ORIGINAL ARTICLE

The Correlation between Epilepsy and the Blood Serum Level of Trace Elements

ZAHRAA M. AL-TAEE[1], ADNAN H. ALJOTHERY[2], ALI HMOOD AL-SAADI[3]
[1,3]Department of Biology, College of Science, University of Babylon, Al-Hillah City, Babel Iraq.
[2]Department of Pediatrics, Hammurabi College of Medicine, University of Babylon, Hillah, Iraq
Correspondence to Zahraa M. Al-Taee, Email: sci.zahraa.mohmmed@uobabylon.edu.iq

ABSTRACT

Background: Epilepsy is a common dysfunction of the nervous system in children. Altered levels of zinc, copper, and calcium in the blood can be considered an important cause of seizures and their recurrence.
Aim: To investigate the difference in serum zinc, copper and calcium levels between the control group and the patient group.
Methods: Case, control study on 121 epileptic patients, aged from 2 months to 15 years, from the visitors of consult clinic in Babil hospital for maternity and children and Outpatient pediatricians clinics in AL-Hillah city and 58 apparently healthy children of similar age and sex. Venous blood withdrawn from patients and controls then serum levels of zinc, copper, and calcium were measured.
Results: After measuring the levels of zinc, copper and calcium in the serum of 187 children, including 121 children with epilepsy and 66 children without any diseases, it was found that the average zinc among patients was higher than in control. As for copper, a significant difference was found for the mean, as it was less among patients as compared to control. And, for measuring the level of calcium in the serum, there was no significant difference between patients and control.
Conclusion: From the results of our research, we conclude that the level of zinc in the blood serum was higher in children with epilepsy,this increase in zinc levels appears to be due to antiepileptic treatments, while the level of copper in the blood serum was lower in patients than in healthy children ,This result is contrary to most studies that have studied serum copper levels in children with epilepsy, and there was no significant difference in the level of calcium in the blood serum between the two groups of patients and healthy.
Keywords: Epilepsy, Children, Trace elements, Zinc, Copper, Calcium.

INTRODUCTION

The neuro-biologic, emotional, psychological, and social ramifications of seizure recurrences describe epilepsy, which is a progressive brain disorder marked by an ongoing (i.e., persistent) predisposition to produce seizures unprovoked by any immediate central nervous system insult. Epilepsy affects both sexes and people of all ages, and it is seen all over the world[1].

Trace element balance is essential for a stable nervous system since they release certain enzymes that function as antioxidants[2]. The physiological effects of trace elements on neuronal excitability can play a role in the etiology of intractable epilepsy[3]. Several studies have indicated that changes in micronutrient homeostasis led to seizures[2].

In order to get a better response, many vital minerals and trace elements are essential for the safe growth of nervous system and the nervous system's susceptibility to excitability[4]. Zinc and copper homeostasis can play a role in seizure susceptibility, growth, and termination, especially in genetically determined epilepsy[5].

Anticonvulsant and proconvulsant properties of zinc have been discovered[6]. Zinc has long been recognized for its capacity to bind to and modulate the activity of a number of targets, including glutamate, gamma-aminobutyric acid (GABA), and glycine receptors[7]. Zinc can also reach neurons[8], where it has a host of effects on intracellular signaling. On the other side, copper dysregulation has an impact on synaptic transmission and excitability. Copper can act as a signal and modulate signaling through multiple pathways, according to study. Copper plays a unique role in oxidation-reduction reactions. Copper's advantages, on the other hand, come at a price. Copper's reactive properties, which make it valuable as an enzymatic cofactor, also make it a concern for the production of reactive oxygen species and resulting oxidative damage in uncontrolled conditions[4,3].

Zinc ions interact with a number of receptors involved in neuronal excitation and inhibition. Decreased levels of zinc was shown to cause reduced cell viability and increased apoptotic rates in an in vitro neuronal cell model when zinc ion chelating agent (TPEN) was used to induce zinc deficiency. Zinc supplementation will undo these improvements[5]

Copper is also essential for the absorption of iron and the proper action of Vitamin C. Copper deficiency is very uncommon. High zinc levels, on the other hand, may impede proper copper absorption due to interactions with zinc. Since they fight for the same absorption sites in the intestine, they are incompatible. As a result, if one of these nutrients is in excess in the diet, the other is likely to be insufficient[6].

Serum copper levels were slightly higher in children with epilepsy, Such factors that can be attributable to increased hepatic synthesis, reduced degradation, changes in intestinal and urinary excretion, differing amounts of copper delivery, or altered distribution, or differing requirements, and altered patterns of copper exposure in different tissues, are probably due to its effects on the nervous system, endocrine, cardiovascular, and skeletal systems. The interaction of copper (Cu) has been shown to lower ATPase (also known as ADPase and ADPase) and Na-K-ATPase, as well as prevent serum and osmotic

pressure homeostasis (Na-K-ATPase), leading to - increased presence of calcium in the brain during episodes of sudden cell death, causing epileptic fits[5].

The epilepsy could be caused by a change in serum - [Ca2+] due to a disturbance in the PTH stage, which causes inhibitory neurons to be suppressed, excitatory neurons to be activated, or a more general influence on certain brain circuitry. Surprisingly, some CaSR mutations have been linked to seizures in people who do not have any changes in their systemic parathyroid hormones or serum Ca2+ levels[7].

MATERIALS AND METHODS

Samples collection: Samples were collected during the period 12/2/2020 – 30/12/2020 , from the visitors of consult clinic in Babil hospital for maternity and children and Outpatient pediatricians clinics in AL-Hillah city, A written Agreement was signed by every participants' parents after their understanding of the project aim and tests that would be performed. we collected 181 samples, 121 from children undergo epilepsy and 58 sample of healthy children ,their age between 2months to 15 years for both groups .Three milliliters of venous blood was obtained by 5ml disposable syringe (without tourniquet) , drained into gel plain tube for serum preparation, which would be used in biochemical tests during the next 6 hours .

Trace element level in serum: Zinc was measured in the blood serum using the (ZINC (Colorimetric Test with 5-Bromo-PAPS)) from Spectrum, Catalog No.(330) .

Copper was measured in the blood serum using the (Copper (Colorimetric Test with Dibrom- PAESA) from Spectrum, Catalog No.(232) .

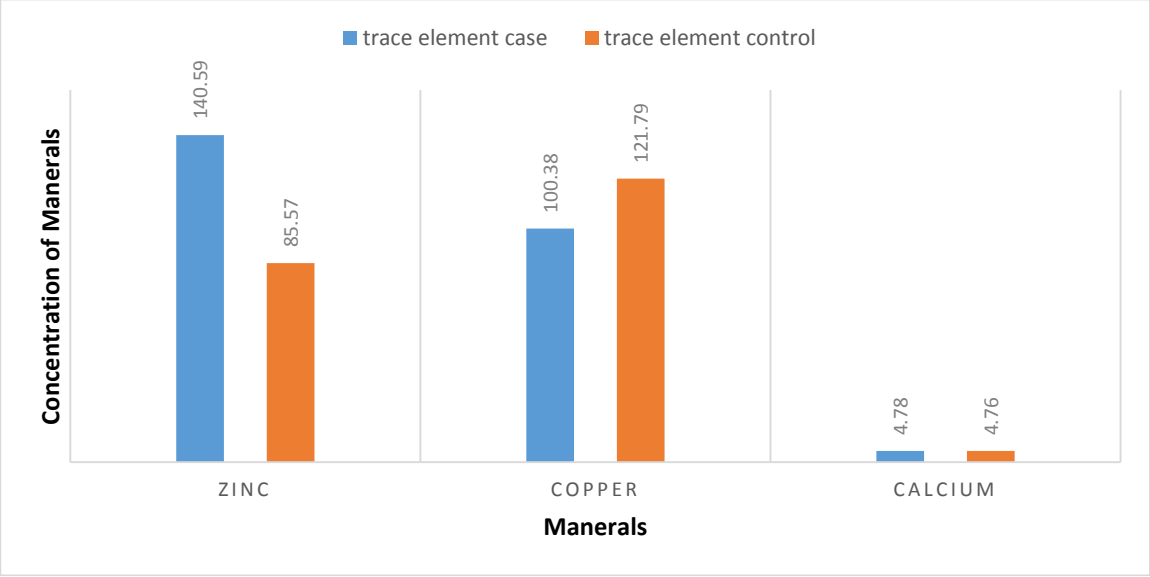
Calcium was measured in the blood serum using the (Calcium Arsenazo III (Single Reagent) from Spectrum, Catalog No.(227) .

Statistical analysis: All statistical analyses were carried out using SPSS (IBM Corp. Published 2012) software. Version 21.0 of IBM SPSS Statistics for Windows. Armonk, NY: IBM Corp. USA) and Microsoft Excel (2010, Microsoft Corp. USA). The outcomes were all expressed as mean ± SEM. Statistically important was deemed a $p < 0.05$. To determine the existence of significant differences, the Unpaired-Sample T Test was used. Analyzing regression to determine the existence of associations. Chi-square test to compare variables of categorical association and genetic association, according to Sole *et al*[8]**.**

RESULTS

The patient group consisted of 75 males and 46 females while there were 38 males and 26 females in the control group. Age within the studied groups ranged between 2 months and 16 years.The mean serum of zinc was highly significant in epileptic children than control group (140±59 , 85.57±2.56 ;*p≤0.05* ,respectively). The mean serum of copperwassignificantly lower inepileptic children than control group (100.38±4.44,121.79±5.31; *P≤0.05*,respectively*)*.For calcium there was no sig. difference between epileptic children and control as demonstrated in figure (1).

Figure 1: Difference in the mean of Zinc, Copper and Calcium between the control and patient groups



DISCUSSION

This study aimed to investigate the serum levels of trace elements such as zinc, copper and calcium among children with epilepsy and to compare their levels with the control group (healthy children), as these elements have an important role in the health of the nervous system and brain cells[9,10,11]. As can be seen from diagram 1, the mean zinc level in the case group was higher than the control group(140±59 , 85.57±2.56 ;*p<0.05*,respectively),this increase may be due to taking nutritional supplements, and taking antiepileptic treatments causes an increase in the level of zinc, as explained by Andin *et al*, who said:There was a statistically significant increase in the mean serum zinc concentration after valproic acid treatment in children with epilepsy[2].In another study by Jia, it was also found that

zinc levels were raised when taking antiepileptic drugs[12], Mean serum zinc concentrations were found to be slightly higher in epileptic children regardless of gender compared to those in controls (around 114g/dL), and copper levels were found to be lower in epileptic children (around 85g/dL) compared to healthy controls (110g/dL)[13]. In other studies, lower levels of zinc were found among children with epilepsy from these studiesthe mean serum zinc concentration was 59.1 µmol/L (59.2-22 g/L) This fell by 30.5% short of the mean zinc serum level of the control group (versus the zinc level in the unsupplemented group; *P ≤ 0.01*) When copper was compared to the mean values in the test group, the sample had no significant differences in total mean concentration of copper and no significant statistical significance[3].

The mean serum of copperwassignificantly lower inepileptic children than control group (100.38±4.44,121.79±5.31; *P≤0.05*,respectively), For the various categories, the mean serum copper and chromium levels were lower in the epileptic patients (85g/dL) Salah and his group discovered that there was a statistically substantial increase in serum copper levels in children with rheumatic fever, with children with rheumatic fever having serum copper levels 154.0±22.9 when they have fever and 154.2±22.3 when they are well, the control group That was statistically important. 1.11 µg/ml of copper was found in the epileptic community, while 0.96 µg/ ml of copper was found in the non-epileptic group[14].

In our study there was no significance difference between patients and healthy children participated in the study which it's similar to Saket' study as indicated that the element Ca showed no difference between the groups[15].

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