International Journal of Contemporary Pediatrics
Addlur S et al. Int J Contemp Pediatr. 2021 Apr;8(4):683-688
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20211077

Original Research Article

Correlation of serum magnesium levels in febrile convulsions in children: a cross sectional comparative study

Shalini Addlur[1], Rohit Khandelwal[2]*, Shivalingappa B. Mangajjera[2], Leeni Mehta[3]

[1]Junior Consultant, Columbia Asia Hospital, Bangalore, Karnataka, India
[2]Department of Paediatrics, Vydehi Institute of Medical Sciences and Research Centre, Bangalore, Karnataka, India
[3]Consultant Physician, Apollo Group of Hospitals, Bangalore, Karnataka, India

Received: 19 January 2021
Revised: 02 March 2021
Accepted: 05 March 2021

***Correspondence:**
Dr. Rohit Khandelwal,
E-mail: docrl16@gmail.com

ABSTRACT

Background: Febrile convulsions is one of the most common type of seizures seen in children. It has been suggested that low serum magnesium (Mg) has occasionally been associated with epilepsy. A positive correlation of the hypomagnesemia with the severity of epilepsy was also found. The present study aimed to estimate the levels of serum magnesium in children with febrile convulsions and to compare serum magnesium levels with normal children.
Methods: Fifty patients who were eligible after screening for inclusion and exclusion criteria were included in the study group after a signed written informed consent and 50 controls were also taken. A detailed history, clinical examination and these investigations were done – complete blood count (CBC) (Hb, DC and ESR), serum calcium, serum magnesium, serum electrolytes, random blood sugar and cerebrospinal fluid (CSF) analysis.
Results: The serum magnesium level was normal in 45 patients (90%) with febrile convulsions, low levels in 4 cases (8%) and high levels seen in 1 case (2%). Serum magnesium levels were normal in all 50 controls. In this study, the serum magnesium levels has got no correlation in patients with febrile convulsion. So, routine magnesium supplementation need not be prescribed in normal subjects to prevent febrile convulsions.
Conclusions: Routine measurement of serum levels of Mg, glucose and calcium are warranted in subject with febrile convulsions. However, large prospective studies are further required in future to establish the correlation of serum Mg and febrile convulsions so that a standard guidelines can be set up which could be followed universally.

Keywords: Serum magnesium, Febrile convulsions, Blood glucose

INTRODUCTION

Febrile convulsion is one of the most common seizure disturbances in children with an approximate rate of 3 to 4 percent.[1] Most febrile seizures are brief, do not require any specific treatment or workup, and have benign prognoses.

Magnesium (Mg) is the fourth most common cation in the body and third most common intracellular cation. It is mainly found in muscle, other soft tissues, bone and erythrocyte. Mg plays an important role in establishing the electrical potential across cell membranes as a result of its involvement in the Na/K ATPase system. Mg is needed for enzymes that play role in cell membrane stability and nerve conduction, and hypomagnesaemia leads to nerve and muscle excitability.[2,3]

It is also involved in neuronal function and it inhibits the facilitatory effects of calcium on synaptic transmission and also exerts a voltage dependent blockage of N-methyl-D-aspartate (NMDA) receptor channel. It has been suggested that low serum Mg has occasionally been associated with

significant effects on the central nervous system especially in epilepsy. A positive correlation of the hypomagnesemia with the severity of epilepsy was also found: the more severe the epilepsy, the lower was the plasma Mg. A significant increase of Mg concentration in cerebrospinal fluid (CSF) of epileptics was found. The most likely origin of Mg in CSF in epilepsy is the CNS tissue from which Mg is released. It is suggested that these alterations of Mg concentrations in plasma and CSF originate from a functional impairment of the cell membranes, which might occur in epilepsy.[4]

Studies done by Chhaparwal et al, Mishra et al, Ahmad et al and Papierkowski et al indicate that deficiency of Mg have contributing effect in the incidence of febrile convulsion.[5-8] Limited data is available on the levels of serum magnesium in children with febrile convulsions. Therefore a study was planned to estimate the levels of serum magnesium and establish the correlation between serum levels of magnesium in children with febrile convulsions.

METHODS

This study was a duration based prospective analytical case-control study conducted in the Department of Paediatrics, Vydehi Institute of Medical Sciences and Research Centre, Bangalore for a period of 1 year from March 2010 to February 2011.

Inclusion criteria

Children between the ages of 6 months to 5 years, who were developmentally normal, with febrile convulsions, children with febrile convulsion admitted for the first time to our hospital, age matched subjects admitted with minor ailments with no convulsions were taken as controls were included in the study.

Exclusion criteria

Children with history of congenital anomalies of central nervous system (CNS), neonatal seizure, neuro infection and other metabolic conditions causing seizure, children who had received magnesium supplements, and children with febrile convulsion who were admitted for the second time and evaluated previously in our institution were excluded from the study. Patients who were eligible after screening for inclusion and exclusion criteria were included in the study. Study was started after obtaining the signed written informed consent by the patient's caretaker.

A detailed history was obtained with regards to the fever – type, duration; convulsions – type, duration, number of episodes of convulsion, prior hospitalization and medications; co-morbid diseases, past history of convulsions, birth and developmental history, family history. The details were entered on case report form. A detailed clinical examination was done and observations were noted. Following investigations were carried out – complete blood count (CBC) (Hb, DC and ESR), serum calcium, and serum magnesium (measured using catalyst method immediately after admission by Synchron CX^R systems and change in absorbance at 520 nanometers), serum electrolytes, random blood sugar, and CSF analysis. Patients who were included in the study group were admitted in paediatric ward and managed according to the standard protocols for the particular ailments.

Ethical approval from the Institutional ethics committee was taken. 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 have been used to generate graphs, and tables.

RESULTS

Age

The mean age of presentation of febrile convulsion was found to be 20.88±11.38 months (Table 1).

Temperature

The mean temperature at which children had febrile convulsion was 101.44±0.99 ^oF.

Total leukocyte count

There was no statistical significance between the cases and controls.

Sex

Of all the 50 children with febrile convulsion, 37 were males accounting for 74%. The rest 13 (26%) were females with the ratio being M: F=2.8:1.

Cause of febrile convulsion

The most common cause for febrile convulsion in this study was upper respiratory tract infection – 43 cases (86%). Acute pharyngotonsillitis, seen in 34 children (68%), the second most common cause being acute pharyngitis seen in 9 children (18%), followed by acute diarrhoeal disease in 5 (10%) and one case of acute otitis media and viral fever (Table 2).

Family history

A positive family history was seen in 13 cases (26%).

Consanguinity

A positive consanguinity was seen in 6 cases (12%).

Blood sugar levels

High blood sugar levels were seen in 22 patients with febrile convulsion (44%). Normal blood sugar levels were seen in 28 cases (56%) (Table 3).

Serum magnesium

The levels of serum Mg was normal in 45 patients (90%) with febrile convulsion, low levels were seen in 4 cases (8%) and high levels seen in 1 case (2%). Serum magnesium levels were normal in all 50 controls (Table 4).

Serum magnesium levels was considered low if <1.7 mg/dl and high if >2.8 mg/dl.

Serum calcium

The levels of serum calcium were normal in both the cases and controls.

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

Parameter	Cases		Control		P value
	Mean±SD	Range	Mean±SD	Range	
Age (months)	20.88±11.38	6-60	27.46±15.01	6-60	0.015
Temperature	101.44±0.99	100-103	98.98±0.59	98.6-100	0.001
Total leukocyte count	13362.46±2313.84	8000-17200	9927.8±2690.881	4800-14500	0.001

Unpaired t test is applied; p value is significant if <0.05

Table 2: Comparison of causes in both the groups.

Cause	Cases		Control		Grand total	P value
	No.	%	No.	%	No.	
Diarrhoeal disease	5	10	12	24	17	
ASOM	1	2	0	-	1	
URI	43	86	38	76	81	0.172
Viral fever	1	2	0	-	1	
Grand total	50		50		100	

Fishers exact test is applied; p value is significant, if <0.05

Table 3: Comparison of blood sugar level in both the groups.

Blood sugar	Cases		Control		Grand total	P value
	No.	%	No.	%	No.	
High	22	44	0	-	22	
Normal	28	56	50	100	78	0.001
Grand total	50	100	50	100	100	

Fishers exact test is applied; p value is significant, if <0.05

Table 4: Serum magnesium levels in both the groups.

Serum Mg level	Cases		Control		Grand total	P value
	No.	%	No.	%	No.	
High	1	2	0	-	1	
Low	4	8	0	-	4	0.071
Normal	45	90	50	100	95	
Grand total	50	100	50	100	100	

Fishers exact test is applied; p value is significant, if <0.05.

DISCUSSION

Febrile convulsion is a terrifying event for the parents, which seeks emergent medical attention. Attempts have been made to identify predisposing risk factors like family history, metabolic disturbances (especially serum Mg, glucose and calcium).

Study population was divided in two groups: 50 children with febrile convulsion (cases) and 50 children without febrile convulsion (controls). Demographic parameters (e.g. gender, age) were comparable in both the groups. In cases, majority were males 74% and remaining were females (26%). This suggests a male preponderance. M: F=2.8:1. In control group, 62% are male and remaining were female (38%). No significant difference was seen in

mean age of cases (20.88 months) and control (27.46 months). In our study, both cases and control have comparable diagnoses. Cases had significant family history of febrile convulsion as compared to control (26% versus 6%). History of consanguinity and parity was not a risk factor.

Serum magnesium

We found no significant difference between the levels of serum magnesium levels of children with and without febrile convulsion ($p>0.05$), though 2% children in cases had high level and 8% had low level of serum magnesium as compared to control group who had normal serum magnesium levels in all children.

In atypical febrile convulsion, 9.09% had low magnesium levels, 90% had normal magnesium levels while in typical febrile convulsion, 89.74% had normal magnesium level, 7.69% had low magnesium level and 2.56% patients had high magnesium levels. Most of the patients had convulsion in between 10 to 15 minutes duration. Out of them, 35 patients (90%) had normal serum magnesium levels, 3 had low magnesium level and one patient had high serum magnesium levels. Our results are similar to those of other workers.[9-11]

Recent evidences indicate that the deficiency of Mg can play a significant role in febrile convulsions. Rutter et al in a study on 83 children with febrile convulsion and Woodbury et al showed no clear abnormality in plasma or CSF magnesium levels and concluded that magnesium levels do not play a role in the causation of febrile convulsion.[9,12] Chhaparwal et al 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.[5] In a study by Mishra et al levels of Mg and other elements were evaluated in CSF in Indian children with febrile seizure. The study subjects included 20 cases of febrile convulsion, 26 patients of encephalitis and 22 children of fever with meningismus. Author found that serum and CSF levels of magnesium, zinc, GABA were significantly reduced in children with febrile convulsions. There was a significant positive correlation between CSF and serum magnesium in study subjects and these findings suggest a relationship between low levels of Mg and predisposition to febrile convulsion in children.[6]

In Iran, Ahmed et al retrospectively studied the serum level of magnesium in 60 children of 3-72 months of age with febrile convulsion. The children of control group had no seizure. Study found that serum levels of magnesium and zinc were deficient in children of febrile convulsions and supplements of magnesium and zinc was suggested in diet of affected children for prophylaxis of febrile seizure recurrences.[7] A similar finding was found by Papierkowski, who estimated Mg and zinc levels in blood serum and cerebrospinal fluid in 18 children of 8 months-5 years with febrile convulsions.[8] Baek et al included 133 patients with febrile seizure and 141 control patients and found that hypomagnesemia (<0.50 mmol/l) was more common in patients with febrile seizure than in controls (42.9% versus 6.9%, $p<0.001$) and it was an independent risk factor for febrile seizure (OR, odds ratio=22.12, 95% CI=9.23–53.02, $p<0.001$). It was concluded that hypomagnesemia was more common and serum iMg^{2+} level was lower in patients with febrile seizures than in controls. However, further evidence is needed for the causal relationship between low magnesium and febrile convulsions.[13]

Kannachamkandy et al studied 35 children between six months to five years with febrile seizures as cases and 35 children with febrile illnesses without seizures as controls and concluded that high serum copper levels and low serum magnesium levels were significantly associated with febrile seizures.[14] Sherlin et al included children between the ages of 6 months to 5 years with febrile convulsions and found that serum Magnesium levels were low in 32% of the cases with febrile convulsion indicating that serum Magnesium levels has got positive correlation in patients with febrile convulsion.[15] Goutham et al in his study included two groups of 45 patients each with 6-60 month of age with febrile convulsion and fever without seizure respectively and got a positive co relation between levels of serum magnesium and febrile convulsion. However more studies at a larger level required to establish a strong correlation between the two.[16] Bharathi et al did an observational prospective study on 120 children aged 6 months to 5 years of age with history of fever and convulsions where no association was found with gender, age, and temperature of the patient and subtype of febrile convulsions but statistically significant association was found with hypomagnesemia and 'typical febrile convulsions' but no such association was found with atypical febrile convulsions.[17]

Obvious reason for above finding could be the need of magnesium for enzymes that play role in cell membrane stability and nerve conduction, and therefore hypomagnesaemia leading to nerve and muscle excitability.[18] Magnesium is also involved in neuronal function and it inhibits the facilitatory effects of calcium on synaptic transmission and also exerts a voltage dependent blockage of N-methyl-D-aspartate (NMDA) receptor channel. Low serum magnesium has occasionally been associated with significant effects on the central nervous system especially in epilepsy. A positive correlation of the hypomagnesemia with the severity of epilepsy was also found: the more severe the epilepsy, the lower was the plasma Mg.[4]

Blood glucose

Hyperglycaemia is relatively frequent in the course of severe illnesses and may be looked upon as the possible

result of an uncoordinated insulin response to the increased glucose that the body may need during periods of stress, it is generally agreed that it does not constitute a pre-diabetic condition. Hyperglycemia and hyperglycorrhagia are common associations of febrile seizures.19 Rapid release of cortisol and adrenaline after seizures as a stress reaction induces elevated glucose concentration in blood and CSF.[9] Fever intensity is also independently correlated with elevated CSF glucose level following febrile seizures.[20]

In our study, significantly high number of cases had high blood sugar as compared to control (p=0.001).The findings of our study are in the line of published literature. In a study by Rutter et al hyperglycaemia was a frequent finding and was reflected in raised CSF glucose levels whereas blood glucose levels were only transiently raised and none of the children had diabetes mellitus.9 In a study in 1199 children, Valerio et al found that hyperglycemia was significantly more prevalent in children affected by febrile seizures (12.9%) than any other diagnosis. It was more frequent in patients with body temperature >39 degrees C (14%) than in those with a temperature ≤39 ºC (4%; p<0.0008). Hyperglycemia was more prevalent in clinical conditions of fever associated with seizures or pain (12.9% and 12.5%, respectively) than fever alone (4.4%).[21]

Hyperglycemia is regarded as a consequence of convulsion-induced release of both cortisol and adrenaline.[1] Interleukin 1 beta (IL-1), an endogenous pyrogenic cytokine, inhibits insulin release and stimulates the secretion of cortisol.[22-24] This may explain why high number of cases had high blood sugar in our study. In fact many authors also reported significantly high blood glucose in the CSF in febrile children with and without convulsions than in non-febrile, non-convulsive children. Both fever and seizures increased the CSF glucose levels.[20]

Blood calcium

It is well documented that low levels of calcium are responsible for initiation of seizures. However, in our study serum calcium in seizure remained comparable to the control as reported by Rutter et al, Prasad et al and Sakha et al.[9,25,26] However, Govil et al and Sood et al showed higher levels of calcium in epileptic children.[11,27] Calcium facilitates the release of acetylcholine by nerve impulses, which may be responsible for neuromuscular irritability. Hypomagnesemia and hypercalcemia combine to produce a membrane state, which becomes responsive to an otherwise sub-threshold stimulus. Kiviranta et al reported in one study that during an 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.[20,28] Van Stuijvenberg et al in a study done in children with seizures associated with fever found that abnormal biochemical blood test results are rare and outside the morbidity range and in children with a low probability of a normal result as calculated by the score chart, the test may be indicated.[29] On the other hand, Kenney et al have shown that routine measurements of biochemical tests are not necessary in febrile convulsion.[30]

The limitations of this study are that the sample size was small compared to the general population and the patients were not followed up later with the repeat blood levels of magnesium.

CONCLUSION

In this study, the serum magnesium levels has got no correlation in patients with febrile convulsion. So, routine magnesium supplementation need not be prescribed in normal subjects to prevent febrile convulsions. The estimation of serum levels of magnesium, glucose and calcium are essential for the rational understanding of pathogenesis and management of febrile seizure. The changes in these parameters might be associated to the type of seizure. The association between serum electrolytes changes and incident febrile seizure suggests that alteration in serum electrolytes is likely to play a clinically significant role in causing febrile seizures.

Therefore, routine measurement of serum levels of Mg, glucose and Ca are warranted in subject with febrile seizure. However, large prospective studies are further required in future to establish the correlation of serum magnesium and febrile convulsions so that a standard guidelines can be set up which could be followed universally.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Michael V. Nelson Textbook of Pediatrics. 17th ed. Philadelphia: WB Saunders. 2004.
2. Garty BZ, Olomucki R, Lerman-Sagie T, Nitzan M. Cerebrospinal fluid zinc concentrations in febrile convulsions. Arch Dis Child. 1995;73(4):338-41.
3. 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.
4. Benga I, Baltescu V, Tilinca R, Pavel O, Ghiran V, Muschevici D, et al. Plasma and cerebrospinal fluid concentrations of magnesium in epileptic children. J Neurol Sci. 1985;67(1):29-34.
5. Chhaparwal 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.
6. 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. J Pediatr Neurol. 2007;5:39-44.
7. Ahmad T, Zarichehr V, Ali TS, Mahbobeh KS, Abbas MS. Assessment of the relation between serum zinc & magnesium levels in children with febrile convulsion. Iranian J Pathol. 2009;4(4):157-60.
8. Papierkowski A, Mroczkowska-Juchkiewicz A, Pawłowska-Kamieniak A, Pasternak K. Magnesium and zinc levels in blood serum and cerebrospinal fluid in children with febrile convulsions. Polski Merkuriusz Lekarski: Organ Polskiego Towarzystwa Lekarskiego. 1999;6(33):138-40.
9. Rutter N, Smales OR. Calcium, magnesium, and glucose levels in blood and CSF of children with febrile convulsions. Arch Dis Child. 1976;51(2):141-3.
10. Shah QA, Jamil AA, Gupta VP, Kabiraj MM, Shah AH. Changes in Serum Electrolytes in Childhood Epilepsy: A Hospital Based Prospective. Greenwich J Sci Tech. 2001;2:18-27.
11. Govil MK, Mangal BD, Alam SM, Mahendru RK, Srivastava DK, Mudgal JC. Serum and cerebrospinal fluid calcium and magnesium levels in cases of idiopathic grand mal epilepsy and induced convulsions. J Assoc Phys India. 1981;29(9):695-9.
12. Woodbury J, Lons K, Carretta R, Hahn A, Sullivian J. Cerebrospinal fluid and serum levels of magnesium, calcium. Neurology. 1968;18:700.
13. Baek SJ, Byeon JH, Eun SH, Eun BL, Kim GH. Risk of low serum levels of ionized magnesium in children with febrile seizure. BMC Pediatr. 2018;18(1):297.
14. Kannachamkandy L, Kamath SP, Mithra P, Shenoy J, Bhat KG, Baliga BS. Association between serum micronutrient levels and febrile seizures among febrile children in Southern India: A case control study. Clin Epidemiol Global Health. 2020;8(4):1366-70.
15. Sherlin I, Balu Ramu. Magnesium Level in Febrile Convulsions. Int J Sci Res. 2014;3(10):850-1.
16. Goutham A, Dhingra P, Shankar P. Serum Magnesium Level in Febrile Convulsion. Int J Gen Pediatr Med. 2017;2(1):7-10.
17. 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. Int Arch Integrated Med. 2016;3:61-8.
18. Rude RK. Magnesium metabolism and deficiency. Endocrinol Metab Clin North Am. 1993;22(2):377-95.
19. Wallace S. Investigation at presentation. The Child with Febrile Seizures. London: Wright. 1988;70-80.
20. 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.
21. Valerio G, Franzese A, Carlin E, Pecile P, Perini R, Tenore A. High prevalence of stress hyperglycaemia in children with febrile seizures and traumatic injuries. Acta Paediatr. 2001;90(6):618-22.
22. Reimers JI. Interleukin-I beta induced trasient diabetes mellitus in rats. A model of the initial events in the pathogenesis of insulin-dependent diabetes mellitus. Dan Med Bull. 1998;45:157-80.
23. Dinarello CA. Biology of interleukin-1. FASEB J. 1988;2:108-15.
24. Lang CH, Cooney R, Vary TC. Central interleukin-1 partially mediates endotoxin-induced changes in glucose metabolism. Am J Physiol. 1996;271(2):309-16.
25. Prasad R, Singh AR, Das BK, Upadhyay RS, Singh TB, Mishra OP. Cerebrospinal fluid and serum zinc, copper, magnesium and calcium Levels in children with idiopathic seizure. J Clin Diagn Res. 2009;1841-6.
26. Sakha K, Barzar M. Evaluation of Serum Sodium and Ionized Calcium Levels in Febrile Convulsions. Pediatr Med Chir. 1985;7(2):249-52.
27. Sood AK, Handa R, Malhotra RC, Gupta BS. Serum, CSF, RBC, Urinary Levels of Magnesium and Calcium in Idiopathic generalized tonic clonic Seizures. Indian J Med Res. 1993;98:152-9.
28. Kiviranta T, Tuomisto L, Airaksinen EM. Osmolality and electrolytes in cerebrospinal fluid and serum of febrile children with and without seizures. Eur J Pediatr. 1996;155(2):120-5.
29. Van Stuijvenberg M, Van Gijssel EN, Steyerberg EW, Moons KG, Derksen-Lubsen G, Moll HA. Seizures associated with fever: clinical data as predictors for normal biochemical blood levels. Eur J Pediatr. 1998;157(7):592-8.
30. Kenney RD, Taylor JA. Absence of serum chemistry abnormalities in pediatric patients presenting with seizures. Pediatr Emerg Care. 1992;8(2):65-6.

Cite this article as: Addlur S, Khandelwal R, Mangajjera SB, Mehta L. Correlation of serum magnesium levels in febrile convulsions in children: a cross sectional comparative study. Int J Contemp Pediatr 2021;8:683-8.