Original Article / Orijinal Makale

Viral Enfeksiyonu ve Basit Febril Konvülziyonu Olan Çocuklarda Serum Selenyum ve Bakır Düzeyleri

Serum Selenium and Copper Levels in Children with Simple Febrile Seizure and Viral Infections

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ÖZET

Amaç: Sağlıklı bir sinir sistemi için eser elementler son derece önemlidir. Eser elementlerin düzeyi viral enfeksiyonlar ve ateşli nöbetler sırasında değişiklik gösterir. Bu çalışmanın amacı febril nöbet ve viral enfeksiyonu olan çocukların serum selenyum ve bakır düzeylerini belirlemektir.

Gereç yöntem: Basit febril konvülziyon geçiren ve viral enfeksiyonu saptanan 40 çocuk çalışmaya alındı. Kontrol grubu olarak ise ateşi ve viral enfeksiyonu olup nöbet geçirmeyen 40 çocuk seçildi. Her iki gruptan alınan serum örnekleri ölçüldü ve karşılaştırıldı.

Bulgular: Basit febril konvülziyon grubunda serum selenyum düzeyleri istatistiksel anlamlı olarak düşük bulundu(p=0.043). Selenyum ve bakır düzeyleri ile yaş, cinsiyet, vücut kitle indeksi, nöbet süresi ve ateş yüksekliği arasında ilişki saptanmadı.

Sonuç: Basit febril konvülziyon geçiren çocuklarda selenyum düzeyinin düşük olması oksidatif hasar ve antioksidan savunma mekanizmalarının aktifleşmesine bağlı olabilir. Selenyum düzeyindeki anlamlı düşüklük febril nöbetleri başlatabileceği gibi nöbetin tekrarlamasına da neden olabilir. Basit ve tekrarlayan febril nöbetlerde selenyum düzeyini araştıran çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Febril konvülziyon, selenyum, bakır, çocuk

ABSTRACT

Purpose: Trace elements are essential for a healthy nervous system. Their levels are shown to be affected in both viral infections and febrile seizures. The aim of this study is to evaluate the serum selenium and copper levels in children with febrile seizures and viral infection.

Method: This study consisted of 40 patients with simple febrile seizures and viral infection (study group) and 40 patients with fever and viral infection (control group). Serum samples were collected for selenium and copper from the study group within one hour following seizure. The serum samples were measured and compared.

Results: Serum selenium levels were significantly lower in the simple febrile seizure group (p=0.043). There was no significant relation between selenium and copper levels with age, sex, body mass index, degree of fever or duration of febrile seizure.

Conclusion: Significantly decreased levels of selenium in children with simple febrile seizures may be the result of oxidative damage and the activation of antioxidant defense mechanisms. The lower serum levels of selenium in patients with SFS may trigger FS or may contribute to its recurrence. Further studies are required to assess selenium levels comparing simple and recurrent febrile seizures.

Keywords: Febrile seizure, selenium, copper, children

Introduction

Febrile seizures (FS) are the most common type of childhood seizure disorder with a prevalence of approximately 3-4%, depending on the study population. (1) Based on the seizure type FS are divided into simple and complex. Simple febrile seizures (SFS) are single and generalized seizures with a duration lasting less than 15 minute. Complex febrile seizures are either focal or prolonged (>15 min), or multiple seizures occur within 24 hours. Although the prognosis of FS is generally good, the long-term effects of FS on brain development have not yet been clearly identified (2-4).

Trace elements are essential for a healthy nervous system because they play important roles in many pathways of central nervous system via specific enzymes including oxidative system. Gluthation peroxidase which is involved in antioxidative defense mechanisms is a selenium (Se) dependent enzyme, whereas, copper (Cu) takes place in the structure of superoxide dismutase, which is also an important antioxidant enzyme. The increased production of free radicals due to oxidative stress or the decreased functioning of antioxidative defense mechanisms may lead to seizures (5). Selenium and Cu play role in preventing oxidative injury, therefore they may also have an effect on preventing seizures (6). The significantly decreased levels of Se in children with SFS have been shown in previous studies (7-9). However, serum Se level is also reported to be low during viral infections (10-12). Conversely, in Se deficiency, benign strains of viruses can mutate to highly pathogenic strains. In addition, some human and animal studies suggest that Se intake can affect the progression of viral infections and that Se status can be associated with viral response (13,14)

Fever and infections are known precipitating factors of seizures. Most of the children experience fever during viral infections but it is not known why FS develops only in some of them. There are few studies on the evaluation of serum Se and Cu in children with SFS and the results are controversial (7-9,15). Also, these studies involve patients with unclassified infection. We suggest that this represents a confounding factor in these studies. Thus, our study represents the first study that was conducted on a group of patients with confirmed viral infection and FS. While designing this study, we aimed to determine whether there is a direct relationship between serum Se and Cu levels and SFS in children with viral infection.

Material and Methods

The present study included forty children with viral infection and SFS and forty age- and sex-matched control subjects with viral infection who were admitted to the pediatric emergency department of Keçiören Education and Research Hospital. Children were defined as FS patients if seizures occurred during fever with an axillary temperature of 38ºC or higher. Simple febrile seizure was defined as a single seizure which is generalized and lasts less than 15 minutes. All the patients were admitted to our emergency room within 30 min after the initiation of febrile seizure. Inclusion criteria for the control group were fever without a history of seizure, admission to hospital because of fever and other flu like symptoms (runny or stuffy nose, fatigue, cough, sneeze) and finally diagnosis with viral infection and not using antibiotics. The diagnosis of viral infection was made by history, clinical or laboratory findings, serologic analysis for viruses in serum and lymphocyte concentration in peripheral blood smear. The exclusion criteria for SFS group included children who had evidence of electrolyte imbalance, metabolic diseases, developmental retardation, malnutrition and/or chronic disease, history of hypoxia, seizures and head trauma. Meningitis was excluded by clinical or laboratory findings, including lumbar puncture. Lumbar puncture was performed in 8 out of 40 patients and all them were under 2 years of age.

Serum samples were obtained within 1 hour following the seizures in the SFS group. Immediately after centrifugation the supernatant was frozen and stored at -80ºC until it was analyzed. Serum levels of Se and Cu were measured using electrochemiluminescence immunoassay (Hitachi Elecsys 2010 analyser system, Roche Diagnostics Ltd, Manheim, Germany). The normal range of serum Se level is 36-125 µg/dl. Routine blood tests in the emergency department (Complete blood count, electrolytes, kidney and liver function) were recorded for each patient. The body mass index (BMI) was calculated for all children as the weight in kilograms divided by the height in meters squared.

The study design was approved by the ethics committee of our hospital (IRB no: 2014/512) Before enrollment, written informed consent was obtained from the primary caretaker of each patient.

Statistical analysis was performed using SPSS 17.0 for Windows (SPSS Inc., Chicago, IL, USA). Chi-square test was used for data analysis of qualitative variables and mean values were compared using independent t-test. Logistic regression analysis was performed to find independent predictors of patients with SFS. Receiver operating curve (ROC) analysis was performed to cutoff value of the Se and Cu levels. A value of $p < 0.05$ was considered significant.

Results

Forty patients with SFS (26 boys and 14 girls) and 40 control patients (28 boys and 12 girls) were enrolled in this study. The mean age of the SFS and control groups were 21.5 ± 12.5 months and 21.6 ± 13.4 months, respectively. There was no significant difference between the SFS and control groups for age, BMI or body temperature (Table 1). Electrolytes, kidney and liver functions of all patients in both groups were normal.

Levels of serum Se in the SFS group and control group were 13- 97 mg/dL and 20-92 mg/dl, respectively. A total of 3 patients in the SFS group and 7 patient in the control group had hyposelenium levels (<36 µgr/dl). Serum Se levels were significantly lower in the SFS group when compared to the control group (p=0.043), but we could not identify a cut-off point for selenium levels. There was no significant difference in the value of Cu between two groups (p=0.115). There was no significant relation between Se and Cu levels with age, sex, BMI and degree of fever. Table 1 shows serum Se and Cu levels in both groups. When the children in the SFS group were divided into two groups according to the duration of FS (seizure duration ≤5 minutes versus seizure duration >5 minutes) the serum Se and Cu concentrations between the 2 SFS and control groups were similar ($p > 0.05$)

Discussion

Causation of FS is believed to be multifactorial with both environmental and genetic factors (16). Oxidative stress and the decreased functioning of antioxidative defense mechanisms are
suggested to be involved in seizure disorders (17, 18). Selenium and Cu play role in preventing oxidative injury so they may also prevent seizures (6, 19, 20) The correlation between Se deficiency and epilepsy has also been shown in several studies (21,22). Only a few studies have evaluated Se in children with FS (7-9,15). Khoshdel et al. reported that serum Se levels of children with SFS were not lower than that of febrile children without seizure (15). In contrast, significantly decreased levels of Se in children with SFS were reported in three previous researches (7-9) Mahyar et al. found hyposelenemia (level <46 µg/dl) in 60% of SFS children (9). We found hyposelenemia (level<36 µg/dl) in 7.5% of SFS children and 17.5% of control group in our study. Abuhandan et al reported that decreased Se levels were independent predictors for simple febrile convulsions, and the Se levels below 49.05 mg/ml showed 73.3% sensitivity and 66.7% specificity for the risk of developing SFS (8). We could not find any cut off level for Se

related with SFS. Amiri et al also reported low serum Se levels in children with SFS and they showed that there was no significant relation between Se levels with age, sex, and degree of fever (7). Our results were similar with this study.

Viral infections appear to be related to increased oxidative stress in the host. Therefore, Se is a key nutrient for prevention of development of virulence. Selenium deficiency has been more reported during several infectious conditions, like different types of influenza virus (23-26). Some human and animal studies suggest that Se intake can affect the progression of viral infections and that Se status can be associated with virologic response (13,14). In the present study, we found lower serum Se levels in patients with SFS compared to the control group. This result reveals that viral infection itself does not have an additional effect on Se levels in children with SFS and viral infection.

Copper can act on various types of ion channels, including N-methyl-D-aspartate receptors and voltage-gated calcium channels (27,28) which, as noted earlier, are important contributors to neuronal excitability and synaptic communication. However, a meta-analysis demonstrates that Cu deficiency does not play an important role in the pathogenesis of epilepsy (29). There is only one study about serum Cu levels and SFS in children. In this study Amiri et al showed that there was no significant difference in the value of copper between SFS and control group (7). Our result was in accordance with this study.

There are some limitations in our study. Firstly, we didn't investigate dietary habits or socioeconomic status for Se in children. However, Hıncal et al did not find any relation between Se levels and the dietary habits or socioeconomic status (30). Secondly, we didn't measure serum Se levels of SFS patients during the recovery period. Knoshdel et al reported that, serum Se levels significantly increased after three months in seizure and control groups (15). Therefore, serum Se levels in the recovery period would upgrade this study. Thirdly, we didn't include patients with complex FS or febrile status. However, we found similar Se and Cu levels in children who had seizures ≤5 minutes and > 5 minutes, and these results suggest that the seizure duration does not affect the serum Se and Cu levels in SFS.

This is the first study to evaluate trace element levels in children with SFS and confirmed viral infection, and it showed that the serum Se levels in patients with SFS were significantly lower but the serum Cu levels were not different from the children with fever and viral infection of the same age. In addition, there was no difference between the levels of trace elements in patients who had seizures ≤5 minutes and those > 5 minutes.

In conclusion, the present results show that SFS is associated with reduced serum Se concentrations. Selenium has been studied in childhood epilepsy and particularly in resistant epilepsy and low levels have been found compared to those of normal children (22) and improvement in the clinical state and electroencephalogram with oral Se substitution has been reported. (31,32). Although selenium levels were in normal range in both groups, significantly decreased levels of Se in children with SFS may be the result of oxidative damage and the activation of antioxidant defense mechanisms. The lower serum levels of selenium in patients with SFS may trigger FS or may contribute to its recurrence. Further studies are required to assess Se levels comparing simple and recurrent febrile seizures.

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