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RESEARCH ARTICLE
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Role Of Serum Zinc Level and Its Supplementation In Children With Febrile Seizures

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ABSTRACT

Aim of study: This study aims to determine the role of serum zinc level as a triggering factor for febrile seizure in Children and its value for better management.

Methods: This study involved 90 kids aged 6 months to 6 years who had 30 simple and 30 complex febrile seizures and were patients at Al-Zahra University Hospital. Her 30 children, who were the same age and sex, served as the study's control group. A comprehensive medical history, clinical assessments of the general and neurological systems, and measurements of the serum zinc levels were all performed on each subject.

Results: There was a highly statistically significant difference (p 0.000) in serum zinc levels between the patient and control groups after zinc supplementation, with the difference being higher in the complex group and between the simple and complex groups. The frequency of seizures dropped.

Conclusion: Zinc has been implicated in the development of febrile seizures and is beneficial for measurement in children with febrile seizures.

Keywords: *serum zinc, febrile seizure, Children*

INTRODUCTION

According to the International League against Epilepsy (ILAE, 2017) (Amneneah AM et al., 2022), febrile seizures occur in 2-5% of children between the ages of 6 months and 6 years. The American Academy of Pediatrics (AAP) (Leung AK et al., 2018) states that neither a metabolic condition nor a central nervous system infection can cause febrile seizures.

There is good news regarding febrile seizures. Seizures brought on by fever have not yet been explained.

Through coenzyme activity and effects on ion channels and receptors, some elements are thought to play a significant role in febrile seizures (Mosili P et al., 2020). Seizures that are febrile can be brought on by iron, zinc, and magnesium deficiencies. It has been investigated how zinc affects the nervous system (Mahmoud AT et al., 2021). According to these studies Our aim was to determine the role of serum zinc levels as a provoking factor for febrile seizures in children and its value for better management.

SUBJECTS AND METHODS

Type and place of the study

This is a comparative intervention study conducted in the Neurology and Pediatrics Outpatient Clinic and the General Department of Neurology at Al-Zahra University Hospital, Al-Azhar University.

This was performed on her 90 children, divided into simple (30 children) and complex (30 children) control groups ranging in age from her 6 months to her 6 years. I was. They were divided as follows.

Patient group: Next was divided into two groups.

Group A:Thirty infants had simple febrile seizures.

Group B:Thirty infants had complex febrile seizures.

2 -control group: Thirty infants had fever without seizures.

Patient group

Simple febrile seizures lasting under 15 minutes, generalized seizures, or complex febrile seizures lasting over 15 minutes with normal growth and development occurred in infants aged 6 months to 6 years.

Control group

Infants and children of the same age and sex with fever without seizures.

Exclusion criteria

Children younger than 6 months or older than 6 years have a neuropathy or central nervous system infection.

Children who have recently taken zinc.

Children with chronic illness, malnutrition, or mental and metabolic retardation.

structural brain lesions

Patients with epilepsy or seizures without fever.

Ethical consideration

The Ethics Committee of the Faculty of Women's Medicine at Al-Azhar University in Cairo, Egypt, gave its approval to the study protocol. Participation in the study was optional. Each participant provided their written informed consent prior to being enrolled in the study. To protect participant privacy, the data are untitled and encrypted.

METHODS

All cases and controls were subjected to the following:

History taken, with particular attention to the occurrence of febrile seizures. Medical history, including associated febrile illness, seizure type (generalized or focal), and postictal condition. A complete clinical and neurological examination. Axillary temperatures of all cases and controls were recorded with a mercury-in-glass thermometer at the time of presentation. A family history of febrile seizures.

Investigation

Determination of serum zinc levels within 6–24 hours of seizure onset in both study groups, and determination of serum zinc levels after his 3 months of daily oral zinc supplementation with 2 mL, followed by re-evaluation of serum zinc levels.

Sampling

Within 6–24 hours of the onset of fever with paroxysms in both study groups and 3 months following oral zinc supplementation with 2 mg, a blood sample of 5 cc was taken. The serum was separated, stored at -20 °C, and measured using a colorimetric technique in sterile 5 ml Holliday tubes containing the gel. a 5-bromo-PAP-based colorimetric technique. 2-(5-bromo-2-pyridylazo)zinc formed a red chelate complex with this compound. -5-(N-propyl-N-sulfopropylamino)-phenol

Using a traditional EEG, assess neurophysiology

On a Nihon Kohden model 1200 electroencephalograph, spontaneous electrophysiological activity was captured using the international 10/20 system for placing surface

electrodes. There was a photostimulation challenge. An average of 32 channels and digital bipolar were used in the reference montage. Functional test that involves monitoring the EEG over

Statistical analysis

Data were gathered, put together, coded, and entered into IBM SPSS version 23 of the Statistical Package for Social Science. Quantitative information was presented as mean, standard deviation, and range for parametric distributions and as median interquartile range (IQR) for nonparametric distributions. Quantitative and percentage expressions were also used for qualitative variables.

RESULTS

Table (1) Before zinc supplementation, this table demonstrated a highly significant difference in serum zinc levels between the case group and the control group.However, after zinc supplementation, there was no significant difference between the simple group and the complex group.

Prior to zinc supplementation, post-hoc analysis revealed that there were highly significant differences between the simple and control groups as well as the combined and control groups.

Prior to zinc supplementation, the simple group and combined group had cut-off points that revealed a highly significant difference (an increase in the number of patients in the simple group).

Figure (1) has her Hypozainceima cutoff point of less than 56 ng/dl receiver operating characteristic curve (ROC) with a specificity of 100% a sensitivity of 71.67%, a positive predictive value of 100% and NPV 63.8%is shown .

Table (2) shows a highly significant difference in seizure frequency between the simple and complex groups before and after zinc supplementation.

TABLE 1: Comparison between studies groups as regard mean serum zinc level before and after zn supplementation.

		Simple group	Complex group	Control group	Test value	P-value	Sig.
		No. = 30	No. = 30	No. = 30			
Zn before	Mean ± SD	49.20 ± 10.45	49.90 ± 14.45	63.27 ± 4.77	16.588••	0.000	HS
	Range	29 – 69	28 – 73	57 – 73			
	≤ 56 ng\dl	24 (80.0%)	19 (63.3%)	0 (0.0%)	42.840*	0.000	HS
	< 63mcg\dl	27 (90.0%)	23 (76.7%)	17 (56.7%)	8.877*	0.012	S
Zn after	Mean ± SD	82.77 ± 8.92	84.80 ± 11.85	–	-0.751•	0.456	NS
	Range	70 – 105	65 – 115	–			
Zn improvement	Mean ± SD	33.57 ± 8.56	34.90 ± 9.39	–	-0.575•	0.568	NS
	Range	18 – 50	21 – 53	–			
Post hoc analysis							
		Simple Vs complex		Simple Vs control	Complex Vs control		
Zn before		0.800		0.000	0.000		

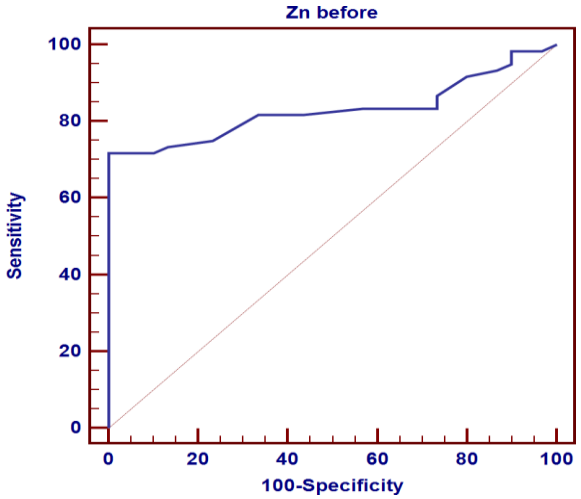

FIGURE 1: Receiver operating characteristic curve (ROC) showed cut off point of hypozainceima less than 56ng\dl with sensitivity71.67% and specificity100% with positive predictive value 100%and NPV 63.8% .

Cut off point	AUC	Sensitivity	Specificity	+PV	-PV
≤56	0.830	71.67	100.00	100.0	63.8

TABLE 2: Comparison between simple and complex groups as regard of frequency of fits before and after zinc supplementation

		Simple group	Complex group	Test value	P-value	Sig.
		No.=30	No.=30			
Frequency off its before	Mean±SD	1.10±0.55	2.67±0.80	-6.512≠	<0.001	HS
	Range	1–4	1–4			
Frequency off its after	Mean±SD	0.43±0.57	0.97±0.49	-3.626≠	<0.001	HS
	Range	0–2	0–2			
Wilcoxon Rank test	Test value	-4.264	-4.787			
	P-value	<0.001	<0.001			

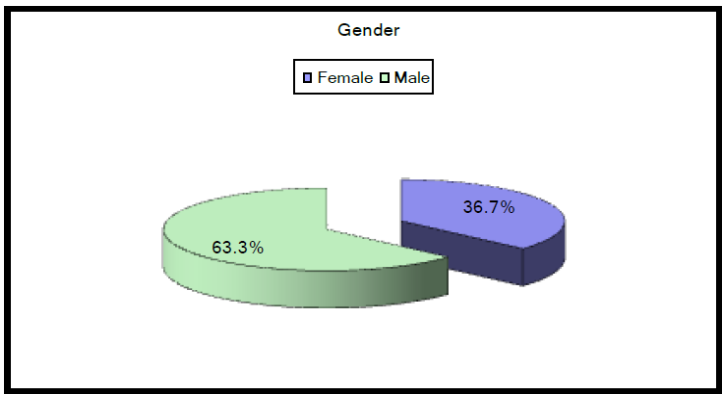

FIGURE 2: Demographic data of the studied groups regarding sex distribution

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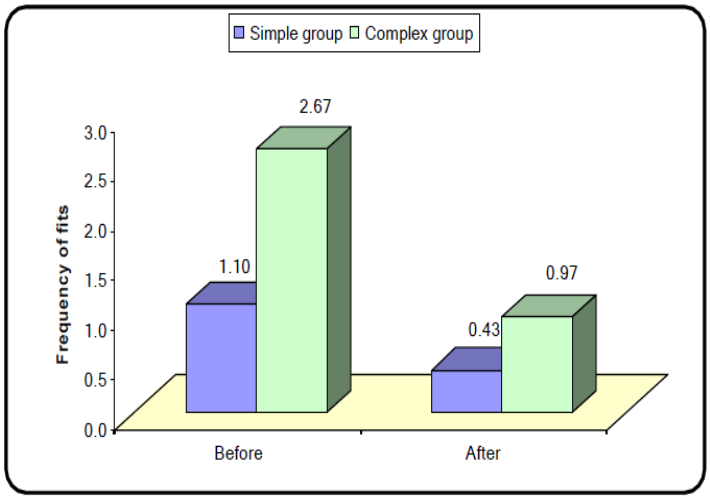

FIGURE 3: Comparison between simple and complex groups as regard of frequency of fits before and after zinc supplementation

TABLE 3: EEG changes before and after zinc supplementation

EEG	Beforezinc	Afterzinc	Test value	P-value	Sig.
Normal	37(61.7%)	43(71.7%)	1.350	0.245	NS
Generalized 3HZ spike with slow waves discharge	18(30.0%)	16(26.7%)	0.164	0.685	NS
Sharp wave with slowness	5(8.3%)	1(1.7%)	2.807	0.093	NS

DISCUSSION

The most prevalent type of seizures in children are called febrile seizures (FS). A child with FS typically ages from 6 months to 6 years old. She may be genetically predisposed to FS, despite the fact that the primary cause of the condition is still unknown. The rate-limiting enzyme for GABA synthesis, glutamate decarboxylase, is known to require zinc as a cofactor. Additionally, it increases affinity for neurotransmitter receptors like glutamate receptors and encourages calcium's inhibitory effects on NMDA receptors. 2020 (Hosseini et al.).

Patients with FS frequently experience acute infections and fever, but it is unclear what causes low serum zinc levels (Kumar et al., 2011).

Through modulation of GABA, zinc has anticonvulsant effects as a direct antagonist of NMDARs. Pyridoxalkinase, a enzyme involved in the production of pyridoxal phosphate, is activated by zinc. The latter catalyzes GABA synthesis and increases glutamate decarboxylase activity. Another explanation is that zinc prevents opiate-induced inhibition of GABAergic neurons by blocking opiate binding in the hippocampal mossy fiber system. Additionally, there is (Okposio et al., 2012).

In our study, the relationship between serum zinc levels and Febrile Seizures was examined, and the potential impact of zinc supplementation on decreasing frequency of simple and complex FS in children was considered.

Males made up 63.3% of the study population, with female to male ratio of1: 1.7. It is unclear whether boys are more susceptible to FS simply because they experience higher fevers, or whether there is a biological basis for these sex differences. This was consistent with findings from other studies. 1.4 to 1.7 ratio, according to Margareza et al. Tamiraras et al.'sstudyfrom 2020 also revealed prevalence in men. However,

Ganesh et al. (2008)'s research findings did not reveal a appreciable male prevalence.

Our study revealed a highly significant difference in serum zinc levels between the case and control groups before zinc supplementation, so we performed a post hoc analysis. As a result, we discovered no difference between the simple and complex groups and a highly significant difference between simple and control. We agreed with Sampathkumar and Kannan's 2018 findings, which showed there was no discernible difference between the serum zinc levels of simple FS and complex FS in their study, indicating zinc may be involved in the pathogenesis of febrile seizures.

A different study found that kids with complex FS had significantly lower serum zinc levels than kids with simple FS, but this is probably because the sample size was so small. 2021: Debroy and others.

In a different 2018 study, Sampathkumar et al. examined the zinc levels in the serum and CSF of children with FS. Zinc levels were noticeably low in both the serum and CSF, he discovered. In light of this finding, he suggested that prescribing zinc supplements might aid in preventing FS.

In our study, serum zinc on a cut off of less than 56 ng/ml has a sensitivity of 71.67% and a specificity of 100% for the prediction of FS, with a positive predictive value (PPV) of 100% and a negative predictive value (NPV) of 0%.

In the study by De Benoist et al. (2007), a serum zinc level of less than 65 g/dl served as the cutoff for zinc deficiency. Since another study published in 2021 discovered that serum zinc has a sensitivity of 80% and specificity of 100% for predicting FS with PPV = 100% and NPV = 83%, we can think of it as a good negative test for FS. 2021 Mahmoud and others

In the second phase of our research, for three months ,FS cases received divided doses of 2 mg/kg/day of zinc sulfate. They were then reevaluated in terms of seizure frequency and serum zinc level. Among 60 children (30 with simple FS and 30 with complex FS)

The mean and standard deviation (1.10 0.55 & 2.67 0.80, respectively) were used to calculate the frequency of FS in simple and complex groups, with a highly significant difference. After the zinc was added, there were highly significant differences in the frequency of FS with mean SD in the simple and complex groups, changing to (0.43 0.57&0.97 0.49&0.43 0.57, respectively).

Our results were in agreement with those of Fallah R et al. In his randomized clinical study, 100 kids (18 to 60 months old) with simple FS and normal serum zinc levels were referred to the hospital and randomly divided into two groups to receive either a placebo or 2 mg/kg/day of zinc sulfate for six months. The recurrence of FS was tracked for a year through follow-up,

Abdelrahman, et al. (2020) showed improvement in FS cases with low serum zinc levels by administering 22.5 mg of elemental zinc daily in divided doses for three months. Then, their serum zinc level and frequency of seizures were reevaluated. The mean level was 0.89 0.15 mg/l in 28 kids with low serum zinc levels, and the P1 value was less than or equal to 0.001. In response to supplementation of zinc, 23 (82.1%) children did not have any seizures, while four (14.3%) children experienced one recurrence of FS and one child experienced two recurrences.

The main results of our study showed that serum zinc levels were lower in febrile seizures (both simple and complex), and that supplementing zinc therapy with 2 mg/kg/day zinc reduced the frequency of febrile illnesses.

CONCLUSION

Our study found that patients with febrile seizures had lower serum zinc levels than patients without febrile seizures, indicating a potential connection between serum zinc concentration and the onset of febrile seizures.

Additionally, taking zinc supplements increased seizure frequency and decreased the frequency of febrile illnesses.

REFRENCES

1. Abdelrahman A , Shokeir A , Abd Elmagid S. Serum zinc level in children presenting with febrile seizures. Alexandria Journal of Pediatrics.2020; 33(3), 144

2. Amneenah AM, Alqatani HAH. Association between Serum Zinc level and Febrile Seizures. The Egyptian Journal of Hospital Medicine .July 2022; Vol. 88, Page 2288-2292
3. Arul J, Kommu PPK, Kasinathan A, et al. Zinc Status and Febrile Seizures: Results from a Cross-sectional Study. J Neurosci Rural Pract. 2020 Oct;11(4):597-600. doi: 10.1055/s-0040-1715992. Epub 2020 Sep 8. PMID: 33144797; PMCID: PMC7595794.
4. De Benoist B, Darnton-Hill I, Davidsson L, et al. Conclusions of the joint WHO/UNICEF/IAEA/IZiNCG interagency meeting on zinc status indicators. Food Nutr Bull.2007; 3:480– 484.
5. Debroy P , Baruah A. Serum Zinc and Magnesium Levels in Children with Febrile Seizure: A Hospital Based Cross-Sectional Study.2021
6. Fallah R, Sabbaghzadegan S, Karbasi SA, et al. Efficacy of zinc sulfate supplement on febrile seizure recurrence prevention in children with normal serum zinc level: a randomised clinical trial. Nutrition.2015; 31:1358–1361.
7. Heydarian F, Nakhaei AA, Majd HM, et al. Zinc deficiency and febrile seizure: a systematic review and meta-analysis. Turk J Pediatr. 2020;62(3):347-358. doi: 10.24953/turkjped.2020.03.001. PMID: 32558408.
8. Hosseini, F., Nikkhah, A., And Goli,A. (2020). Serum zinc level in children with febrile seizure. Iranian Journal of Child Neurology,; 14(1), 43.
9. Kumar L , Chaurasiya O, Gupta A. Prospective study of level of serum zinc in patients of febrile seizures, idiopathic epilepsy and CNS infections. People's Journal of Scientific Research.2011; 4(2): 1-4.
10. Leung AK, Hon KL, Leung TN. Febrile seizures: an overview. Drugs Context. 2018 Jul 16;7:212536. doi: 10.7573/dic.212536. PMID: 30038660; PMCID: PMC6052913.
11. Mahmoud AT, Albassuoni MA, Abd El Nabi SA, et al. Serum zinc and iron levels in children with febrile seizures. Menoufia Med J 2021;34:611-6
12. Mahmoud T , Albassuoni A , Abd El Nabi A,et al. Serum zinc and iron levels in children with febrile seizures. Menoufia Medical Journal.2021; 34(2), 611.
13. Margaretha L, Masloman N. Correlation between serum Zinc level and simple febrile seizure in children. Pediatr Indon.2020; 50:326–330
14. Mosili P, Maikoo S, Mabandla MV, et al. The Pathogenesis of Fever-Induced Febrile Seizures and Its Current State. Neurosci Insights. 2020 Nov 2;15:2633105520956973. doi: 10.1177/2633105520956973. PMID: 33225279; PMCID: PMC7649866.
15. Okposio M , Sadoh W , Ofovwe G , et al. Serum zinc level in nigerian children with febrile convulsion. Journal of Pediatric Neurology.2012; 10: 187-191.
16. Sampathkumar P, Kannan KS. A comparative study of serum zinc levels in children with febrile seizures and children with fever without seizures in an urban referral hospital. Int J Contemp Pediatric.2018; 5:977-982.
17. Sampathkumar P, Kannan KS. A comparative study of serum zinc levels in children with febrile seizures and children with fever without seizures in an urban referral hospital. Int J Contemp Pediatric.2018; 5:977-982.
18. Tamilarasu N , Kumaravel S , Ramesh Babu B . A Study of Serum Zinc Levels in Children with Febrile Seizures in a Referral Hospital.2020
19. Whelan H , Harmelink M , Chou E , et al. Complex febrile seizures—a systematic review. Disease-a-Month.2017; 63(1), 5-23.