Abstract
Objective
To evaluate the serum zinc level of the patients with simple febrile seizure and compare them with febrile children without seizure.

Materials & Methods
This prospective case-control study was performed on 60 patients aged 6 months to 6 years from Apr. 2009 to Jan. 2010 in Ghaem, Imam Reza and Dr. Sheikh Hospitals in Mashhad. The serum zinc level was assessed and compared between the cases (30 individuals who suffered from simple febrile seizure) and the controls (30 individuals who had fever without seizure).

Results
Mean serum zinc level was 663.7 μg/l and 758.33 μg/l in the case group and the control group, respectively (P<0.001).

Conclusion
It was revealed that the serum level of zinc was significantly lower in children with simple febrile seizure in comparison with febrile children without seizure.

Keywords: Simple febrile seizure, children, zinc, CSF (cerebrospinal fluid)

Introduction
Febrile seizure is a common neurologic disorder (1). It occurs in children aged 5 or 6 months to 6 years of age (2, 3). The etiology of febrile seizure is unknown but genetic factors or electrolyte disturbances may have a role in its occurrence or recurrence (4, 5). To date, it is revealed that febrile seizure can be induced by several factors (6). Gamma-aminobutyric acid (GABA) is an important inhibitory neurotransmitter. Zinc has a regulatory effect on glutamic acid decarboxylase and the synthesis of GABA (2,4).

Ehsanipour et al. performed a study in Rasoul-e- Akram Hospital between January 2003 and January 2005 and stated that patients with febrile seizure had a lower serum zinc level compared to the other two groups consisting of the patients with fever without seizure and those with afebrile seizure (4).

In another study by Ganesh et al which was carried out in a major children hospital between June 2005 and May 2006 on 3-month to 5-year-old patients, it was revealed that serum zinc level was significantly lower in patients with simple febrile convulsion compared to the control group (7).
On the other hand, according to another report by Garty et al on 66 patients at Schneider Children Hospital, there was no difference in CSF zinc level between patients with febrile seizure and the control group (8). Therefore, with regard to the importance of febrile seizure and its possible contributing factors including serum zinc level, this study was designed.

**Materials & Methods**

This prospective case-control study was performed on 60 patients aged 6 months to 6 years between Apr. 2009 and Jan. 2010 in Ghaem, Imam Reza and Dr. Sheikh Hospitals in Mashhad. Serum zinc level was evaluated in 30 patients (case group) with simple febrile seizure and 30 patients (control group) who had fever without seizure. During the first 6 hours from admission, 3 cc blood was taken from patients and serum was separated and stored in -20 °C. Then, samples were evaluated using atomic absorption spectrophotometry method.

Inclusion criteria were as follows:
- Being 6 months to 6 years of age,
- Having simple febrile seizure with the seizure attack lasting less than 15 minutes,
- Having one seizure attack during illness
- Having a generalized seizure attack,
- Having normal growth and development

Exclusion criteria were as the following:
- Being younger than 6 months or older than 6 years,
- Having a history of previous seizure attack(s) or recent zinc intake,
- Having afebrile convulsion,
- Failure to thrive,
- Acute meningitis.

Data was analyzed by SPSS version 11.5. Chi-square test, t-test and Mann Whitney test were used. A p-value ≤0.05 was considered significant.

This study was approved by the Ethic Committee of Mashhad University of Medical Sciences.

**Results**

Demographic data is shown in table 1.

The mean age of the cases and the controls showed no significant difference (P=0.961). Forty percent of the cases and 43.3% of the controls were female.

Mean body temperature was 38.92˚C (SD 0.41) in the case group and 39.23˚C (SD 0.64) in the control group (P-value: 0.29).

Mean number of days of fever before admission in the case and the control group was 0.63 (SD 0.22) and 2.56 days (SD= 2.46), respectively (P-value:0.001). Serum zinc level of the cases and the controls are shown in table 2.

**Discussion**

It was detected that serum zinc level was significantly lower in patients who suffered from simple febrile seizures compared to patients who had fever without febrile convulsions.

In one study by Papierkowski et al in Poland that was performed on 33 patients aged 8 months to 5 years old including 18 patients in the case group with febrile seizure and 15 healthy individuals in the control group, serum and CSF zinc and magnesium levels were evaluated. It was observed that cases had significantly lower levels of serum and CSF zinc and magnesium compared to controls (9). According to Burhanoglu et al from Turkey, low levels of serum and CSF zinc levels were seen in patients with febrile convulsion(10).

Another Amiri et al from Ghazvin hospital that was performed on 60 patients which 30 patients with febrile seizure in the case group and others in the control group. Serum zinc, selenium and copper levels were evaluated. It was revealed that serum zinc and selenium levels were significantly lower in children with febrile convulsion (1).

In another study by Ehsani pour which was carried out in Rasoul - e- Akram Hospital from Jan 2003 to Jan 2005 on 92 patients aged 6 months to 5 years, 3 groups of patients were evaluated (34 patients who suffered from febrile seizure, 40 cases who had fever without seizure and finally 18 patients with non-febrile seizure). It was observed that patients with febrile seizure had a lower serum zinc level compared to other groups (4).

Similarly, findings of our study and the results of other studies confirmed low serum zinc levels in patients with febrile seizure.

On the other hand, in one report by Garty et al from Schneider Children Hospital, there was no significant
relationship between CSF zinc level of the patients with febrile seizure and the control group (8). They had some delay in performing lumbar puncture when the fever was resolved while our cases and controls had a fever when samples were obtained.

Zinc, as a major element of some enzymes, has an important role in some tissues like central nervous system and can affect some inhibitory mechanisms of CNS (11). It has an important role in Gamma Amino Butyric Acid (GABA) synthesis through glutamic acid decarboxylase synthesis. So, a low serum zinc level can cause decrease GABA concentration (3,4). Also, zinc can suppress some excitatory mechanisms in CNS. It may directly raise the threshold of the seizure level through inhibiting N-methyl D-aspartate (NMDA) receptors or via improving calcium inhibitory function (3,4,11,12).

In the end, we had some limitations in our study including sampling and storage of the samples in different hospitals and then transferring them to the laboratory for evaluation.

In conclusion, low serum zinc levels can predispose children aged 6 months to 6 years to simple febrile seizure.

It is suggested that zinc supplementation be considered in patients who are at risk of febrile seizure.

**Table 1.** Demographic data of the case and control group

<table>
<thead>
<tr>
<th></th>
<th>Female/male</th>
<th>mean age (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Case</strong></td>
<td>12/18</td>
<td>21.25± 11.53</td>
</tr>
<tr>
<td><strong>Control</strong></td>
<td>13/17</td>
<td>21.4± 12.06</td>
</tr>
</tbody>
</table>

**Table 2.** serum zinc level (µg/L) in the case and the control group

<table>
<thead>
<tr>
<th>Group</th>
<th>Maximum(µg/l)</th>
<th>Minimum(µg/l)</th>
<th>Mean(µg/l)</th>
<th>SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Case</strong></td>
<td>853</td>
<td>393</td>
<td>663.7</td>
<td>107.6</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>Control</strong></td>
<td>1022</td>
<td>616</td>
<td>758.33</td>
<td>80.29</td>
<td></td>
</tr>
</tbody>
</table>

**References**


