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Original Research Article

Correlation of Serum Magnesium and Calcium Levels in Febrile Convulsions in Children

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Abstract

Background: Numerous studies have demonstrated a link between the incidence of febrile convulsions and the levels of magnesium, zinc, and copper in serum and cerebrospinal fluid (CSF). Convulsions caused by the central nervous system's hyperexcitability are a hallmark of hypomagnesaemia. One of the most prevalent kinds of seizures in children is febrile convulsions. There have been hints that epilepsy and low serum magnesium (Mg) may occasionally be related. Additionally, a favorable link between the severity of epilepsy and hypomagnesemia was discovered. Seizures classified as febrile are those that happen between the ages of six and sixty months, with a temperature of 38 degrees Celsius or above, are not brought on by an infection of the central nervous system or other metabolic disturbance, and do not have a history of previous afebrile seizures. A seizure is a brief episode of symptoms and/or signs brought on by abnormally high levels of synchronous or excessive neuronal activity in the brain.

Aim: To Study the Serum levels of Magnesium and Calcium in children: 6 months - 5 years of age with febrile convulsions and to establish the correlation between serum Magnesium and Calcium levels and febrile convulsions

Material and Method: This study was carried out in the Department of Pediatrics using a duration-based prospective analytical case-control design. Cases were defined as children who needed to be hospitalized due to febrile seizures and were between the ages of six months and five years. As controls, we included children in the same age range who were admitted to the hospital due to a febrile illness without seizures. The study objectives were conveyed to the parents/guardians of the chosen study subjects in their native tongue. They received an informative letter on the participant. In all, forty the research age group of children, ranging from 6 months to 5 years, was admitted to the pediatric unit. Patients who wished to participate in the trial or their guardians gave written, informed consent.

Results: The mean age of presentation of febrile convulsion was found to be 18.77±10.32 months. The mean temperature at which children had febrile convulsions was 95.33±0.88ºF. The differences between the cases and controls were not statistically significant. There were 24 children (68%), with 24 cases of acute pharyngotonsillitis; 7 cases (18%) of acute pharyngitis; 3 cases (10%) of acute diarrheal illness; and 1 case each of acute otitis media and viral fever. According to the current study's analysis of the mean serum calcium levels, all of the subjects in the control group had normal serum calcium levels, and the association between the two groups was found to be statistically significant. Among the cases, 90% of the subjects had normal levels and 10% had abnormal levels.

Conclusion: There is no link between the serum magnesium levels and febrile convulsion in participants in this study. Therefore, in healthy patients, routine magnesium supplementation is not necessary to avoid febrile convulsions. Calculating serum magnesium and calcium levels is crucial for a logical comprehension of the etiology and treatment of febrile seizures. The type of seizure may be related to changes in these characteristics.

Keywords: Magnesium, Calcium, Febrile Seizures, Convulsion. Hypomagnesemia.

Introduction

One of the most frequent seizure disorders in children is febrile convulsion, which affects 2 to 5% of cases. Seizures classified as febrile occur when a child is between the ages of six months and sixty months, has a temperature of 38 degrees Celsius or above, is not the product of a central nervous system infection or any other metabolic disturbance, and does not have a history of previous afebrile seizures. A comprehensive neurological and general examination, as well as a full history, are necessary for every child who arrives with a febrile seizure. [1] A child between the ages of six and sixty months is said to be experiencing febrile seizures when they have a

temperature of 38 degrees or higher, which is not related to a central nervous system infection or any type of metabolic imbalance, and which does not occur in the absence of a previous history of afebrile seizures. [2] When a child, between the ages of six months and five years, experiences a feverish seizure without any accompanying cerebral infection, metabolic disruption, or history of afebrile seizures, it is referred to as a febrile seizure. [3] A febrile seizure is the developing brain's age-dependent reaction to a high body temperature. Studies have been conducted in an effort to determine the risk factors, which include metabolic and micronutrient abnormalities as well as family history. [4–5]

Third among intracellular cations, magnesium is the fourth most prevalent cation in the body. Between 50 and 60 percent of magnesium in the body is found in bone, where it acts as a reservoir since 30 percent of it can be exchanged to enter the extracellular area. Just 25% of the intracellular magnesium is exchangeable; the majority is attached to proteins. The majority of intracellular magnesium is found in muscle and liver because these tissues have higher magnesium concentrations due to their higher metabolic rates. Magnesium levels in plasma typically range from 1.5 to 2.3 mg/dl. Nerve conduction and membrane stability depend on magnesium. It is mostly present in bone, erythrocytes, muscle, and other soft tissues. Because of its involvement in the Na/K ATPase system, magnesium plays a crucial function in creating the electrical potential across cell membranes. Enzymes involved in nerve transmission and cell membrane integrity require magnesium, and hypomagnesemia causes excitability of the muscles and nerves. [6,7] Since magnesium is a chemical gatekeeper, a magnesium deficit leads to an increase in calcium entry into the nervous system, which ultimately results in overstimulation, spasm, and convulsion. [8] In numerous enzymatic processes, magnesium serves as a cofactor. In addition to maintaining the electrical potential of nerve tissues and cell membranes, it is involved in energy metabolism, protein synthesis, RNA synthesis, and DNA synthesis. It plays a part in controlling the metabolism of calcium and potassium fluxes. Decreased calcium plasma concentration and potassium depletion in muscles are caused by a drop in magnesium levels. It modulates the calcium and potassium channels and facilitates membrane stability by regulating the activity of the enzyme. It is also in charge of keeping the sodium and potassium transmembrane gradients intact. [9,10] Magnesium has a role in neuronal activity and blocks the facilitative effects of calcium on synaptic transmission. It also blocks the N-methyl-D-aspartate (NMDA) receptor channel in a voltage-dependent manner. On rare occasions, low serum magnesium has been linked to substantial effects on the central nervous system, particularly in cases of epilepsy. Researchers have discovered a favorable association between children's propensity for febrile convulsions and low serum magnesium levels. [11] Low serum magnesium levels have been linked to major impacts on the central nervous system, particularly in cases of epilepsy. Information regarding serum magnesium levels in children experiencing febrile convulsions is scarce. Thus, a study was designed to determine the correlation between serum levels of magnesium in children experiencing febrile convulsions and to estimate the amounts of magnesium in the blood.

Material and Methods

This study was carried out in the Department of Pediatrics using a duration-based prospective analytical case-control design. Cases were defined as children who needed to be hospitalized due to febrile seizures and were between the ages of six months and five years. As controls, we included children in the same age range who were admitted to the hospital due to a febrile illness without seizures. The study objectives were conveyed to the parents/guardians of the chosen study subjects in their native tongue. They received an informative letter on the participant. In all, forty the research age group of children, ranging from 6 months to 5 years, was admitted to the pediatric unit. Patients who wished to participate in the trial or their guardians gave written, informed consent.

Cases: are defined as seizures that occurs between the age of 6 and sixty months, with a temperature of 38° C or higher, that are not the result of central nervous system infection or any metabolic imbalance, and that occur in the absence of a history of prior a febrile seizure.

Controls: Age and sex-matched children admitted to the pediatric ward with fever but without seizures. Fever in controls was defined as the axillary temperature above 99°F or Oral temperature above 100°F

Inclusion Criteria:

- Children from 6 months to 5 years of age with normal Neurological development with a diagnosis of Febrile Convulsions.
- Children with febrile convulsions were admitted for the first time to our hospital

Exclusion criteria:

- Seizures due to CNS infections and metabolic causes
- Children with a History of Neonatal seizures
- 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

A thorough history of the presenting complaints was taken before the children were enrolled in the trial. This included information on the length of the fever, the time it took for the seizures to start, the type of seizures, how long they lasted, any prior history of seizures, and any family history of seizures. A history of any symptoms that might have contributed to the febrile episode, such as a cold or cough, nasal or ear discharge, burning during micturition, or sobbing during it, was also documented.

A thorough medical history was taken, covering the kind and duration of the fever, the co-occurring conditions, the convulsions' historical history, the number of episodes, the type, duration, and the number of hospitalizations and drugs, as well as the birth and developmental history and family history. The case report form was filled up with the information. A thorough clinical assessment was conducted, and findings were recorded. The study group's patients were admitted to the pediatric ward and treated in accordance with established guidelines for specific conditions.

Blood Sample Collection:

Using stringent aseptic measures, three milliliters of whole blood were drawn via venipuncture in a sterile, metal-free, acid-propylene-washed plastic test tube. To facilitate the erythrocytes' settling down, the sample was left undisturbed for five hours. After that, the serum was separated using aseptic centrifugation at 2500 revolutions per minute. Quantitative colorimetric techniques were used to measure the serum magnesium and calcium levels using a star 21 plus semi-auto analyzer (Rapid Diagnostics Group of Companies Pvt Ltd, India). In the study, the serum micronutrient levels that were within a given reference range for a given sex and age were considered normal. In the study, micronutrient levels were classified as low or high if they fell below the lower limit of the sex- and age-specific ranges, respectively, or over the upper limit.

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)	18.77±10.32	25.42±13.01
Temperature	95.33±0.88	92.85±0.55
Total leukocyte count	12351.43±2218.78	8924.6±2587.771

The mean age of presentation of febrile convulsion was found to be 18.77±10.32 months. The mean temperature at which children had febrile convulsions was 95.33±0.88ºF. There was no statistical significance between the cases and controls. Of all the 40 children with febrile convulsion, 30 were males accounting for 74%. The rest 10 (26%) were females.

Table 2: Comparison of causes in both groups.

Cause	Cases		Control	
	No.	%	No.	%
Diarrhea disease	4	10	10	24
ASOM	1	2	0	-
URI	34	86	30	76
Viral fever	1	2	0	-
Grand total	40		40	

The most common cause for febrile convulsion in this study was upper respiratory tract infection – 34 cases (86%). Acute pharyngotonsillitis was seen in 24 children (68%), the second most common cause being acute pharyngitis seen in 7 children (18%), followed by acute diarrhea disease in 3 (10%) and one case of acute otitis media and viral fever.

Table 3: Serum magnesium levels in both groups.

Serum Mg level	Cases		Control	
	No.	%	No.	%
High	1	2	0	-
Low	3	8	0	-
Normal	36	90	40	100
Grand total	40	100	40	100

The levels of serum Mg were normal in 35 patients (90%) with febrile convulsion, low levels were seen in 4 cases (8%) and high levels were seen in 1 case (2%). Serum magnesium levels were normal in all 40 controls. Serum magnesium levels were considered low if 2.8 mg/dl. The association was found to be statistically significant between the two groups on comparing Mean Serum Magnesium.

Table 4: Comparison of Serum Calcium among Both the groups

		Cases	Control
Serum Calcium	Normal	35(90%)	40(100%)
	Abnormal	5(10%)	0(0%)

In the present study on analyzing the mean serum calcium levels, it was found that among the cases group nearly 90% of them had normal levels and 10% of them had abnormal serum calcium levels and in the control group all the subjects had normal serum calcium levels and the association between both the groups was found to be statistically significant.

Discussion

The purpose of this study was to compare the serum levels of calcium and magnesium in children with febrile convulsions to those of febrile children without convulsions. The fourth most common cation in the body and the third most common cation inside cells is magnesium (Mg). It is mostly present in bone, erythrocytes, muscle, and other soft tissues. [12] It also affects how neurons operate, blocking the facilitative effects of calcium on synaptic transmission and blocking the N-methyl-D-aspartate (NMDA) receptor channel in a voltage-dependent manner. [13] Magnesium works as an anticonvulsant, reverses cerebral vasospasm, and lessens the release of acetylcholine at the neuromuscular junction by opposing calcium ions at the presynaptic junction. It also lessens neuronal excitability. [14]

Rutter et al. 1976 [15] in a study on 83 children with febrile convulsion and Woodbury et al. 1968 [16] 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. Chhaparwal et al. 1971 [17] 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 [18] 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. Van Stuijvenberg et al. 1998 [19] 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.

Magnesium has an impact on calcium metabolism as well. It is necessary for the synthesis of cyclic adenosine monophosphate (cAMP), which regulates the release of parathyroid hormone. Unsurprisingly, hypocalcemia is frequently linked to magnesium insufficiency. [20,21] in contrast our study had only 7 cases (5.83%) of hypocalcemia and it was absent in Balu ram and sherlin 2014 [22] study in our study. The most common other metabolic abnormalities associated with hypomagnesemia were hypocalcemia followed by hypoglycemia and hyponatremia.

A study by Bharathi et al. 2016 [23] 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 [24] In another study Talebian, et al. 2009 [25] 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. In our study, the mean serum magnesium levels were 2.10 mg/dl and 1.95 mg/dl in children with febrile convulsion, and febrile children without convulsion respectively. Similar results are demonstrated in Y. Sree Krishna, et al. 2013 [26] Nahid K khosroshahi, et

al.2015 [27] N.Nutter et al. 1976 [28], and Burhanoglu study et al. 1996 [29] However the mean serum magnesium levels in these studies are high when compared to our study. In contrast to our study Talebian, et al.2009 [25] Papierkowski Namakin et al.1999 [30] Sreenivasaiah et al. 2016 [31], and Dr. Sherlin banu et al.2 014 [32] revealed that the serum 78 magnesium levels are significantly lower than compared to normal children but those studies were done in limited.

The mean serum magnesium level in N. Nutter et al. 1976 [28] and Y. Sree Krishna, et al. 2013 [26] studies were 2.3mg/dl and 2.1 mg/dl respectively. The mean serum magnesium level in controls was 1.95 mg/dl which is slightly lower than the children with febrile seizures. In Talebian, et al. 2009 [25] Namalkin K et al. 2016 [24], and N. Nutter et al. 1976 [28] studies the mean serum magnesium levels are in the upper limit of normal levels. In our investigation, serum calcium levels were found to play a major influence in children experiencing febrile seizures. However, the case and control groups' mean serum calcium levels are comparable. According to this study, children who experience febrile seizures have normal serum magnesium levels. It suggests that the pathophysiology of febrile convulsions may not be significantly influenced by serum magnesium levels. Because all of the children in our study were primarily from the nearby metropolitan area, our study sample was not representative of the total population. Children that experience febrile seizures frequently are not included in this study.

Conclusion

There is no link between the serum magnesium levels and febrile convulsion in participants in this study. Therefore, in healthy patients, routine magnesium supplementation is not necessary to avoid febrile convulsions. Calculating serum magnesium and calcium levels is crucial for a logical comprehension of the etiology and treatment of febrile seizures. The type of seizure may be related to changes in these characteristics. Changes in serum electrolytes are likely to be a clinically relevant factor in the onset of febrile seizures, as evidenced by the correlation between changes in serum electrolytes and incidence febrile seizures. More extensive clinical investigations are necessary to confirm the connection between febrile convulsions and hypomagnesemia. It is advised to conduct more research to ascertain how magnesium supplementation affects the prevention of febrile convulsions. Patients with febrile convulsions showed a positive association between their serum magnesium levels and the case-control research. To prove that there is a significant positive link between serum magnesium levels and febrile convulsions, more extensive research including a large number of cases is necessary.

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