The Role of Serum Zinc Level in Febrile Convulsion Etiology

Febril Konvulsiyon Etyolojisinde Serum Çinko Düzeyinin Rolü

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Abstract

Objective: Although the mechanism of febrile convulsion is not yet clear, some changes in the level of trace elements such as zinc have been suggested to be responsible for the pathogenesis.

Material and Methods: This study was carried out with 88 children, 40 girls, 48 boys between 6-72 months of age who visited the Pediatric Emergency Department of Okmeydanı Research and Training Hospital from Agust 2009 to November 2009. The children were divided into three groups. The first group included 45 patients with complaints of febrile convulsion, the second group included 23 children who had visited for fever but did not have convulsions, and the third group consisted of 20 healthy children.

Results: Mean serum zinc concentration of patients who had febrile convulsions was 110.49±35.03 µg/dL, whereas mean serum zinc concentrations of children with fever and healthy children were 107.12±21.66 µg/dL and 116.12±32.07 µg/dL, respectively.There is no statistically significant difference between the three groups in terms of zinc levels. We did not find any difference between serum zinc levels in patients who had one or more convulsions.

Conclusion: Our findings do not support the hypothesis that febrile convulsion is related to reduced serum zinc concentration, thus necessitating further studies involving larger sample sizes in order to understand the role of zinc in the pathogenesis of febrile convulsion. *(J Pediatr Inf 2012; 6: 90-3)*

Key words: Febrile convulsion, zinc

Received/Geliş Tarihi: 31.03.2012
Accepted/Kabul Tarihi: 03.08.2012

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doi:10.5152/ced.2012.27

Özet

Amaç: Febrile konvulsiyonunun oluş mekanizması tam olarak bilinmemekle beraber, çinko gibi bazı eser elementlere ait patolojilerin, febril konvulsiyonun ortaya çıkışında rol oynayabileceği düşünülmektedir. Çalışmamızda amaç febril konvulsiyon ile serum çinko düzeyi arasındaki ilişkiyi araştırmaktır.

Gereç ve Yöntemler: Bu çalışmaya, Ağustos 2009-Kasım 2009 tarihleri arasında Okmeydanı Eğitim ve Araştırma Hastanesi Çocuk Acil Polikliniği'ne başvuran yaşları 6-72 ay arasında değişen, 40'ı kız, 48'i erkek toplam 88 çocuk alındı. Çocuklar üç grup altında incelendi. Birinci grup febril konvulsiyon geçiren 45 çocuktan oluşurken, ikinci grubu yüksek ateşi olan ancak konvulsiyon geçirmemiş 23 çocuk, üçüncü grubu da 20 sağlam çocuk meydana getirdi. Tüm çocuklardan, serum çinko düzeyi ölçümü yapmak üzere kan alındı. Üç grubun serum çinko düzeyleri istatistiksel olarak karşılaştırıldı.

Bulgular: Febril konvulsiyon geçirmiş olan grubun serum çinko düzeyi ortalaması 110.49±35.03 µg/dL, ateşli çocukların ortalaması 107.12±21.66 µg/dL, sağlıklı çocukların ortalaması ise 116.12±32.07 µg/dL olarak bulundu. Üç grubun serum zinc düzeyleri arasında istatistiksel olarak anlamlı bir fark saptanmadı. İlk kez konvulsiyon geçirmiş ve iki veya daha fazla kez konvulziyon geçirmiş olan hastaların serum çinko düzeyleri arasında da anlamlı bir farklılık bulunmadı.

Sonuç: Çalışmamızda, febril konvulsiyon ile serum çinko düzeyi arasında bir ilişki gösterilmemiş olup, çinkonun febril konvulsiyon patogenezi ile olan ilişkisini saptayabilmek için daha fazla çalışmaya ihtiyaç olduğu düşünülmektedir. *(J Pediatr Inf 2012; 6: 90-3)*

Anahtar kelimeler: Febrile konvulsiyon, çinko

Introduction

The most frequent cause of childhood seizures, febrile convulsions, are generally of a benign nature; however, they remain a serious condition currently due to the recurrence rates seen in some cases and the slight risk they carry of developing into epileptic attacks. The etiology of febrile convulsions is still not clear. However, genetic factors, immunization conditions, neurotransmitter anomalies and hippocampal lesions have been stressed (1).

There has been a recent focus on the functions of trace elements in the central nervous system and these elements are thought to play a role in the production of some neurotransmitters in the brain. Being one of these essential elements, zinc is present in nucleic acids, gene regulating proteins and more than 200 metalloenzymes. At the same time, it plays a role in neurotransmission and the central nervous system membrane stabilization by being present in the vesicles in the presynaptic region (2, 3). Due to these reasons, it was thought that zinc deficiency may have a role in the pathogenesis of febrile convulsion.

This study aims to determine zinc levels in children who have febrile convulsions and thus help reveal possible associations between zinc deficiency and febrile convulsions.

Material and Methods

Febrile convulsions are the most common type of convulsion during childhood (3). The etiology of febrile convulsions is still not clear (1). Participants were 45 patients aged between 6-72 months who presented to the Pediatric Emergency Department of Okmeydanı Research and Training Hospital between August 2009-November 2009 due to one or more febrile convulsions of a generalized tonic-clonic type. At the same time, there was a control group of 23 patients in the same age range who presented to our hospital for fever but did not have a convulsion, and another control group of 20 healthy children. Children who had focal convulsions, received antiepileptic treatment, had a known chronic disease or eating problem or were using zinc preparation were excluded from the study.

All patients who presented to our emergency polyclinic for febrile convulsions received emergency intervention, followed by detailed history recording and physical and neurological examination. Patients were informed about the study; those who volunteered to participate signed informed consent forms; and approximately 3 cc venous blood was obtained in tubes rinsed with deionized water. Blood samples were centrifuged immediately for 10 minutes at 1500 rpm and blood serum was removed into an eppendorf tube to be stored at -80 °C.

Zinc detection from blood was carried out in a Perkin-Elmer A-Analyst 800 tool atomic absorption spectrophotomety after diluting the serum 5 fold in 1/1000 priton.x.100 solution.

Statistical analyses of the findings were performed in the NCSS (Number Cruncher Statistical System) 2007&PASS 2008 Statistical Software (Utah, USA) program. The analyses made use of descriptive methods (median, minimum,maximum, frequency values) as well as Kruskal-Wallis Test for the comparison of quantitative parameters across groups. For comparisons of parameters between two groups, Mann-Whitney U test was used. Qualitative data were compared by using the Yates's Continuity Correction test. A level of $p<0.05$ was considered statistically significant.

Results

A total of 88 children aged between 6-72 months were enrolled in the study. Of these, 40 (45.5%) were female and 48 (54.5%) were male. The median age of children was 22 (16-72) months. They were examined in three groups: "Convulsion patients" (n=45), "Febrile patients" (n=23) and "Healthy children" (n=20). Of the 45 convulsion patients, 19 (42.2%) were girls and 26 (57.8%) were boys; of the 23 febrile patients, 11 (47.8%) were girls and 12 (52.2%) were boys; and of the 20 healthy children, 10 (50%) were girls and 10 (50%) were boys (Table 1).

Among the children who had febrile convulsions, 62.2% were first-time febrile convulsion patients, 26.7% were second time patients, 6.7% were third time patients

Table 1. Demographic assessment of groups

	Convulsion Patients	Febrile Patients	Control Patients	p
	Median (min-max)	Median (min-max)	Median (min-max)	
+Age(month)	18 (8-72)	35 (6-72)	22.5 (9-70)	0.395
+Zinc Level(µg/dl) ++Gender	110.49 (55.90-211) n (%)	107.12 (78-156) n (%)	116.12 (57-189) n (%)	0.673
Girls	19 (%42.2)	11 (%47.8)	10 (%50.0)	0.815
Boys	26 (%57.8)	12 (%52.2)	10 (%50.0)	

Table 2. Assessment of age, zinc level and family history in the convulsion group with respect to the number of febrile convulsions

Convulsion Group	Number of Febrile Convulsions		P
	1st time (n=28)	2nd time or more (n=17)	
	Median (min-max)	Median (min-max)	
+Age (month)	16 (8-72)	24 (12-70)	0.078
+Zinc Level (µg/dL)	98.90 (55.90-211)	112 (57.9-156.8)	0.673
++Family History	n (%)	n (%)	
Yes	14 (50.0%)	6 (35.3%)	0.514
No	14 (50.0%)	11 (64.7%)	

and 4.4% were fourth time febrile convulsion patients. Among those who were having a febrile convulsion for the first time, 44.4% had a family history; and among those who were having a second or more febrile convulsion, 35.3% had a family history. The median age for a first convulsion was 16 (8-72) months and 64% of cases have their first febrile convulsion were between 12-24 months.

No statistically significant difference was found between the age of patients (p=0.395) and gender distributions of children in different groups (p=0.815). Median serum zinc level was 110.49 (55.90-211) µg/dL in the febrile convulsion group; 107.12 (78-156) µg/dL in the febrile group, and 116.12 (57-189) µg/dL in the healthy control group (p=0.673). The difference between these levels was not statistically significant (Figure 1).

No statistically significant difference was observed between the median age (p=0.078), zinc levels (p=0.673) and family history rates of children who had febrile convulsions for the first time and those who had 2 or more convulsions before (p=0.514) (Table 2). Similarly, no statistically significant relationship was found between the ages and zinc levels of all three groups.

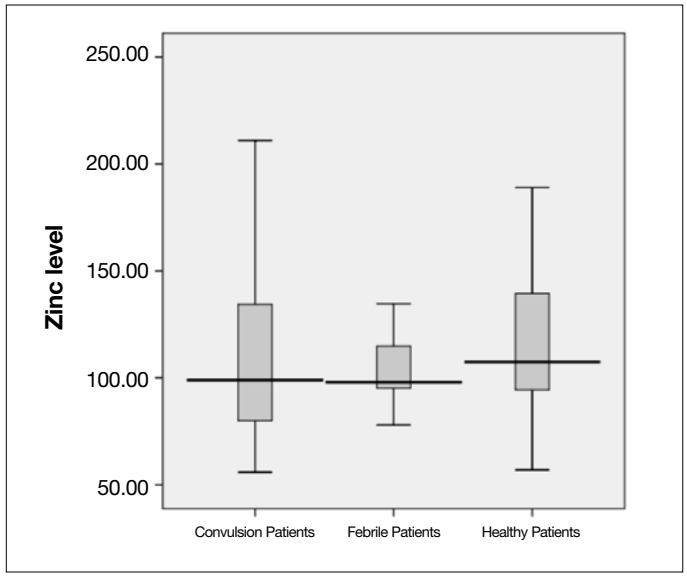

Figure 1. Zinc level distributions of groups

Discussion

Febrile convulsions are the most common type of convulsion during childhood. It is particularly common during early childhood when the convulsion threshold is low, a tendency for infections is higher and fever response is more intense. Previous studies have shown that first febrile convulsions most frequently occur between 12-24 months and peaks between 18-22 months (3-5). Similar to the literature, we also found that the median age for a first convulsion was 16 (8-72) months and 64% of cases have their first febrile convulsion between 12-24 months.

The etiology of febrile convulsions is still not understood clearly. Various factors such as the child's age, genetic predisposition, level of fever, cytokines, changes in the level of aminoacids and trace elements, central thermoregulation disorders, a delay in central nervous system maturation, and infections are mentioned in its etiopathogenesis. Today, there is a consensus that the most importance factor for febrile convulsion risk is genetic predisposition (6, 7). Esch et al. (8) studied 142 children with febrile convulsions prospectively and found a family history rate of 40%. In the same study, almost half of the patients with recurrent febrile convulsion were reported to have a prior family history (9). In our study, the family history rate of those who were having their first febrile convulsion was 44.4% while that of those who were having a second or more febrile convulsion was 35.3%. Even though family history rate was not higher among children who had more than 2 convulsions, it is noteworthy that both groups had rather high family history rates.

In recent years, the functions of trace elements in the central nervous system have been stressed, and these elements are thought to play a role in the production of some neurotransmitters of the brain. Zinc is one of the most important of these trace elements. It enters the structure of many metalloenzymes and acts as a neurotransmitter or neuroregulator in the central nervous system (9). Therefore, its association with febrile convul-

sions has been a widely studied topic recently. Serum zinc levels are generally known not to vary by gender (11, 12). In our study, we did not find a significant difference between the serum zinc levels of girls and boys.

In a study conducted in Iran, Ehsanipour et al. (13) compared the serum zinc levels of 34 febrile convulsion patients, 40 high fever patients who did not have convulsions, and 18 afebrile convulsion patients. In the febrile convulsion group, serum zinc levels were found to be significantly lower than the other two groups. Similarly, the serum zinc levels of the fever group were also significantly lower than the afebrile convulsion group. The study concluded that serum zinc levels fall during febrile diseases and the fall is most noticeable among patients who had had febrile convulsions. Likewise, Ganesh et al. (14) studied 38 children with febrile convulsions and 38 healthy children in India and found serum zinc levels of 32.17 µg/dL in the febrile convulsion group and 87.6 µg/dL in the control group. It was concluded from these findings, which were statistically significant, that Indian children with febrile convulsions had lower serum zinc levels and more studies were needed regarding zinc replacement in children in order to reduce the incidences of febrile convulsions.

On the other hand, Uluhan et al. (14) studied 25 pediatric febrile convulsion patients and 20 healthy children in Akdeniz University and found serum zinc levels of 86.76±4.04 µg/dL in the febrile convulsion group and 96±7.62 µg/dL in the control group, but did not find a significant difference between the two groups. The lower serum zinc levels in the febrile convulsion group was explained by the facts that zinc levels fall in cases of acute infection and stress, and that zinc is found in concentrated levels in recovering tissue. Also Çelik et al. (15) studied 25 pediatric febrile convulsion patients and 20 healthy children but did not find a significant difference between the two groups.

In this study, we found no significant difference between the serum zinc levels of our groups. Likewise, no relationship was detected between serum zinc levels and age, gender and the number of febrile convulsions. Previous studies on the association of serum zinc levels with febrile convulsions have also yielded inconclusive results. Therefore, studies with much larger sample sizes and detail are needed to reveal the relationship between zinc levels and febrile convulsions.

Conflict of Interest

No conflict of interest is declared by the authors.

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