

A Correlation between the Levels of Calcium and Serum Magnesium and Febrile Convulsions in Children

Pankaj Kumar Jain¹, Sambhav Yadav²¹Associate Professor, Department of Paediatrics, Krishna Mohan Medical College and Hospital, Mathura²Assistant Professor, Department of Paediatrics, Krishna Mohan Medical College and Hospital, Mathura

Received: 16-07-2023 / Revised: 15-08-2023 / Accepted: 21-09-2023

Corresponding Author: Dr. Sambhav Yadav

Conflict of interest: Nil

Abstract

Introduction: Several investigations have shown a correlation between the prevalence of febrile convulsions and the concentrations of copper, zinc, and magnesium in serum and CSF. Hypomagnesaemia is characterized by convulsions brought on by the hyperexcitability of the central nervous system. Feverish convulsions are among the most common types of seizures that affect youngsters. Some evidence suggests that there may occasionally be a connection between low serum magnesium (Mg) and epilepsy. Furthermore, a positive correlation between the degree of epilepsy and hypomagnesaemia was found. Seizures that occur between the ages of six and sixty months, have a temperature of 38 degrees Celsius or above, are not caused by a central nervous system infection or another metabolic disorder, and do not have a history of prior afebrile seizures are categorized as febrile seizures. A brief episode of symptoms and/or signs caused by excessive or abnormally high levels of synchronous brain neuronal activity is known as a seizure.

Aim: To investigate the serum levels of calcium and magnesium in children with febrile convulsions aged six months to five years, and to determine whether there is a relationship between these parameters and febrile convulsions.

Material and Method: The Department of Pediatrics applied a duration-based prospective analytical case-control approach to conduct this study. Children between the ages of six months and five years who required hospitalization due to febrile seizures were classified as cases. Children in the same age range who were hospitalized for a febrile illness but did not have seizures served as controls. The parents/guardians of the selected study subjects were informed of the study's aims in their mother tongue. An educational letter about the participant was given to them. Forty children in the research age group, aged between six months and five years, were hospitalized to the pediatric unit. Patients who wished to participate in the trial or their guardians gave written, informed consent.

Results: The levels of serum Mg were normal in 33 patients (82.5%) with febrile convulsion, low levels were seen in 5 cases (12.5%) and high levels were seen in 2 case (5%). Serum magnesium levels were normal in all 40 controls. The levels of serum Calcium were normal in 32 patients (80%) with febrile convulsion, low levels were seen in 6 cases (15%) and high levels were seen in 2 case (5%). Serum Calcium levels were normal in all 40 controls.

Conclusion: There is no connection between the study participants' serum magnesium levels and febrile convulsions. Consequently, regular magnesium supplementation is not required in healthy people in order to prevent febrile convulsions. The determination of serum magnesium and calcium levels is essential to a rational understanding of the cause and management of febrile seizures. Changes in these traits might be connected to the type of seizure.

Keywords: Calcium, Magnesium, Febrile Seizures and Convulsion.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Febrile convulsion is a common seizure disorder in children, accounting for 2 to 5% of cases. When a child has seizures that are categorized as febrile, they happen when they are between the ages of six and sixty months, have a temperature of 38 degrees Celsius or higher, are not the result of a metabolic disturbance or an infection of the central nervous

system, and do not have a history of previous afebrile seizures. Every child who presents with a febrile seizure requires a thorough neurological and general evaluation in addition to a complete medical history. [1] When a child between the ages of six and sixty months has a temperature of 38 degrees or higher, and it is not associated with an

infection of the central nervous system or any kind of metabolic imbalance, and it does not happen in the absence of a prior history of afebrile seizures, it is considered to be experiencing febrile seizures. [2] A febrile seizure occurs when a child, aged six months to five years, has a feverish seizure without any concomitant brain infection, metabolic disturbance, or history of afebrile seizures. [3] The age-dependent response of the developing brain to a high body temperature is known as a febrile seizure. Research has been done to identify the risk factors, which include anomalies related to metabolism and micronutrients as well as family history. [4–5]

Magnesium ranks third among intracellular cations and is the body's fourth most common cation. Since 30 percent of magnesium can be transferred to enter the extracellular area, between 50 and 60 percent of magnesium in the body is found in bone, where it serves as a reservoir. Of the magnesium found within cells, only 25% is exchangeable; the rest is bound to proteins. Muscle and liver contain the majority of intracellular magnesium because their greater metabolic rates result in higher magnesium concentrations in these organs. The normal range of magnesium concentrations in plasma is 1.5–2.3 mg/dl. Magnesium is necessary for both membrane stability and nerve conduction. The majority of soft tissues, including muscle, erythrocytes, and bone, contain it. Due to its participation in the Na/K ATPase system, magnesium is essential for generating the electrical potential that exists between cell membranes. Magnesium is necessary for the enzymes that transmit nerve signals and maintain the integrity of cell membranes; hypomagnesemia makes muscles and neurons excitable. [6,7] A deficiency in magnesium causes an increase in calcium access into the nervous system, which in turn causes overstimulation, spasm, and convulsion since magnesium is a chemical gatekeeper. [8] Magnesium is a cofactor in several enzymatic reactions. It is important in energy metabolism, protein synthesis, RNA synthesis, and DNA synthesis in addition to preserving the electrical potential of nerve tissues and cell membranes. It contributes to the regulation of potassium and calcium flux metabolism. A decrease in magnesium levels results in decreased calcium plasma concentration and potassium depletion in muscles. By controlling the enzyme's activity, it modifies the calcium and potassium channels and promotes membrane integrity. Additionally, it maintains the integrity of the transmembrane gradients for potassium and sodium. [9,10] Magnesium affects neuronal activity and prevents calcium from facilitating synaptic transmission. Additionally, it selectively blocks the voltage-dependent N-methyl-D-aspartate (NMDA) receptor channel. Seldom has low serum magnesium been associated with

significant effects on the central nervous system, especially in epilepsy instances. Low serum magnesium levels have been found to be positively correlated with children's risk of febrile convulsions. [11] Serum magnesium levels below normal have been associated with significant effects on the central nervous system, especially in epileptic patients. There is little information available about serum magnesium levels in children who are having febrile convulsions. Therefore, a study was designed to measure the amounts of magnesium in the blood and establish a correlation between the serum levels of magnesium in children exhibiting febrile convulsions.

Material and Methods

The Department of Pediatrics used a duration-based prospective analytical case-control approach to conduct this study. Children between the ages of six months and five years who required hospitalization due to febrile seizures were classified as cases. Children in the same age range who were hospitalized for a febrile illness but did not have seizures served as controls. The parents/guardians of the selected study subjects were informed of the study's objectives in their mother tongue. An educational letter about the participant was given to them. Forty children in the research age group, aged between six months and five years, were hospitalized to the pediatric unit. Written, informed consent was provided by patients or their guardians who wished to take part in the trial.

Inclusion Criteria:

- Children diagnosed with febrile convulsions between the ages of six months and five years, provided they have normal neurological development.
- For the first time, children with febrile convulsions were admitted to the hospital.

Exclusion Criteria:

- Seizures due to CNS infections and metabolic causes
- Children on magnesium supplements and/or who received magnesium recently
- Children admitted with febrile convulsions but who were already evaluated during previous admission in our institution were excluded from the study

Blood Sample Collection: Three milliliters of entire blood were venipunctured using strict aseptic procedures and placed in a sterile, metal-free, acid-propylene-washed plastic test tube. The sample was left undisturbed for five hours to help the erythrocytes settle down. After that, aseptic centrifugation was used to separate the serum at a speed of 2500 revolutions per minute. The serum levels of calcium and magnesium were measured

quantitatively using colorimetric techniques with a star 21 plus semi-auto analyzer (Rapid Diagnostics Group of Companies Pvt Ltd, India). Serum micronutrient levels within a reference range for a specific age and gender were deemed normal in the study. Micronutrient levels were categorized as low or high in the study based on whether they were over the upper limit or below the lower limit of the sex- and age-specific ranges, respectively.

Statistical Analysis: Statistical analysis was done and the data was analyzed using mean standard deviation, Chi-square test/Fisher exact test, and proportions has been used to find the significance of study parameters. The statistical software namely statistical package for the social sciences (SPSS) 16.0 were used for the analysis of the data and Microsoft has been used to generate graphs, and tables.

Result

Table 1: Comparison of age, temperature, Hb, and TLC in both groups.

Parameter	Cases	Control
	Mean±SD	Mean±SD
Age (months)	9.73±2.32	39.24±17.01
Temperature (°F)	94.93±0.74	91.99±0.51
Total leukocyte count	12432.43±2198.78	9124.6±2176.77

The mean age of presentation of febrile convulsion was found to be 9.73±2.32 months. The mean temperature at which children had febrile convulsions was 94.93±0.74°F. There was no statistical significance between the cases and controls. Of all the 40 children with febrile convulsion, 30 were males accounting for 75%. The rest 10 (25%) were females.

Table 2: Comparison of causes in both groups.

Cause	Cases		Control	
	No.	%	No.	%
Diarrhea disease	5	12.5	15	37.5
ASOM	2	5	0	-
URTI	30	75	25	62.5
Viral fever	3	7.5	0	-
Grand total	40		40	

The most common cause for febrile convulsion in this study was upper respiratory tract infection – 30 cases (75%). followed by acute diarrhea disease in 5 (12.5%) and 3 case of viral fever and 2 cases of ASOM.

Table 3: Serum magnesium levels in both groups.

Serum Mg level	Cases	Control	Serum Calcium level	Cases	Control
	No.	No.		No.	No.
High	2	0	High	2	0
Low	5	0	Low	6	0
Normal	33	40	Normal	32	40
Grand total	40	40	Grand total	40	40

The levels of serum Mg were normal in 33 patients (82.5%) with febrile convulsion, low levels were seen in 5 cases (12.5%) and high levels were seen in 2 case (5%). Serum magnesium levels were normal in all 40 controls. The levels of serum Calcium were normal in 32 patients (80%) with febrile convulsion, low levels were seen in 6 cases (15%) and high levels were seen in 2 case (5%). Serum Calcium levels were normal in all 40 controls.

Discussion

Comparing the blood levels of calcium and magnesium in febrile children with convulsions to those in febrile children without convulsions was the aim of this investigation. Magnesium (Mg) is the third most prevalent cation within cells and the fourth most frequent cation overall in the body. The majority of soft tissues, including muscle,

erythrocytes, and bone, contain it. [12] Additionally, it alters the way that neurons function by inhibiting the facilitative effects of calcium on synaptic transmission as well as the voltage-dependent blockage of the N-methyl-D-aspartate (NMDA) receptor channel. [13] By opposing calcium ions at the presynaptic junction, magnesium reduces the release of acetylcholine at the neuromuscular junction, reverses cerebral vasospasm, and acts as an anticonvulsant. It also reduces the excitability of neurons. [14]

Chhparwal et al 1971 [15] determined Mg levels in the serum and in the CSF in 100 Indian children presenting with febrile convulsions and found out that children with febrile convulsions had low serum and CSF concentrations of magnesium and stated that there are certain biochemical changes that occur during the febrile state which possibly precipitate febrile convulsions.

Kiviranta et al 1995 [16] reported in one study that during acute febrile disease, mild disturbance of water and electrolyte balance occurs frequently and, in another study, it was suggested that changes in serum electrolyte levels, might enhance the susceptibility to seizure and its recurrence during a febrile disease in childhood.

The metabolism of calcium is impacted by magnesium as well. It is required for cyclic adenosine monophosphate (cAMP) production, which controls parathyroid hormone release. Not surprisingly, low magnesium levels are often associated with hypocalcemia. [17,18] In contrast our study had only 7 cases (5.83%) of hypocalcemia and it was absent in Balu ram and sherlin 2014 [19] study in our study. Hypocalcemia, hypoglycemia, and hyponatremia were the most frequent additional metabolic disorders linked to hypomagnesemia.

A study by Bharathi et al. 2016 [20] found a positive correlation between hypomagnesemia to simple febrile seizure, with no significant association between serum magnesium level and atypical febrile seizure in children.

Namalkin K et al. 2016 [21] In another study Talebian, et al. 2009 [22] study also the sex ratio was found to be contrasting to our study but there were no significant differences in the prevalence of Seizures among gender. The mean serum magnesium levels in the children with febrile convulsion and the feverish children without convulsion in our study were 2.10 mg/dl and 1.95 mg/dl, respectively.

Serum calcium levels were discovered to be a significant factor in children having febrile seizures during our experiment. The mean serum calcium levels in the case and control groups, however, are similar. This study found that the serum magnesium levels of children who have febrile seizures are normal. It implies that serum magnesium levels may not have a major impact on the pathophysiology of febrile convulsions. Our study sample was not representative of the entire population because all of the children were predominantly from the adjacent urban region. This study does not include children who often have febrile seizures.

Conclusion

There is no connection between the study participants' serum magnesium levels and febrile convulsions. Consequently, regular magnesium supplementation is not required in healthy people in order to prevent febrile convulsions. The determination of serum magnesium and calcium levels is essential to a rational understanding of the cause and management of febrile seizures. Changes in these traits might be connected to the type of

seizure. The association between changes in serum electrolytes and the prevalence of febrile seizures suggests that variations in serum electrolytes may play a clinically important role in the start of febrile seizures. Further comprehensive clinical studies are required to validate the association between hypomagnesemia and febrile convulsions. Further research is recommended to determine the impact of magnesium supplementation on the prevention of febrile convulsions. Serum magnesium levels in patients experiencing febrile convulsions were positively correlated with the case-control study. In order to demonstrate a statistically significant positive correlation between serum magnesium levels and febrile convulsions, a larger number of cases and more thorough investigation are required.

References

1. Mahyar A, Ayazi P, Fallahi M, Javadi A. Risk factors of the first febrile seizures in Iranian children. *Int J Pediatr.* 2010;2010:862897.
2. Leung A, Robson L, Febrile seizures. *J pediatric health care.* 2007;2(4):250-5.
3. Nelson textbook of pediatrics: Robert M. Kliegman, MD, Richard E. Behrman, MD, Hal B. Jenson, MD and Bonita F. Stanton, MD. 19th edition 2011.
4. Aly IA, Kmal HM, Soliman DR, Mohamed MH. Iron profile parameters and serum zinc & copper levels in children with febrile convulsions in Banha. *J Am Sci.* 2014;10:320–327.
5. Garty BZ, Olomucki R, Lerman-Sagie T, Nitzan M. Cerebrospinal fluid zinc concentrations in febrile convulsions. *Arch Dis Child.* 1995;73(4):338-41.
6. Steering Committee on Quality Improvement and Management, Subcommittee on Febrile Seizures American Academy of Pediatrics. Febrile seizures: clinical practice guideline for the long-term management of the child with simple febrile seizures. *Pediatrics.* 2008;121:1 281–1286.
7. Hamed SA, Abdellah MM. Trace elements and electrolytes homeostasis and their relation to antioxidant enzyme activity in brain hyperexcitability of epileptic patients. *J Pharmacol Sci.* 2004;96(4):349-59.
8. Castella-Guerra L, Del Carmen Fernandez, Lopezchozas. Electrolytes disturbances and seizures. *Epilepsia,* 2006,47(12):1990-8.
9. Mishra OP, Deepak Singhal, Ram S Upadhyay, Rajniti Prasad, and Divya Atri. CSF Zinc, Magnesium, Copper and GABA Levels In Febrile Seizures. *Journal of Pediatric Neurology,* 2007; 5: 39-44.
10. Ivanai Cepelak, Slavica Dodig. Magnesium-More Than A Common Cation. *Read 517. Medical Sciences,* 2013; 39: 47-68.

11. Mishra OP, Prasad R, Singh AR, Das BK, Upadhyay RS, Singh TB. Cerebrospinal fluid zinc, magnesium, copper, and gamma-aminobutyric acid levels in febrile seizures. *Journal of Pediatric Neurology*. 2007;5:39-44.
12. Shinnar S. Febrile seizures. In: Swaiman KF, Ashwal S, Ferriero DM, ed. *Pediatric neurology: principles and practices*. 4th edition. Philadelphia: Mosby, Elsevier, 2006; 1:1078- 86.
13. Waruiru C, Appleton R. Febrile seizures: an update. *Arch Dis Child*, 2004; 89(8): 751-6.
14. Suter C, Klingman W. Neurologic manifestations of magnesium depletion states. *Neurology (Minneap.)*, 1955; 5: 691-9.
15. Chhapparwal BC, Kohli G, Pohowalla JN, Singh SD. Magnesium levels in serum and in C.S.F. in febrile convulsions in infants and children. *Indian J Pediatr*. 1971;38(280):241-5.
16. Kiviranta T, Airaksinen EM, Tuomisto L. The role of fever on cerebrospinal fluid glucose concentration of children with and without convulsions. *Acta Paediatr*. 1995;84(11):1276-9
17. Chhapparwal BC, Kohli G, Pottowali JN, et al. Magnesium levels in serum and in CSF in febrile convulsions in infants and children. *Indian J Paediatrics*, 1971; 38(5): 241-5.
18. Benga I, Baltescu V, Tilinca R, et al. Plasma and cerebrospinal fluid concentrations of magnesium in epileptic children. *J Neurol Sci.*, 1985; 67(1): 29- 34
19. Sherlin, Baluramu. Serum magnesium level in febrile convulsions. *International Journal of Science and Research IJSR*, 2014; 3(10)
20. Bharathi S, Chiranjeevi K. Study of serum magnesium levels and its correlation with febrile convulsions in children aged 6 months to 5 years of age. *IAIM*. 2016;3:61-68.
21. Namakin K, Zaradast M, Sharifzadeh GH, Bidar T, Zargarian S. Serum Trace Elements In Febrile Seizures: A Case-Control Study. *Iran J Child Neural*, 2016; 10(3): 57-60.
22. Ahmad Talebian, Zarichehr Vakili, Safar Ali Talar. Assessment of The Relation Between Serum Zinc and Serum Magnesium Levels In Children With Febrile Convulsion. *Iranian Journal of Pathology*, 2009;4(4): 157- 160.