



Relationship of Febrile Convulsion with Iron Deficiency Anemia and Zinc Deficiency

Febril Konvülsiyonlu Çocuklarda Demir Eksikliği Anemisi ve Çinko Eksikliği İlişkisi

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ABSTRACT

Objective: Febrile convulsion (FC) is the most common type of seizure in children. Its incidence is 2–5%. Iron and zinc, as a major element of some enzymes, play an important role in the central nervous system (CNS) and can affect some inhibitory mechanisms of CNS. The aim of this study is to evaluate the association of FC with iron deficiency anemia and zinc deficiency and the relationship of FC with its pathogenesis.

Methods: We prospectively evaluated the demographic and clinical characteristics of FC in 57 children aged 3–60 months who presented to the pediatric emergency department as the case group and 25 healthy children who presented to outpatient clinics as the control group in Şişli Hamidiye Etfal Training and Research Hospital, a tertiary state hospital in İstanbul, between January 2013 and July 2013. Anemia was defined as a hemoglobin (Hb) level of <11 g/dL. The serum zinc levels were determined by atomic absorption spectrophotometry.

Results: The male to female ratio was 1.71/1. The mean age at the first seizure was 21.6±11.8 months. The most common cause of FC was upper respiratory tract infection (84.2%). Twenty (35.1%) patients had a family history of FC and 8 (14%) had a family history of epilepsy. The most common seizure type was generalized tonic-clonic seizures (78.9%). There was no statistically significant difference between the case and control groups in the anemia ratio, Hb level, Htc, MCV, RDW, RBC count, platelet count, TIBC, and ferritin level. There were statistically significant lower rates of mean serum zinc levels and hypozincemia in the case group.

Conclusion: There was no statistically difference between FC and anemia. The serum zinc levels were found to be lower in patients with FC. The relationship between low zinc levels and convulsion is not understood whether it is a cause or result. It can emphasize the hypothesis that there is a relation between serum zinc levels and febrile convulsion in children. (*JAREM 2016; 6: 94-7*)

Keywords: Seizure, febrile, iron, zinc

ÖZ

Amaç: Febril konvülsiyon (FK) çocuklarda en sık görülen nöbet tipidir. FK görülme sıklığı %2-5'tir. Demir ve çinko, bazı enzimlerin yapısında bulunan büyük elementler olarak, santral sinir sisteminde (SSS) önemli göreve sahiptir ve SSS'de bazı baskılayıcı mekanizmaları etkileyebilir. Bu çalışmanın amacı FK'nın demir eksikliği anemisi ve çinko eksikliğiyle ilişkisini değerlendirmektir.

Yöntemler: Şişli Hamidiye Etfal Eğitim ve Araştırma Hastanesi'ne Ocak 2013-Temmuz 2013 arası başvuran; yaşları 3-60 ay arası olup çocuk acil polikliniğine FK ile başvuran 57 hastanın ve kontrol grubu olarak çocuk polikliniğine başvuran 25 sağlıklı çocuğun prospektif olarak demografik ve klinik özellikleri değerlendirildi. Anemi; hemoglobin (Hb) düzeyinin 11 g/dL'den düşük olması olarak tanımlandı. Serum çinko düzeyleri atomik absorpsiyon spektrofotometresi metoduyla ölçüldü.

Bulgular: Erkek/kız oranı 1,71/1 idi. Ortalama FK ilk yaşı 21,6±11,8 aydı. En sık FK odağı üst solunum yolu enfeksiyonuydu (%84,2). Hastaların 20'sinde (%35,1) FK geçiren aile öyküsü vardı ve 8 (%14) hastanın epilepsi için aile öyküsü vardı. Olgu ve kontrol grupları arasında anemi oranı, Hb, Htc, MCV, RDW, RBC, trombosit, TIBC ve ferritin düzeyleri açısından istatistiksel olarak anlamlı farklılık yoktu. Olgu grubunda kanda çinko düzeyi düşüklüğü ve ortalama serum çinko düzeyi istatistiksel olarak anlamlı derecede düşüktü.

Sonuç: Febril konvülsiyon ve anemi arasında istatistiksel olarak farklılık yoktu. FK'lı hastalarda serum çinko düzeyleri daha düşüktü. Düşük çinko düzeyi ve FK arasındaki ilişkinin neden mi sonuç mu olduğu anlaşılabilir. Bu sonuç; çocuklarda serum çinko düzeyi ve FK arasında ilişki olduğu hipotezini güçlendirmektedir. (*JAREM 2016; 6: 94-7*)

Anahtar Kelimeler: Konvülsiyon, febril, demir, çinko

INTRODUCTION

Febrile convulsion (FC) is the most common type of seizure in children (1). It occurs in children aged 6 months to 6 years (2). Its incidence is 2–5% or 4.8/1000 person-year (3).

FCs are mostly seen in males. The male to female ratio is 1.4:1 (4). FCs are seen 4 times more in patients with a family history of FC than in the general population (5). Although the pathogenesis

of FC remains unknown, the most important etiopathogenetic factors may be age, accompanying infection, fever, and genetics (6). Most FCs seen at 6 months to 3 years peak at 18 months (7, 8). The reason for frequent convulsions in this age group which has tendency to recurrent infections; hypersensitivity of maturing brain to increase in body temperature (9). FCs mostly seen during the course of high fever and convulsion may be the first sign in 25–50% of the patients (10). The most commonly defined

risk factor is family history in first degree family members. Cohort studies in patients with febrile convulsion; risk of siblings was determined as 10–45% (11). Cognitive dysfunction, psychomotor retardation, behavioral problems, pica, breath holding spells, restless leg syndrome, and thrombosis could be associated with iron deficiency. The effect of iron deficiency in a developing brain and mechanisms such as altered development of hippocampus neurons, impairment of energy metabolism, delayed maturation of myelin, slowed visual and auditory evoked potentials, and alterations in synaptic neurotransmitter systems including norepinephrine, dopamine, glutamate, gamma-aminobutyric acid (GABA), and serotonin may be responsible for these symptoms (12, 13). Zinc has a regulatory effect on glutamic acid decarboxylase and the synthesis of GABA (14).

Considering the conflicting pathogenesis of FC, we designed a study to investigate the relationship of FC with iron deficiency anemia and zinc deficiency.

METHODS

We prospectively evaluated the demographic and clinical characteristics of FC in 57 children aged 3–60 months who presented to the pediatric emergency department as the case group and 25 healthy children who presented to outpatient clinics as the control group in Şişli Hamidiye Etfal Training and Research Hospital between January 2013 and July 2013.

Febrile convulsion was defined as a seizure occurring in a child with a documented temperature of at least 37.8°C.

Febrile convulsion has been defined as a seizure associated with a febrile illness in the absence of central nervous system infection or acute electrolyte abnormalities in 6–60-month-old children without previous afebrile seizures. FCs are further classified as simple and complex. Complex FC is defined as a seizure lasting more than 15 min and recurring within 24 h or a focal seizure (15).

The exclusion criteria comprised receiving an iron or zinc combination within the past month, the presence of any chronic systemic diseases (cardiac, renal, metabolic, malignancy, and rheumatologic, etc.), and having neurodevelopmental delay, previous afebrile seizure, or acute central nervous system infection (meningitis or encephalitis).

A venous blood sample was obtained from all children in both groups. The hemoglobin (Hb) level, hematocrit (Htc), mean corpuscular volume (MCV), red blood cell distribution width (RDW), platelet count, mean platelet volume (MPV), serum iron level, total iron binding capacity (TIBC), biochemical tests, and ferritin, C-reactive protein (CRP) and zinc levels were measured.

Iron deficiency anemia is defined as an Hb level of <11 g/dL; MCV of <70 fl at 12–24 months, <73 fl at 24–48 months, and <76 fl at 2–12 years; and ferritin level of <10 µg/L. Serum iron levels of <30 µg/dL, total iron binding capacity of >350 µg/dL, transferrin saturation (a percentage calculated as serum iron concentration/TIBC×100) of less than 16%. Zinc deficiency was considered as serum zinc level of <70 µg/dL.

Informed consent was taken from the parents, and the study was approved by the ethics committee of Şişli Hamidiye Etfal Training and Research, İstanbul, Turkey.

Statistical Analysis

In the descriptive statistics of the data, mean, standard deviation, rate, and frequency are used. The distribution of variables was checked with the Kolmogorov–Smirnov test. For the analysis of qualitative data, the independent samples t-test and Mann-Whitney U test were used. For the analysis of quantitative data, the Chi-square test was used; in conditions where the Chi-square test cannot be used, Fischer's test was used. Statistical Package for the Social Sciences 21.0 (SPSS Inc.; IBM Company, Armonk, New York, USA) was used in the analysis.

Results at 95% confidence interval and p-values of <0.05 were considered to be significant.

RESULTS

We studied 57 children (36 males and 21 females) with FC and a control group of 25 healthy children (13 males and 12 females).

The mean age of patients in the case and control groups was 25.8±11.9 months and 24.8±14.2 months, respectively. The mean age at first seizure was 21.6±11.8 months. The most common cause of FC was upper respiratory tract infection (84.2%). Twenty (35.1%) patients had a family history of FC and 8 (14%) a family history of epilepsy. Simple FC was seen 91.2%, and generalized-type FC was seen 98.2% of the patients. The most common seizure type was generalized tonic-clonic seizures (78.9%). Recurrence was seen in 18 (31.6%) patients.

There was no statistically significant difference between the case and control groups in the anemia ratio, Hb level, Htc, MCV, RDW, RBC count, platelet count, TIBC, and ferritin level (Table 1). MPV, mean serum iron level, and iron level were lower in the case group. Additionally, the transferrin saturation index was lower in the case group.

There were statistically significant lower rates of mean serum zinc level and hypozincemia in the case group (p=0.009 and p=0.003, respectively) (Table 2).

Table 1. Comparison of some hematological parameters

	Case	Control	p
Hb level	11.7±1.2	11.7±1.1	0.899
MCV	76.0±5.7	77.9±3.7	0.121
Plt count	312070±111023	301280±82158	0.664
TIBC	380.4±73.5	388.3±41.8	0.618
Ferritin level	42.4±29.7	32.4±23.2	0.138

Hb: Hemoglobin; MCV: Mean corpuscular volume; Plt: Platelet; TIBC: Total iron binding capacity

Table 2. Comparison of zinc levels

		Case	Control	p
Zinc	Mean	75.2±20.0	87.4±16.6	0.009
	<70	26 45.6%	3 12.0%	0.003
	70–120	28 49.1%	21 84.0%	
	>120	3 5.3%	1 4.0%	

There were no difference between the groups with low and normal serum zinc levels in age, gender, FC type, recurrence ratio, and anemia.

DISCUSSION

Genetic factors play an important role in FC. However, genetic inheritance is not fully understood. Wallace (5) found a 17% FC history in first degree family members; in Ling's report (16), this number was 26.6%, while in Kolfen et al. (17) study, this was 16%. Moreover, in the Turkish population, consanguineous marriage ratio was 22% (18). In our study, we found that the FC history of first degree family members higher than literature (35.1%).

There was no statistically significant difference between the case and control groups in the anemia ratio, Hb level, Htc, MCV, RDW, RBC count, platelet count, TIBC, and ferritin levels.

Akbayram et al. (19) indicated that in Turkey, in children with FC, serum iron levels are lower than those in the healthy children group. Similar to this, we found a statistically significant difference ($p=0.03$) between the case and control groups at mean serum iron level and low serum iron ($Fe<30 \mu\text{g/dL}$) ratio.

Pisacane et al. (20) showed that in a case-control study in Italy for 6–24 months, 156 FC patients had a 30% anemia ratio, patients with fever but no convulsion had a 14% ratio, and healthy children had a 12% ratio. They described an association between iron deficiency anemia and FC. Fallah et al. (21) reported that in Iran, in a cross sectional case control study, iron deficiency anemia was found at a rate of 26% in first unprovoked afebrile seizure, at a rate of 22% in FC, and at a rate of 10% in healthy children. Although the anemia ratio in the case group that we found was consistent with that found in literature (26.3%), there was no statistically difference with that in the control group.

Serum zinc levels are known not to change depending on gender (22). We showed no gender difference between patients with normal and low zinc levels.

Çelik et al. (23) reported that there was no significant difference between serum zinc level in 25 children with FC and healthy 25 children as the control group. Kafadar et al. (24) found that there was no significant difference between the FC and control group. Uluhan et al. (25) reported 25 FC patients had a mean serum zinc level of $86.76\pm 4.04 \mu\text{g/dL}$ and that 20 healthy children, as the control group, had a mean serum zinc level of $96\pm 7.62 \mu\text{g/dL}$. There was no statistically significant difference. In one report by Cho et al. (26) from Korea in Pusan Hospital, there was no significant difference between the serum zinc level in children with FC and the control group. This difference with our result may be due to their small sample size (the study was performed on 11 patients in each group).

On the other hand, Ehsanipour et al. (14) reported a comparison of serum zinc levels and found that 34 patients had FC, 40 had fever, and 18 had afebrile convulsion. In the case group, zinc levels were found to be significantly lower than those in other groups. Further, in other studies, mean serum zinc levels were found to be lower in patients with FC (27, 28). Salehiomran and Mahzari (29) reported that the mean serum zinc level was $0.585\pm 0.166 \text{ mg/L}$ and $0.704\pm 0.179 \text{ mg/L}$ in the case and control groups, re-

spectively. The mean serum zinc level was significantly lower in the FC group than in the control group. Our study showed that the mean serum zinc level was $75.2\pm 20.0 \mu\text{g/dL}$ in the case group and $87.4\pm 16.6 \mu\text{g/dL}$ in the control group. Low serum zinc level ratio was 45.6% in the case group and 12% in the control group. The mean serum zinc level and low serum zinc level ratio were significantly lower in the case group than in the control group.

CONCLUSION

Although anemia criteria were lower in the case group, there was no statistically difference between FC and anemia. Serum zinc levels were found to be lower in patients with FC. The relationship between low zinc levels and FC is not understood whether it is a cause or result. To find the truth about relationship of FC with anemia and zinc levels, more sophisticated investigations are needed.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Şişli Hamidiye Etfal Training and Research.

Informed Consent: Written informed consent was obtained from the parents of the patients who participated in this study.

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Hasta Onamı: Yazılı hasta onamı bu çalışmaya katılan hastaların ailelerinden alınmıştır.

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