, and the difference was significant (12).

The reason(s) for reduction of serum zinc level in patients afflicted with febrile seizure is not clear. However, fever and acute infection may have some roles in developing such condition (13). It is believed that the release of tumor necrosis factor (TNF) and interleukin (IL) during fever or tissue injury may result in reduction of serum zinc level (6). Izumi *et al.* proposed that the hypozincemia during fever trigger the NDMA receptor, one of the members of glutamate family of receptors, which may play an important role in the initiation of epileptic discharge during febrile seizures (14). Although our study also implies that the hypozincemia occurs during febrile seizure, nevertheless, we are not fully sure that the hypozincemia is involved in epileptic discharge, as our control group was healthy children without fever.

The role of zinc in nervous system function has been broadly discussed in literature (15, 16). Brain contains an abundant value of zinc, especially in hippocampus region. Five to fifteen percent of zinc is concentrated as vesicle zinc in glutamatergic synapses (15). Zinc acts as a neurotransmitter and improves the communicating and locomotive function, and also evolution of neurological system (9). Zinc deficiency diminishes hippocampal zinc and leads to seizure discharge (16). Regarding the findings of the studies carried out by different researchers; noticeable prevalence of febrile seizures; the risk of recurrent seizures, epilepsy and brain damage; and also the crucial role of zinc in central nervous system (9, 15-17), the question is to what extent the zinc plays a role in the pathophysiology of febrile seizures and how much the prophylactic prescription of zinc could be capable of preventing febrile seizure. More studies are required to address these questions.

In conclusion, this study revealed that the serum zinc level in children afflicted with their first febrile seizure is lower than in healthy children and the difference is statistically significant.

Acknowledgements

We thank Mr. Amir Javadi for his assistance. This project was founded by the Research Department of Qazvin University of Medical Sciences.

Conflict of interests

The authors declare that they have no competing interests.

REFERENCES

1. Johnston MV. Febrile seizure. In: Behrman RE. Nelson textbook of Pediatrics, Philadelphia: Sunders; 2004. P. 1994-1995.

2. Daoud A. Febrile convulsion: review and update. J Pediatr Neurol. 2004; 2(1): 9-14.
3. Daoud AS, Batieha A, Abu-Ekteish F, Gharaibeh N, Ajlouni S, Hijazi S. Iron status: a possible risk factor for the first febrile seizure. Epilepsia. 2002 Jul; 43(7):740-743.
4. Pisacane A, Sansone R, Impagliazzo N, Coppola A, Rolando P, D'Apuzzo A, Tregrossi C. Iron deficiency anaemia and febrile convulsions: case-control study in children under 2 years. BMJ. 1996 Aug 10; 313(7053): 343.
5. Burhanoğlu M, Tütüncüoğlu S, Coker C, Tekgül H, Ozgür T. Hypozincaemia in febrile convulsion. Eur J Pediatr. 1996 Jun; 155(6): 498-501.
6. Ehsani F, Vahid-Harandi M, Kany K. [Determination of serum zinc in children affected by febrile convulsion and comparison with control group]. The Journal of Iranian Medical Sciences University. 2006;12: 219-276. Farsi
7. Tütüncüoğlu S, Kütükçüler N, Kepe L, Coker C, Berdeli A, Tekgül H. Proinflammatory cytokines, prostaglandins and zinc in febrile convulsions. Pediatr Int. 2001 Jun; 43(3):235-239.
8. Hambidge M. Human zinc deficiency. J Nutr. 2000 May;130(5S Suppl):1344S-1349S.
9. Mahyar A. The preventive role of zinc from communicable and non-communicable diseases in children, NCD Malaysia, 2005; 4: 21-25.
10. 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):349-359.
11. Gündüz Z, Yavuz I, Koparal M, Kumandaş S, Saraymen R. Serum and cerebrospinal fluid zinc levels in children with febrile convulsions. Acta Paediatr Jpn. 1996 Jun; 38(3):237-241.
12. Mishra OP, Singhal D, Upadhyay RS, Prasad R, Atri D**.** Cerebrospinal fluid zinc, magnesium, copper and gamma-aminobutyric acid levels in febrile seizures. Journal of Pediatric Neurology. 2007; 5: 39–44.
13. Garty BZ, Olomucki R, Lerman-Sagie T, Nitzan M. Cerebrospinal fluid zinc concentrations in febrile convulsions. Arch Dis Child. 1995 Oct; 73(4):338-341.
14. Izumi Y, Ishii K, Akiba K, Hayashi T. Hypozincemia during fever may trigger febrile convulsion. Med Hypotheses. 1990 May; 32(1):77-80.
15. Cole TB, Robbins CA, Wenzel HJ, Schwartzkroin PA, Palmiter RD. Seizures and neuronal damage in mice lacking vesicular zinc. Epilepsy Res. 2000 Apr; 39(2): 153-169.
16. Tapiero H, Tew KD. Trace elements in human physiology and pathology: zinc and metallothioneins. Biomed Pharmacother. 2003 Nov;57(9):399-411.
17. Yang ZX, Qin J. Interaction between endogenous nitric oxide and carbon monoxide in the pathogenesis of recurrent febrile seizures. Biochem Biophys Res Commun. 2004 Mar 5;315(2):349-355.