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Trace Elements Concentrations in Children with Epilepsy

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Abstract
Background: Epilepsy one of the most common and serious brain disorders, is characterized by spontaneous and stereotyped disturbance of sensation, behavior, emotion or motor function resulting from the rapid and local discharges of gray matter Microminerals and trace elements act as crucial components for the development of immunity and provide antioxidant defense in human body The aim of this study were to evaluate the association of trace element (Zn, Cu, and Mn) with epilepsy in children. **Methods:**Case control study was conducted in Pediatrics Department at Zagazig University Hospital. Laboratory Investigations Including: Serum Trace elements (Zn, Cu, and Mn). **Results:** Our study showed that, there was a statistically significant decrease in serum zinc (Zn) among cases group than control group. In the present work, there were no statistically significant difference in serum copper (Cu) among cases group compared to control group. Our study showed that, there was a statistically significant decrease in serum manganese (Mn) among cases group than control group. **Conclusion:** Results of this research work demonstrated that depleted serum trace elements (Zn, Mn) might be associated with epilepsy. In this context, micromineral supplement may be recommended to reduce the risk of being epileptic.
Key words: trace element- epilepsy in children.- Evaluation-

Introduction:

Epilepsy one of the most common and serious brain disorders, is characterized by spontaneous and stereotyped disturbance of sensation, behavior, emotion or motor function resulting from the rapid and local discharges of gray matter [(1)].
This disorder is heterogenic in nature with idiopathic (genetic basis), symptomatic (identified brain injury) and cryptogenic (unknown) etiologies [(2)].
Microminerals and trace elements act as crucial components for the development of immunity and provide antioxidant defense in human body [(3)].
For maintaining a healthy nervous system and neuronal susceptibility, it is very important to keep these elements in a balanced state, Several reports have suggested that altered level of some trace elements and body electrolytes play an important role in the pathophysiology and recurrence of seizures [(4)].
Zinc (Zn) is abundant in the hippocampus region of the brain which has been implicated as a causative factor of epilepsy, It is a fundamental element for the normal neuronal communication as well as proper functioning and synthesis of the inhibitory neurotransmitter, γ-amino butyric acid (GABA), Altered zinc metabolism and low levels of serum zinc may play an important role in the induction epileptic seizures via activation of *N*-methyl-d-aspartate receptors. [(5)].

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Copper (Cu) is also an important micromineral that acts as a cofactor for different enzymes, including tyrosinase and dopamine hydroxylase [(6)].
Release of Cu during synaptical transmission helps modulate neuronal excitability under normal conditions and depleted serum Cu level leads to epileptiform discharges [(7)].
Manganese (Mn) is a fundamental micronutrient for the proper neuronal development and function. Either deficiency or excess Mn concentration in the body can severely affect the pathological conditions in the central nervous system, Alterations in Mn concentrations, whether excessive or deficient, can be accompanied by convulsions due to the alterations in dopamine, glutamate, and GABA regulatory systems [(8)].
The aim of this study were to evaluate the association of trace element (Zn, Cu, and Mn) with epilepsy in children

Patients and Methods
A. Type of study:
Case control study
B. Study Setting:
This study was conducted in Pediatrics Department at Zagazig University Hospital.
D. Inclusion criteria:
Included:
1. All patients who are newly diagnosed as epilepsy having abnormal EEG and have been experiencing at least one seizure in past 6 month.
2. Both sexes are included.
3. Patient with no previous history of antiepileptic and antioxidant drug administration.
4. Age (1-12 years).

E. Exclusion criteria:
Included:
1. Absence of informed consent.
2. Age group out of range (1- 12 years).
3. Patient with previous history of antiepileptic and antioxidant drug administration.
4. Patient who had sever general medical condition (diabetes mellitus, renal, cardiovascular, liver disease, endocrine disorder).

F. Sample size:
Assuming that mean ±SD of malondialialdehyde in epileptic children versus normal group was 5.41± 3.9 versus 2.9 ± 1.5 so the sample size was 46 case (23 in each group) CI 95% power of test 80% using open epi. The sample size was calculated by community department at Zagazig University.

II. Operational Design:
* Informed consent was obtained from all patients care giver.
* All the participating patients were subjected to the following:
- Full history taking:
- Clinical Examination:
- Systemic and Local examination.
- Laboratory Investigations Including:
- Complete blood count(CBC).
- Serum Trace elements (Zn, Cu, and Mn).

Blood Sample Collection and Storage
- Five-milliliter venous blood sample was drawn from each patient and control in a metal-free sterile tube. The blood sample was kept at room temperature for about 30 minutes

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to clot and centrifuged at 3000 rpm for 15 minutes to extract the serum. Then the serum was taken in an Eppendorf tube and was stored at −80°C until the study day. These samples were then used for analyzing trace elements (Zn, Cu, and Mn).

Ethical Consideration:
Informed consent was taken from the parents of the children to participate in the study. Approval for performing the study was obtained from Pediatric Department, Zagazig University Hospitals after taking Institutional Review Board (IRB) approval.

Statistical Analysis
Data analysis was performed using the software SPSS (Statistical Package for the Social Sciences) version 24. Quantitative variables were described using their means and standard deviations. Categorical variables were described using their absolute frequencies and were compared using Chi square test and fisher exact test when appropriate. Kolmogorov-Smirnov (distribution-type) tests were used to verify assumptions for use in parametric tests. To compare continuous quantitative data of two groups, Mann whitney test (for non-normally distributed data) and independent sample t test (for normally distributed data) were used. The level statistical significance was set at 5% (P<0.05).

Results:
There was no statistically significant difference between Cases group and control group regarding Age (year), sex and Residence **(Table 1).**
This Table shows that 9 (39.1 %) children had mild epilepsy, while 7 (30.4 %) children had moderate and Sever epilepsy **(Table 2).**
There was statistically significant decrease in TLC among cases group than control group. There was no statistically significant difference between Cases group and control group regarding HB and Platelets **(Table 3).**
There was statistically significant decrease in serum Zn among cases group than control group **(Table 4).**
There were no statistically significant difference in Cu among cases group than control group **(Table 5).**
There was statistically significant decrease in serum Mn among cases group than control group **(Table 6).**

Table (1): Comparison between cases group and control group regarding demographic data.

			Cases group (No.= 23)	control group (No.= 23)	X^2	P. value
Age(year)	**Range**		1.3 - 10.5	2.0 - 12.0	t.test 0.052	0.959
	Mean ± SD		5.74± 3.02	5.69 ± 3.19		
Sex	**Female**	**No.**	11	6	2.333	0.127
		%	47.8%	26.1%		
	Male	**No.**	12	17		
		%	52.2%	73.9%		
Residence	**Rural**	**No.**	17	16	0.107	0.743
		%	73.9%	69.5%		
	Urban	**No.**	6	7		
		%	26.1%	30.5%		

X^2 test: Chi square test. t test: Student test
P value >0.05 is non-statistically significant (N-S).

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P<0.05 is statistically significant (S)

Table (2): Severity of illness among the studied cases.

		)No.= 23(	%
Severity of the illness	**Mild**	9	39.1
	Moderate	7	30.4
	Severe	7	30.4

Table (3): Comparison between cases group and control group regarding laboratory findings.

		Cases group (No.= 23)	**control group (No.= 23)**	**t.test**	**P. value**
HB (gm/dl)	**Range**	9.0 - 16.0	11.0 - 13.5	-.023-	0.982
	Mean±SD	12.56 ± 1.67	12.57 ± 0.64		
TLC ($x10^3/mm^3$)	**Range**	5000 - 11300	8000 - 12500	-2.051-	0.046
	Mean±SD	9286.96 ± 1903.18	10217.39 ± 1053.42		
Platelets ($x10^3/mm^3$)	**Range**	170 - 367	230 - 350	-1.065-	0.293
	Mean±SD	282.70 ± 67.05	299.70 ± 36.95		

t test: Student test
P value >0.05 is non-statistically significant (N-S).
P<0.05 is statistically significant (S)

Table (4): Comparison between cases group and control group regarding level of serum Zn.

		Cases group (No.= 23)	**control group (No.= 23)**	**t.test**	**P. value**
Zn(mg/dl)	**Range**	0.30 - 0.55	0.66 - 1.10	-12.521-	0.000
	Mean ± SD	0.41 ± 0.07	0.82 ± 0.14		

t test: Student test
P value >0.05 is non-statistically significant (N-S).
P<0.05 is statistically significant (S)

Table (5): Comparison between cases group and control group regarding level of serum Cu.

		Cases group (No.= 23)	**control group (No.= 23)**	**t.test**	**P. value**
Cu (ug/dl)	**Range**	75 - 140	74 - 140	-.336-	.739
	Mean ± SD	97.61±17.48	99.43 ± 19.38		

t test: Student test
P value >0.05 is non-statistically significant (N-S).
P<0.05 is statistically significant (S)

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Table (6): Comparison between cases group and control group regarding level of serum Mn.

		Cases group (No.= 23)	control group (No.= 23)	t.test	P. value
Mn (µg/dL)	**Range**	3.2 - 6.5	4.5 - 14.0	-8.615-	.000
	Mean ± SD	4.587 ± 1.00	9.41 ± 2.49		

t test: Student test
P value >0.05 is non-statistically significant (N-S).
P<0.05 is statistically significant (S)

Discussion

Our study showed that, there was a statistically significant decrease in serum zinc (Zn) among cases group than control group.

This was in agreement with**Saad et al., [(9)]** who found that, significantly lower zinc levels in the serum of children with epilepsy in comparison with healthy control children.

Similarly, **Kheradmand et al. [(10)]** reported significantly lower serum zinc levels in patients with intractable epilepsy in comparison with a controlled epilepsy group. These data suggest that children with refractory epilepsy may potentially benefit from zinc supplementation treatment.

Zinc (Zn) is abundant in the hippocampus region of the brain which has been implicated as a causative factor of epilepsy. It is a fundamental element for the normal neuronal communication as well as proper functioning and synthesis of the inhibitory neurotransmitter, γ-amino butyric acid (GABA). Altered zinc metabolism and low levels of serum zinc may play an important role in the induction epileptic seizures via activation of *N*-methyl-d-aspartate receptors. Zinc is an important trace element whose intake is related to protein intake. As a result, zinc deficiency is an important component of nutrition-related morbidity worldwide. Zinc supplementation in populations at possible risk of zinc deficiency appears to have beneficial effects on the incidence and outcome of serious childhood diseases [(5)].

In the present work, there were no statistically significant difference in serum copper (Cu) among cases group compared to control group.

This was in agreement with**Saad et al., [(9)]** who found no changes in serum Cu concentration in epileptic patients as compared with the control group.

Studies regarding the results of Cu concentration in epilepsy are contradictory where, **Nazıroğlu and Yürekli, [(11)]** found that depleted blood copper level may be associated with the pathogenesis of epilepsy. Also, **Sarangi et al., [(12)]** reported higher levels of serum Cu in untreated epileptics (p<0.05).

Our study showed that, there was a statistically significant decrease in serum manganese (Mn) among cases group than control group.

This was in agreement with**Dupont and Tanaka, [(13)]** who found a negative correlation between low blood Mn concentration and epilepsy.

Alteration of Mn level alters the dopamine, glutamate, and GABA regulatory systems, which ultimately lead to convulsive disorder, that is, epilepsy [(8)].

Conclusion:

Results of this research work demonstrated that depleted serum trace elements (Zn, Mn) might be associated with epilepsy. In this context, micromineral supplement may be recommended to reduce the risk of being epileptic.

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