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Relationship between serum selenium level and febrile seizure in children

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ABSTRACT

Febrile seizures are the most common type of convulsion in children. Frequent studies have been conducted on the relation between febrile seizures and micronutrient deficiency. Recent studies have shown that selenium deficiency plays a major role in catching epilepsy. The current study was conducted to determine the relationship between serum selenium level and simple febrile seizure. In this cross-sectional descriptive study, children aged 9 months to 5 years suffering from febrile seizure entered the study, who had been hospitalized in Shahid Madani Hospital of Khorramabad in the first half of 2014. Sampling technique was accessible method based on children's inclusion criteria. Among children aged between 9 months and 5 years, 38 subjects diagnosed with simple febrile seizures, 38 children with fever and no seizures, and 38 children aged between 9 month to 5 years, without febrile seizures were selected through accessible sampling method. They were similar to children with febrile seizure in terms of age and gender. Serum selenium level was measured using atomic absorption spectrophotometer. Data related to anthropometric indices, age, gender and location of children were collected using three questionnaires. To compare serum selenium level among these three groups, one-way analysis of variance (ANOVA) or its non-parametric alternative (Kruskal-Wallis test) was used. To measure the relation between demographic variables and serum selenium level, chi-square tests were employed (by converting serum selenium level to dual-mode quality variable). Average selenium level was 76.41±22.31, 78.85±19.2 and 87.28±16.3 in children with febrile seizures, fever with no seizure group and no febrile seizure group, respectively and it showed a significant difference according to ANOVA (pv=0.048). In post hoc analysis, the difference was observed between children with febrile seizures and no febrile seizures' group along with children with fever and no seizures and no febrile seizures' group. In post hoc analysis, the difference between serum selenium levels was not statistically significant between two groups of children with febrile seizures and those with fever and no seizure. In the present study, a decrease of serum selenium level was observed in children with febrile seizures along with children with fever. However, more future studies are recommended.

Keywords: Febrile, Seizure, Serum Selenium, Children.

INTRODUCTION

Febrile seizures are the most common type of convulsion in children. Febrile seizure is that type of convulsion occurring in children aged between 6 and 60 months, who experience boy temperature of 38^{o}C or more in the absence of central nervous system infection or electrolyte disorder without history of previous seizures(1). In simple febrile seizures, convulsion is usually a generalized tonic-clonic seizure, lasts less than 15 minutes and occurs once in a 24-hour period. This type of seizure is observed in children who are neurological normal. If focal symptoms are present, seizures last over 15min, convulsion is repeated during a fever course and the child suffers from

evolutionary disorder, this febrile seizure is known as aseptic or complex (2-4). Prevalence of febrile seizures is 2 to 5% (5-7). This disorder is the most common neurologic disorder in children that accounts for a large part of hospitalization (8 and 9).

Pathogenesis of febrile seizures is not fully recognized yet. Although genetic influences in a child having a febrile seizure are important in terms of the possibility to experience seizures, fever could cause seizures in itself. Normally, febrile seizures occur following febrile infections including human herpes virus 6 (HHV-6), upper respiratory infections and gastrointestinal infections (10-12). Immunologic reactions could be effective as well (13). In previous studies, frequent investigations have been conducted about the relationship between febrile seizure and iron, serum ferritin, zinc and magnesium deficiency (14-21). One of the causes of epilepsy is oxidative stress and generation of reactive oxygen and nitrogen species (21). The brain is highly susceptible to oxidative damage because of generating a high volume of reactive oxygen resulted from high aerobic metabolism. As an antioxidant and cell protective agent, selenium is required for normal brain evolution and its function. The main role of glutathione peroxidase as a selenium-dependent enzyme is reducing organic peroxides and oxygen (22-25).

A high volume of selenium is present in brain, especially in gray matter. Selenium level of the body is related to age, gender, dietary intake and soil selenium volume. Different selenium level in various regions results from different factors including selenium content of the soil in that area, dietary habits and geographical differences in selenium intake (26 and 27). Recent studies have shown that selenium plays a major role in catching epilepsy (28-30). Few studies have reported the possible role of selenium in febrile seizure pathogenesis (31-33).The present study was conducted to determine the relationship between serum selenium level and simple febrile seizure.

EXPERIMENTAL SECTION

In this case-control study, statistical society consisted of all children aged between 9 months and 5 years suffering from febrile seizure referring to Shahid Madani Hospital of Khorramabad in the first half of 2014. This study was approved by Ethics Committee of Research, Lorestan University of Medical Sciences of Lorestan. Sampling was accessible based on children's inclusion criteria. These criteria include absence of idiopathic epilepsy or secondary epilepsy to other diseases including central nervous system infections and absence of secondary epilepsy due to electrolytes disorders. Children with metabolic diseases, blood disorders, chronic diseases, neonatal history of asphyxia and seizure with no fever and neurological complications, excluded the study along with those diagnosed with degenerative diseases of the central nervous system. Sample volume was calculated using the following formula.

$$n = \frac{2\left[z\left(1-\frac{\alpha}{2}\right)+z(1-\beta)\right]^2 \times SD^2}{(\mu_1-\mu_2)^2}$$=38 per group

SD=6.92$z\left(1-\frac{\alpha}{2}\right)=1.96$

$z(1-\beta)=0.84$

$\mu_1-\mu_2=4.7$

In this study, among children aged 9 months to 5 years, 38 children with febrile seizure, 38 with fever and no seizures, who were hospitalized, were selected. Control group were 38 children aged 9 months to 5 years no fever and seizure who were similar to patients with febrile seizure and were selected through accessible sampling method. Weight, height, head circumference and (axillary) temperature were measured according to standard method.

Blood drawn from hospitalized patients in groups 1 and 2 for diagnostic tests was used to determine serum selenium level, and 6ml blood was drawn from control group in the case of their parents' consent. Samples were centrifuged and serum was poured in acid-washed tubes and saved in the fridge in -70^{o}C.

Serum selenium level was measured using atomic frame spectrophotometer. Normal range of serum selenium level is 46-143 mg/Dl.

Tools employed in this study were a questionnaire including information related to indices of children's anthropometric data, age, gender and location of children in three groups. Descriptive statistics were employed to describe personal characteristics and indices of children's anthropometric data and to compare serum selenium level among these three groups, ANOVA or its non-parametric alternative (Kruskal-Wallis test) were employed.

In addition, to measure the relation between demographic variables and serum selenium level, chi-square tests were employed (by converting serum selenium level into dual-mode quality variable).

RESULTS AND DISCUSSION

In this case-control study, 110 children were investigated. Among them, 38 children suffered from febrile seizures, 36 subjects with fever and no seizures and 36 children with no febrile seizures. Average age of children with febrile seizures was 1.87 years old, children with fever and no seizures 2.36 years old and no fever group 2.1 years old (Table 1). According to ANOVA, difference between average age of three groups was not statistically significant (pv=0.21).

Table 1: Comparison of average age of children in study groups

Study groups	Mean ± standard deviation	F value	p-value
Febrile seizures	1.78±1.11	1.55	0.21
Fever and no seizures	2.36±1/62		
No febrile seizures	2.1±0.64		

Statistical test: ANOVA

According to Table 2, the difference between children's frequency distribution of gender in three study groups was not statistically significant (pv=0.96).

Table 2: Comparison of gender frequency distribution of children in study groups

Study groups	Gender			p-value
	Girls Number (%)	Boys Number (%)	Total Number (%)	
Children with febrile seizures	19 (50)	19 (50)	38 (100)	0.96
Children with fever and no seizures	19 (52.8)	17 (47.2)	36 (100)	
Children with no febrile seizures	18 (50)	18 (50)	36 (100)	

Statistical test: chi-square

Mean duration of fever in children with febrile seizure and children with fever and no seizures was 2.3±1.5 and 2.8±1.7 days respectively, and this difference between fever duration in two groups was not statistically significant according to independent t-test (pv=0.16).

In Table 3, the averages of anthropometric values under study are compared. Based on the results of this table, average weight of children with febrile seizure was 11.2kg, children with fever and no seizures, 12.58kg and average weight of control group was 11.83kg. This difference between average weight of children in three study groups was not statistically significant according to the results of ANOVA test (pv=0.2).

In addition, average height of children with febrile seizure, children with fever and no seizure and the control group was 83.38cm, 86.41cm and 85.05cm respectively and this difference was not statistically significant (pv=0.44). Difference between average head circumference of children in three study groups were not statistically significant as well (pv=0.22).

Table 3: Comparison of average anthropometric indices of children in study groups

Study groups	Weight Average ± standard deviation	p-value	Height Average ± standard deviation	p-value	Head circumference Average ± standard deviation	p-value
Febrile seizures	11.2±2.58	0.2	83.38±9.05	0.44	48.5±2.78	0.22
Fever and no seizures	12.58±4.81		86.41±13.96		49.08±3.58	
No febrile seizures	11.83±1.3		85.05±5.81		49.61±1.53	

Statistical test: ANOVA test

In Table 4, values of serum selenium of children in three study groups are compared. As the results of this table show, average serum selenium values in children with febrile seizures, in children with fever and no seizures and in control group were 76.41μg/l, 78.85μg/l and 87.28μg/l respectively. According to ANOVA test, this difference was statistically significant (pv=0.048). In post hoc analysis, there was a difference between children with febrile seizures and the control group along with children with fever and no seizures and the control group. In post hoc analysis, the difference between serum selenium levels was not significant in two groups of children with febrile seizures and children with fever and no seizures (Table 4).

In Table 5, correlation between serum selenium levels and body mass index (BMI) of children was investigated in each study group. As the results of this table show, no significant linear relationship was observed between values of serum selenium and age in children with febrile seizures (pv=0.99 and r=0.001) and children with no febrile seizures (pv=0.26 and r=-0.19). However, there was a direct significant linear relationship between age and serum selenium

level in children with fever and no seizures, in such a way that as age increased, serum selenium level increased significantly and this difference was statistically significant according to Pearson correlation test (pv=0.041 and r=0.34). No significant linear relationship or correlation was observed between BMI and selenium level in 3 study groups (Table 5).

Table 4: Comparison of average serum selenium values in study groups

Study groups	Serum selenium values Mean ± standard deviation	F value	p-value
Febrile seizures	76.41±22.31	3.13	0.048
Fever and no seizures	78.85±19.2		
No febrile seizures	87.28±16.3		

Statistical test: ANOVA test

Table 5: Correlation matrix of measuring the relationship of serum selenium level with age and BMI in study groups

Study groups	Variable	Age	BMI
Children with febrile seizures	Serum selenium values	pv=0.99, r=0.001	pv=0.64, r=0.078
Children with fever and no seizures	Serum selenium values	pv=0.041, r=0.34	pv=0.47, r=0.12
Children with no febrile seizures	Serum selenium values	pv=0.26, r=-0.19	pv=0.76, r=0.052

Statistical test: Pearson correlation coefficient

In Table 6, mean values of serum selenium level in children are compared in study groups in terms of gender.

Table 6: mean values of serum selenium in study groups in terms of gender statistical test: t-test

Study groups	Gender	Serum selenium values Mean ± standard deviation	t value	p-value
Children with febrile seizures	Girl Boy	75.23±23.34 77.6±21.8	0.32	0.74
Children with fever and no seizures	Girl Boy	84.3±19.79 72.77±17.07	-1.87	0.069
Children with no febrile seizures	Girl Boy	85.17±1.91 89.47±14.72	0.8	0.42

Statistical test: t-test

In female children with febrile seizures, serum selenium was 75.23μg/l and in male children it was 77.6μg/l and this difference was not statistically significant according to t-test (pv=0.74). In children with fever and no seizures, mean values of serum selenium were 84.3μg/l and 72.77μg/l in girls and boys respectively and this difference was not statistically significant (pv=0.069). In control group no difference was observed in serum selenium level among male and female children (pv=0.42).

According to t-test, no significant difference was observed in terms of serum selenium level in children with febrile seizures living in urban (76.62) and rural areas (76.62) (pv=0.74).

However, there was a significant difference between children with fever and no seizures living in urban (81.26) and rural areas (68.87) (pv=0.047) (Table 7).

Table 7- average serum selenium level in study groups in terms of location

Study groups	Gender	Serum selenium values Mean ± standard deviation	t value	p-value
Children with febrile seizures	Urban areas Rural areas	76.82±23.27 74.11±22.49	0.32	0.74
Children with fever and no seizures	Urban areas Rural areas	84.26±18.94 68.87±18.23	1.6	0.047

Statistical test: t-test

The current study was conducted to investigate the relationship between serum selenium level and febrile seizure in three groups of, 1) children with febrile seizures; 2) children with fever and no seizures; and 3) healthy children.

Results of this study showed that there is a significant relationship between serum selenium level among children with febrile seizures compared to no fever and seizures group. However, serum selenium level in children with febrile seizures and fever group was not statistically significant.

Febrile seizure is a type of convulsion occurring along with fever in children aged between 6 and 60 months with no disease in central nervous system or no electrolyte disorder (34). Although pathogenesis of febrile seizures is not

fully recognized yet, it is possible for it to accompany the increase in excitatory amino acids including glutamate and decrease in inhibitory amino acids including gamma-aminobutyric acid (35).

The brain is highly susceptible to oxidative damage and oxidative stress increases in seizures, stroke and neurodegenerative diseases.

Abuhandan et al, measured blood level of oxidant and antioxidants in 30 children with febrile seizures compared to control group and concluded that oxidants increase and antioxidants decrease. The increase in oxidative stress in patients may increase danger of febrile seizures (37). Results of their study are similar to the study conducted by Akarsu in 2007 and Günes in 2009 (38 and 39).

To decrease the harmful effects of oxidants including free radicals, there are defense mechanisms in the body including glutathione reductase, glutathione peroxidase, superoxide dismutase and catalase. Rare elements including copper, zinc and selenium are necessary for antioxidant enzymes' function (40).

In 2004, Mahyar et al. measured serum selenium level in 30 children with simple febrile seizure compared to 30 children with fever and no seizures (control group). They concluded that serum selenium level in children with simple febrile seizure was significantly lower compared to control group (41). In a study conducted by Amiri et al., serum selenium level in patients with febrile seizure was significantly lower compared to patients with fever (42).

In a study conducted by Khoshdel et al. in 2011, serum selenium level was measured in 25 children with simple febrile seizure compared to 25 children with fever and no seizures in acute phase and after 3 months. Results showed that in acute phase, no significant difference was observed between mean serum selenium level in simple febrile seizures' group and children with fever and no seizure (43). In 2012, Abuhandan et al. compared serum selenium level of 42 patients with simple febrile seizure and healthy children and concluded that mean serum selenium level in patients with febrile seizure was significantly lower compared to healthy children (44).

In Mahyar and Khoshdel study, children with febrile seizure were compared to children with fever. However, in Abuhandan study, they were compared with healthy children. In our study, three groups of children with febrile seizures, children with fever and healthy subjects were compared and a significant difference was observed between serum selenium level among children with febrile seizures compared to no fever and seizure group that is identical toAbuhandanstudy (44). In 2015 Ahmadipour and Mohsenzadeh et al compared the serum selenium level in asthmatic and healthy children in khorramabad city and found that there was no significant difference between two groups(45).

In this study, the difference between serum selenium levels was not statistically significant between two groups of children with febrile seizure compared to children with fever and no seizure that conforms to the study by Khoshdel et al. (43). However, it does not conform to the study by Mahyar et al. (41).

In our study, selenium level decreased in both groups with fever. It seems that selenium affects inflammatory response and immune system of the body intensively (46).

Studies show that selenium level is low in infections because of taking it as an anti-oxidant (47). In several cases of viral infections, there is the stimulation of selenoprotein production and as a result decrease of serum selenium level (48). In general, it could be stated that selenium level decreases in infections because of using selenium as an antioxidant to remove free radicals.

CONCLUSION

A decrease of serum selenium level was observed in children with febrile seizure along with children with fever it could be stated that selenium level decreases in infections because of using selenium as an antioxidant to remove free radicals. However, more future studies are recommended.

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