SERUM ZINC AND COPPER LEVELS IN UNTREATED EPILEPTIC PATIENTS

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Summary

Epileptic patients exhibit variable alteration in some trace element levels. Zinc and Copper are amongst those trace elements which are necessary for neural function. To investigate the possible correlation between serum zinc and copper concentration and epilepsy, we evaluated serum zinc and copper in 45 epileptics (male=25, female=20) whose seizures have been diagnosed recently as epilepsy. We compared the serum zinc and copper levels in epileptic patients who have not gone under any antiepileptic treatment with 45 healthy individuals (sex and age matched).

Serum zinc and copper concentration of patients were determined by atomic absorption spectrophotometer; the same was done with control group. All data were analyzed by SPSS software and t-test.

Although epileptic patient’s zinc and copper levels were higher than control group (Epileptics: Zn: 100.75±18.49 (µg/lit), Cu: 948.00±32.29 (µg/dl)) (Control Zn: 82.85±1.80 (µg/lit), Cu: 887.13±29.33 (µg/dl)), but the differences were statistically insignificant (P>0.05). We may assume that despite the crucial neural modulating role of zinc and copper in the CNS, the serum zinc and copper levels have no relation with the initiation or aggregation of epilepsy.

Keywords: copper, epilepsy, zinc

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Introduction

Epilepsy can be defined as a condition in which seizures are recurrent. Seizures may develop as a result of the spreading of excitatory postsynaptic potentials, which discharge synchronously from either abnormal neurons or metabolic problems that lower seizures potential. A seizure is the manifestation of an abnormal, hypersynchronous discharge of a population of cortical neurons. This discharge may produce subjective symptoms or objective signs, in which case it is a clinical seizure, or it may be apparent only on an electroencephalogram (EEG), in which case it is an electrographic (or subclinical) seizure.

The incidence of new-onset seizures in the general population is approximately 80 per 100,000 per year; approximately 60% of these patients will have epilepsy, a tendency toward recurrent unprovoked seizures (1, 2).

The annual cost of the estimated 2.3 million cases was projected to be $12.5 billion, with antiepilepsy drugs accounting for 30% of direct medical costs. Indirect costs, such as lost earnings and lost productivity, accounted for 85% of total costs.

Although trace elements are found in little amount in body they have obvious structural functional importance and have an important role on a variety of biological processes (3).

Zinc and copper are endogenous transition metals that can be synaptically released during neuronal activity. Synaptically released zinc and copper probably function to modulate neuronal excitability under normal conditions. However, zinc and copper also can be neurotoxic, and it has been proposed that they may contribute to the neuropathology associated with a variety of conditions, such as Alzheimer’s disease, stroke, and seizures (4).

This current evaluation of zinc and copper in epileptic patient’s serum was designed to investigate whether concentration of these trace elements have any relation with onset or development of epilepsy signs.

Regarding to the contradictory findings, we have reported a comparison between 45 epileptic’s serum Zn and Cu levels with age-matched and gender-matched control
group to investigate possible relation between serum Zn and Cu concentration and epilepsy.

Materials and methods

45 newly diagnosed epileptic patients (male=25, female=20, mean age 28±15.10) with idiopathic generalized seizure (Atonic seizures or myoclonic juvenile, Lennox-Gastaut syndrome, Absence, Tonic-clonoic) and abnormal EEG were enrolled in this study; Patients have been experiencing at least one seizure since last year (clinical diagnosis was according to the admitted criteria by International League Against Epilepsy). Demographic characteristics, seizure types, medical history, clinical examination were obtained about each patient. Patients were chosen among newly registered epileptics who have not ever taken any antiepileptic medicine.

Regarding to the possible effects of environmental and geographical circumstances on body trace element levels, we tried to choose those patients who were inhabitants of Mashad (where this study was running). Exclusion criteria were treatment with any antiepileptic or other drugs which alter the serum zinc and copper levels.

Patient’s serum Zn and Cu were determined by atomic absorption spectrophotometer in toxicology department of Mashad Medical University. Control group was defined according to similar criteria. 45 individuals (male=25, female=20, mean age 26.6±10.67) with no sign of epilepsy or seizure (whose medical documents were available on Mashad Medical University dependent hospitals). Blood samples were determined in the same laboratory with same equipments and standards.

Statistical analysis

Data are expressed as means ±SEM. Statistical comparison between control and test group was performed by using Independent-sample T-test and statistical significance was defined as P<0.05. Calculations were done with the statistical package SPSS 14.0 for windows.
Results

This study included 45 epileptic patients (male=25, female=20) whose disease were newly diagnosed. The patients were not taking any kind of antiepileptic medicines. The serum zinc and copper levels were determined at the beginning of study and before going under treatment.

Control group was established according to the same criteria. Sex and gender matched group included 45 individuals (male=25, female=20) who have never had any kind of seizure or epilepsy. The demographic data of the epileptic and control group are shown in Table I.

Although the epileptic group exhibited higher serum zinc and copper levels (Zn: 100.75±18.49 (µg/lit), Cu: 948.00±32.29 (µg/dl)) than the control group (Zn: 82.85±18.0 (µg/lit), Cu: 887.13±29.33 (µg/dl)) but the differences were insignificant (P>0.05).

Therefore no significant difference and correlation between serum zinc and copper levels and seizures or epilepsy was observed (P>0.05).

Table I: Demographic data of persons contributed in the study

<table>
<thead>
<tr>
<th></th>
<th>Epileptic patients</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>sex</strong></td>
<td>Number (%)</td>
<td>Mean age(years)</td>
</tr>
<tr>
<td>female</td>
<td>44.44(20)</td>
<td>26.90</td>
</tr>
<tr>
<td>male</td>
<td>55.56(25)</td>
<td>28.88</td>
</tr>
<tr>
<td>total</td>
<td>100(45)</td>
<td>28.00</td>
</tr>
</tbody>
</table>
Table II: Serum zinc and copper levels in untreated epileptic patients and control group
Data have been presented as Mean ± SEM

<table>
<thead>
<tr>
<th>group</th>
<th>N</th>
<th>Mean</th>
<th>SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Copper</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>control</td>
<td>45</td>
<td>887.13</td>
<td>29.33</td>
</tr>
<tr>
<td>test</td>
<td>45</td>
<td>948.00</td>
<td>32.29</td>
</tr>
<tr>
<td>Zinc</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>control</td>
<td>45</td>
<td>82.85</td>
<td>18.0</td>
</tr>
<tr>
<td>test</td>
<td>45</td>
<td>100.75</td>
<td>18.50</td>
</tr>
</tbody>
</table>

Fig. 1a&1b. Serum zinc and copper levels in untreated epileptic patients and control group
(1a: Zn ,1b: Cu)
(Cu: µg/lit_ Zn: µg/dl)
Seizures can be defined as paroxysmal events in which there is a significant change in the EEG that correlates with a change in behavior and consciousness.

Estimates of the annual incidence of epilepsy in the general population range from 30 to 57 per 100,000. These rates vary with age, being high in infants and young children, then decreasing throughout adulthood until approximately age 60, when they again begin to increase. The overall prevalence of epilepsy is approximately 6 per 1000(1, 2).

Since the foremost precondition of illness treatment is discerning its etiology, there have been lots of examinations and assumptions to determine the base of epilepsy. Body trace elements are among those factors which have gone under long studies to find any possible correlation between seizure and these elements. Zinc and copper are neuroactive substances that are present in many regions of the CNS (4).

Zn released from glutaminergic presynaptic terminals, modulates postsynaptic N-methyl-D-aspartate (NMDA) receptors for glutamate. During seizure or ischemia large amount of Zn are released from these terminals and can kill postsynaptic neurons (5).

Some studies have revealed that Zinc ions increase neuronal excitability by inhibiting the activity of the NA-K-ATPase enzyme, which is known to concentrate in hippocampus. This hyper excitability results in seizure. It was suggested that there might be kind of relationships between zinc level in hippocampus and gamma-aminobutyric-acid (GABA) concentration which probably make an antiepileptic effect in humans (3).

Approximately 10% of the total zinc in the brain, probably ionic zinc, exists in the synaptic vesicles, and may serve as an endogenous neuromodulator in synaptic neurotransmission. However, dietary zinc deprivation affects zinc homeostasis in the brain. Vesicular zinc-enriched regions, e.g., the hippocampus, are responsive to dietary zinc deprivation, which causes brain dysfunctions such as learning impairment and olfactory dysfunction. On the other hand, the susceptibility to epileptic seizures, which may decrease vesicular zinc, is also enhanced by zinc deficiency (6).

Horning’s study has demonstrated that synaptic concentrations of zinc can be neurotoxic in certain circumstances, such as ischemia or seizures. Much more
experimental studies on the role of Zn and Cu in the CNS have been performed, but conclusions are mostly contradictory.

In a study of C3HeB/FeJ quaking mice, brain copper and zinc levels were determined in 21-day-old and "adult" mice in comparison with normal littermate controls.

The conclusions are explained: “Expressed per gram dry weight of brain, copper was increased 84% over normal mice at 21 days after birth, but was not significantly different from normal in the adults”; it was estimated that zinc was increased 23-24% at both ages therefore mutant quaking mice show abnormal copper content which is in contradiction with later findings on human serum trace element levels (4, 7).

Thiel R.J presented a paper which indicates that “Zn and Cu deficiency might be acknowledging causes of seizure. Yet epileptics often exhibit elevated serum copper levels”.

It was also brought up “Zinc deficiency is known to cause seizure. In chronic alcoholics seizures can be caused by zinc deficiency and tend to improve with zinc supplementation. Zinc ions limit the excitatory responses in the dentate granule cells of those with temporal lobe epilepsy presumably by blocking the N-methyl-D-aspartate receptors. Studies involving three different animal models of epilepsy showed that zinc supplementation protected against the development of seizures, which suggest that zinc may be an essential component of a natural anticonvulsant tissue response to abnormal excitation”(8).

Fukahori & Itoh found that mice which were zinc-deficient had increased seizure susceptibility, those with adequate dietary zinc had no change, but those who took supplemental zinc decreased seizure susceptibility. Based on other reports, some conventional antiepileptic drugs could make oxidative pressure and subsequently alter the metabolism of trace elements, alterations in zinc metabolism could be effective on causing seizure (9,10).

Some reports recommend that seizure type (limbic or generalized tonic-clonic) and number of stimuli seem to be the determinant factors for changes in zinc levels (7). In a study of serum zinc and copper in health and disease included 596 controls and 1616 patients of various diseases, assessment of body trace elements revealed that serum zinc
level was increased in epilepsy. Also the copper levels were found elevated in epilepsy (11).

In contradiction to the mentioned reports, an evaluation of diurnal variation of serum copper and zinc in epileptics receiving anti-convulsants indicates that variations in serum zinc concentrations are a normal physiological process and is unlikely to be related to anti-convulsant drugs or epilepsy (12).

In agreement with the above statement, our study revealed that serum zinc and copper concentration is irrelevant with the incidence of epilepsy and seizure, but since our cases had not taken any antiepileptic medicine, the results may change if being investigated after administrating proper antiepileptic treatments.

Acknowledgment

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