

The Relationship between Zinc Deficiency and Febrile Convulsion in Isfahan, Iran

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Abstract

Objective

Febrile convulsion (FC) is a common cause of seizure in young children, with an excellent prognosis. In addition to genetic predisposition and infections, FCs are generally thought to be induced by metabolic and elemental changes during fever such as Zinc (Zn) deficiency. Regarding the high prevalence of febrile convulsions and the role of Zn deficiency, we investigated the role of Zn in FC patients in Isfahan, Iran.

Materials and Methods

In a controlled cross sectional study, 90 patients aged 9 months to 5 years were studied in a period of 12 months. They were assigned to three groups. Thirty patients were included in the Febrile Seizure group, thirty febrile children without convulsion or previous history of convulsion were included in the febrile group and thirty afebrile healthy ones were enrolled as controls. Venous blood was obtained and Zn concentration in serum was measured using Graphite Furnance Atomic Absorbance Spectrophotometering (GF-AAS).

Results

Patients and the control groups had no difference in either mean age or sex distribution. No significant relationship was observed between serum Zn level and age or sex among patients in the FC group and two other control groups.

Conclusion

Our findings showed that Zinc level was significantly lower in the febrile seizure group compared to two other groups. We tried to categorize various conditions in a more practical form. Also, Zinc is in close relationship with socioeconomic level of the individuals which was well considered in the current survey.

Keywords: Zinc; Zinc deficiency; Febrile Convulsion.

Introduction

Febrile convulsion (FC), a common cause of seizures in young children, generally has an excellent prognosis and is associated with fever. No evidence of intracranial infection, epilepsy, or any other defined cause of seizure exists. FC is age dependent and is rare before 9 months and after 5 yr of age. The peak age of onset is about 14–18 months of age, and the incidence meets 3–4% of young children (1). FC has been studied extensively in past decades; it was tried to help practitioners to assess the risks associated with such manifestation in some of these studies. FC can occur following both viral and bacterial infections (2, 3).

Febrile convulsion susceptibility has been linked to several genetic loci in different families. In addition, previous studies have shown that siblings and parents of patients with febrile seizures have a 4 to 10 percent incidence of epilepsy (4, 5, 6, 7).

However, viral and bacterial infections, especially HSV6, in combination with a low seizure threshold (genetically prone patients) often remain the most common causes of convulsion in young children. Having considered various etiologies for FC, its real underlying mechanism is unclear to date (3, 4).

In addition to genetic predisposition and infections, other parameters are also considered in this regard. Febrile convulsions are generally thought to be induced by metabolic changes during the rise-phase of body temperature. Iron insufficiency may play a role in the pathogenesis, as well. In a prospective study of 150 children, mean ferritin levels were significantly lower in children with a first febrile seizure than matched controls with a febrile illness but no convulsions (29.5 versus 53.3 mcg/L). Plasma ferritin levels ≤ 30 mcg/L occurred in a significantly greater proportion of children with seizures than controls (65 versus 32 percent). Further studies are required to confirm this preliminary finding (8).

Some proposed hypotheses on the induction mechanism of febrile convulsions have suggested hypozincemia during fever (9). Among numerous biological effects of Zinc, considerable evidence shows its role in neurological function. Biochemical changes in neurotransmitters or trace elements like Zinc remain necessary components of >200 metalloenzymes, which play an important role in the CNS; for example, Zinc deficiency lowers serum and CSF concentration of γ -aminobutyric acid (GABA), blocks N-Methyl D-Aspartate (NMDA) receptors which can affect serum and CSF Zn levels. This hypozincemia activates the NMDA receptor, one of the glutamate family of receptors, which may play an important role in the induction of epileptic electrical discharges (9). Consequently, Zinc deficiency is illustrated as one of the nutritional problems worldwide today, especially in developing countries. However, there is no precise reported prevalence of Zinc deficiency in Iranian children. Regarding the assumed role of Zinc deficiency in FC, besides the high prevalence of convulsions in term of fever, we planned to investigate this relationship

in these patients in Isfahan, Iran.

Materials and Methods

In a controlled cross sectional study, 90 patients aged 9 months to 5 years were studied in a period of 12 months (December 2007 to December 2008) in Amin Hospital (A university hospital affiliated to Isfahan Medical School). They were assigned to three distinct groups. Included patients had no history of previous convulsion, developmental delay or neurological deficit. CNS infection and electrolytes imbalance were ruled out, too. Upon attending the pediatric ward of Amin Hospital with a complaint of febrile seizure, thirty patients were included in the study as the Febrile Seizure group. The febrile control group consisted of thirty febrile children without convulsion or previous history of convulsion who were admitted to this hospital for other reasons. We also had another control group of thirty afebrile healthy children, selected through the patients visited in the outpatient pediatric clinic of the hospital, or those who came for vaccination. None of them needed hospital admission in their first visit. Controls were selected with regard to inclusion criteria used for other patients in case groups like age between 9 months to 5 years, no family history of afebrile seizures, and lack of developmental delay. A single seizure with <15 min duration in the presence of fever (Core Temperature >38) without focal features was defined as a simple febrile convulsion provided that it did not occur more than once in 24 h. Acetaminophen was used for its antipyretic effects (rectal suppository or oral syrup with 10-15 mg/kg 4 times a day) and rectal or IV Diazepam was administered to control seizures (0.2 mg/kg).

After controlling FC and performing clinical examination, parents were clearly informed on the main purposes of the study and an informed written consent was signed by parents after confirmation. It must be noted that The Ethics Committee of Isfahan University of Medical Sciences had approved the study protocol. Then, 5cc vein blood was obtained and kept in screw-capped air tight de-ionized pyrex test tubs for Zinc measurement. After collecting all samples, they were transferred to a toxicology laboratory for final measurement. ZN concentration in serum was measured using Graphite Furnance Atomic Absorbance

Spectrophotometering (GF-AAS). Samples were obtained within 6 h after admission to hospital. Data were analyzed using ANOVA with SPSS 11.5 software.

Results

Thirty children with febrile convulsion, 30 febrile children with no seizure and 30 healthy afebrile children were studied. Mean age of the groups are listed in Table

Table 1: Mean age of the groups

Group	Mean (year)	SD
Febrile convulsion	2.6	0.7
febrile children with no seizure	2.73	0.9
healthy controls	2.70	0.8

Of 30 patients in the FC group, 17 were male and 13 were female. There were 15 boys and 15 girls in febrile children with no seizure group and 14 males and 16 females in the control healthy group.

Patients and the control groups had no difference in either mean age or sex distribution (P value>0.5). No significant relationship was observed between serum Zinc level and age or sex among patients in the FC group and two other control groups (P value>0.5).

Comparison of serum zinc concentration level among the three groups is detailed in Table 2.

Mean serum zinc level was compared in the 3 groups. ANOVA showed that this level was significantly lower in FC patients compared to two other groups (Pvalue<0.001) while comparison of serum zinc concentration level between febrile group with no seizure and healthy group showed no significant difference (P value>0.5)

Table 2: Serum zinc concentration level

Group	Mean level of Zinc (mcg/dl)	SD
Febrile convulsion	93.39	73.88
febrile children with no seizure	130.54	25.89
healthy group	130.39	14.74

Discussion

This study showed that Zinc level was significantly lower in the febrile seizure group compared to two other groups. Regarding the concept that Zn deprivation may lead to febrile convulsions, serum/CSF Zn concentration was observed to decrease during infectious diseases among Turkish children (10). Also, the hypothesis proposed by Izumi et al. that ‘hypozincaemia during fever triggers febrile seizure (9) is consistent with our current findings.

Other studies on determining the role of blood or CSF Zn in febrile seizure in children, except for a few mentioned above that confirmed the findings of our current study, remained mainly scanty until 2004 (11).

In Iran, In a case control study in Qazvin, It was revealed that the serum zinc level in children afflicted with their first febrile seizure was lower than healthy children and the difference was statistically significant (12).

In addition, in a prospective case - control study which was performed on 60 children aged 6 months to 6 years from Apr. 2009 to Jan. 2010 in Ghaem, Mashhad, the serum zinc level was assessed and compared between the cases (30 patients with simple febrile seizure) and the controls (30 children who had fever without seizure) and it was found that mean serum zinc level was 663.7 µg /l and 758.33 µg /l in the case group and the control group respectively with P value <0.001 (13).

In 1996, to further understand the role of trace elements

in the pathogenesis of febrile convulsions, serum and CSF zinc (Zn), copper (Cu), magnesium (Mg) and protein levels were measured by Burhanoglu et al, using spectrometry, in patients with febrile convulsion (n=19), bacterial meningitis (n= 9), viral CNS infection (n= 16) and in the control group (n= 10). Finally it was concluded that Serum and CSF Zn levels were lower in children with febrile seizures. Zinc deprivation may play a role in the pathogenesis of febrile seizures (10).

In another study in 1990, Izumi proposed a new hypothesis on the induction mechanism of febrile convulsions that suggested hypozincemia during fever. This hypozincemia activates the NMDA receptor, one of the glutamate families of receptors, which may play an important role in the induction of epileptic discharges (9).

In comparison with these studies, we better clarified the differences between various conditions by assigning the patient to three distinct groups. In other words, we tried to categorize various conditions in a more practical fashion.

On the other hand, Zinc is in close relationship with the level of socioeconomic of the individuals living in a geographic area. to evaluate the role of Zn and history of using food supplementation in developing countries with a low socioeconomic status, Abid Hossain Mollah and his colleagues conducted a prospective cross-sectional study to determine if there was any simultaneous change in zinc (Zn) concentration in serum and cerebrospinal fluid (CSF) in the febrile convulsion children as compared to their matched non-seizure febrile peers in Dhaka, Bangladesh. Serum and CSF-Zn simultaneously decreased in febrile convulsion children when compared to their matched non febrile convulsion peers (14). This finding was further investigated in our study with more emphasis.

However, more prospectively designed multi central studies involving larger sample sizes are essential in order to confirm or decline the findings. For this reason, we designed and conducted this study in Iran. The geographically diverse region of this study compared to few previous ones alongside involving a larger sample to confirm or discredit the findings of previous studies strengthened our survey. This would assist us in adopting a cost-effective strategic plan and formulating

a more effective protocol to prevent febrile convulsion recurrent attacks with adequate Zn supplementation, particularly in developing countries, which could also be included in boosting the power towards better child survival strategies more rationally.

Having mentioned all the advantages, lack of appropriate studies on Zn level (and Hypozincemia) prevented us from reaching a definite conclusion whether infectious diseases are responsible for low zinc levels or the existing hypozincemia is the main reason. Therefore, further studies must be conducted to clearly determine the prevalence of Zinc deficiency in Iranian children.

In conclusion, our findings showed that Zinc level was significantly lower in the febrile seizure group compared to two other groups. We tried to categorize various conditions in a more practical fashion. Also, Zinc is in close relationship with the socioeconomic level of the individuals which was well taken into account in the current survey.

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