Original Research Article

A Study on Association of Serum Electrolytes in Febrile Seizures - A Prospective Observational Study in a Tertiary Care Centre in Hyderabad

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Abstract

Background: Brain, among many other human tissues and organs, may be influenced by electrolyte disturbances. Therefore, electrolytes need to be immediately recognized as they may cause severe and life- threatening complications when neglected or not appropriately treated. Seizures are often seen in patients with sodium disorders. Hence, our main objective of study was to assess the occurrence and association of dyselectrolytemia in febrile seizures. **Methods:** This is a prospective study conducted for one year in a tertiary care institute on 50 children having febrile seizures which is the study Group 1 and another 50 children who had fever but no seizures which constituted the Group 2 group. Serum electrolytes (Sodium, Potassium and Chloride) levels are measured in the above 100 children. Statistical analysis was done to assess the occurrence of dyselectrolytemia in febrile seizures. **Results:** The association between the demographic features of the children and the febrile seizures in them was not seen as the results obtained were not statistically significant. Among 50 children in the Group 1 with febrile seizures, 17 children had abnormal levels of serum sodium in the form of hyponatraemia. All the children in the other group with no febrile seizures had normal serum sodium levels. 11 children who had recurrent febrile seizures in the same febrile period also had low sodium levels. The association of serum potassium levels and chloride levels with febrile seizures was not noted as the results showed no statistical significance. **Conclusions:** Our study concludes that there is a significant association of serum electrolytes especially serum sodium levels with febrile seizures in children. Hence monitoring of the sodium levels in those with febrile seizures is of utmost importance in children not only to decrease the recurrence of seizures but also for effective prevention.

Keywords: Children, Chloride, Electrolytes, Febrile Seizures, Hyponatraemia, Potassium, Recurrent Seizures, Sodium.

Background

Febrile seizures are one of the most common problems in India Incidence in India is 3-5 %. Peak incidence is usually 2nd year of life. FS is usually benign having excellent prognosis. Most FS are simple; however, up to 30 % might have some complex features. The risk of recurrence of FS is related to various factors, including younger age group, prolonged seizure duration, degree of fever, and positive personal and family history of FS [1]. Owing to their association with epilepsy in future, various studies have been conducted to identify the risk factors associated with them viz, family history of febrile seizures, epilepsy, perinatal factors, temperature peak, perinatal factors, genetic factors, maternal smoking and alcohol consumption during pregnancy, but risk factors remain largely unknown [2,3].

Preliminary studies in children support the hypothesis that the cytokine network is activated and may have a role in the pathogenesis of febrile seizures, but the precise clinical and pathological significance of these observations is not yet clear [4].

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During routine electrolyte studies in patients with FS, some researchers found the serum levels of sodium to be lower in children with new repeated episodes of FS within the same febrile period and although serum sodium levels cannot assist in prediction of recurrence of FS in children, relative hyponatremia, may predispose the febrile child to occurrence of simple FS [5,6,7,8,]. As Sodium plays an important role in cell physiology, neuronal cell depolarization, production of electrical discharge and finally seizures result. The need to evaluate and correlate serum sodium levels in febrile convulsions becomes significant [9]. However, the American Academy of Pediatrics Practice doesn't recommend sending serum electrolytes, calcium, phosphorus, magnesium, blood glucose routinely for evaluation of a child with febrile convulsion, unless clinically indicated. [10].

Methods

This is a comparative cross-sectional study conducted for a period of one year from May 2018 to April 2019 in the age group of 6 months to 5years admitted in paediatrics wards of Niloufer hospital. Sample size calculation was calculated based on the previous literature. According to a previous literature [11,12], an estimated occurrence of hyponatremia in febrile seizures, was reported to be 35%. With 95% confidence interval and absolute precision (d) of 10%, sample size of 88 was calculated using the formula $n=z^2(pq/d^2)$, where, z=1.96 at 95% confidence interval, p = 35% (estimated occurrence of hyponatremia/ abnormal sodium), q=100-p (65.0%) and d = absolute precision (10%). Considering 10% of 88 i.e., 8.8 ≈9 as non-response rate, a total sample size of 97 was estimated which was rounded off to

100. A total of 100 was equally divided among the two groups comprising 50 among each group.

Group-1 consisted of 50 Children aged between 6 months to 5 years who had febrile Seizures with recorded temperature of 38 degree Celsius (100.4-degree Fahrenheit) or more. Group-2 consisted of another 50 children of same age group with fever and but did not have seizures. Children presenting with unprovoked seizures, prior history of inborn errors of metabolism, seizures due to significant head trauma, suspected cerebral malaria, nervous system pathology, prior history of birth asphyxia and developmental delay were excluded from the study.

Study was started after obtaining approval from the institutional ethics committee and a signed written informed consent by the patient's care taker. A detailed history was obtained with regards to fever type and duration, convulsions type and duration, number of episodes of seizures, prior hospitalization and medication, co-morbid diseases, past history of seizures, history of consanguinity, family history of epilepsy, birth and developmental history. The details were entered on case report form. A detailed clinical examination was done and observations were noted. All the necessary investigations like complete blood count, serum sodium, serum potassium, serum chloride, and if needed EEG and lumbar puncture were carried out. Patients who were included in the study group were admitted in paediatric ward and managed according to the standard protocols for the particular ailments.

Statistical analysis was done after data was entered in tables, charts and graphs using Microsoft word and Excel and analysed using EPI INFO version 7. Data was summarized in percentages and proportions. The categorical variables age group, gender and dyselectolytemia (normal and abnormal) were presented as proportions. Fisher's exact test was applied to assess the association between abnormal electrolyte levels and presence of febrile seizures. P value of <0.05 was considered statistically significant.

As already mentioned, Group-1 consisted of 50 children with febrile seizures and Group 2 had 50 children with fever and but no seizures. Observations made during the study are shown in the form of tables and charts as follows. In our study, out of 50 children in group-1, with febrile seizures, 41 (82 %) children had simple febrile seizures and 9 (9 %) children had complex febrile seizures according to the definition.

Certain baseline characteristics were analysed in the present study. Analysing the age distribution among the children in Group-1 we noted that, 38% i.e., 19 children were under one year of age. 15 children (30 %) were between 1 to 2 years, 9 children (18 %) were between 2 to 3 years, 5 children (10 %) were in the age group of 3 to 4 years and 2 children (4 %) were 4 to 5 years. Almost similar distribution for age was noted in children admitted in Group-2. P Value (0.187) was calculated and found to be not significant and the groups were comparable. Similarly, gender distribution was analysed in both groups. Male children were 32 (64 %) and females were 18 (36 %) in Group-1, whereas in Group-2, males were 28 (56%) and female children were 22 (44%). Calculated P value (0.414) was not significant. Both the groups were compared based on the family history of Epilepsy. No significant association was noted in this study (P value =0.084 NS) with regards to the family history of Epilepsy. Similarly, no significant association was noted (P=0.373 NS) among the groups with history of Consanguinity. In this study, the mean temperatures recorded in the group with febrile seizures and group with no febrile seizures was 102.168^0F and 102.4^0F respectively. However, no significant association was noted with this parameter (P value =0.322 NS).

Children in both the groups were distributed and studied based on the probable focus of fever (Table 1). Most of the those with febrile seizures (42 %) as well as in the other group (32 %) had Upper Respiratory tract infections, which was the probable focus of fever in our study.

Results

Table 1: Distribution of study subjects based on probable Focus of Fever

Probable Focus	Group 1	Group 2	Total
ASOM	2 (4 %)	2 (4 %)	4 (4 %)
Diarrhoea	6 (12 %)	4 (8 %)	10 (10 %)
Dysentery	1 (2 %)	0 (0 %)	1 (1 %)
Enteric fever	2 (4 %)	5 (10 %)	15 (15 %)
LRTI	0 (0 %)	4 (8 %)	4 (4 %)
URTI	21 (42 %)	16 (32 %)	37 (37 %)
WALRI	2 (4 %)	4 (8 %)	6 (6 %)
Viral fever	12 (24 %)	6 (12 %)	18 (18 %)
No focus	4 (8 %)	9 (18 %)	13 (13 %)
Total	N = 50	N = 50	N = 100
FS – Febrile seizures.		Chi square = 11.951, P value = 0.153 (NS)	

The occurrence of dyselectrolytemia among the children with febrile seizures (Group-1) was compared with the non-seizure group (Group-2). 17 % children in the Group 1 had abnormal sodium levels in the form of hyponatraemia. However, none of the children in the other group i.e., children with fever but no seizures, showed no abnormalities in the Serum Sodium levels. This feature was statistically significant in our study with a P value equal to 0.001 (S) (Table-2).

In this study, 17 children in the study group with febrile seizures had recurrent seizures within the same febrile period. The remaining 33 children in the same group did not have any recurrence. Based on this aspect, another feature that was noted in our study was that the serum sodium levels were found to be low in 18.2% children in Group 1, who had recurrent seizures in the same febrile period. This point was statistically significant (P value =0.001) (Table 3).

Table 2: Association of serum sodium levels with febrile seizures

Serum Sodium Levels	With FS	Without FS	Total
Abnormal (Hyponatraemia)	17 (34 %)	0 (0 %)	17 (17 %)
Normal	33 (66 %)	50 (50 %)	83 (83 %)
Total	50	50	100
FS – Febrile seizures.		Chi square = 20.482, P value = 0.001 (S)	

Table 3: Serum Sodium Levels in Group 1 with Recurrent Seizures within same Febrile Period

	Recurrence Absent	Recurrence Present	Precentage
Sodium levels abnormal	6 (18.2 %)	11 (64.7 %)	17 (34 %)
Sodium levels normal	27 (81.8 %)	6 (35.3 %)	33 (66 %)
Total	33	17	50
Chi square = 10.822, P value = 0.001 (S)			

Table 4: Association of serum potassium levels with febrile seizures

Serum Potassium Levels	With FS	Without FS	Total
Abnormal	1 (2 %)	0 (0 %)	1 (1 %)
Normal	49 (98 %)	50 (50 %)	99 (99 %)
Total	50	50	100
FS – Febrile seizures.		Chi square = 1.010, P value = 0.315 (NS)	

Table 5: Association of serum chloride levels with febrile seizures

	With FS	Without FS	Total
Abnormal	1 (2 %)	1 (2 %)	2 (2 %)
Normal	49 (98 %)	49 (49 %)	98 (98 %)
Total	50	50	100
FS – Febrile seizures.		Chi square = 0.001, P value = 1.000 (NS)	

There was no significant association for both serum Potassium and Chloride levels when they were analysed in both the study groups. The P value was > 0.05. [Table 4 & 5]

Discussion

Febrile seizure is a terrifying event for the parents, seeking emergency medical attention. Attempts have been made to identify predisposing risk factors like family history, gender predisposition, genetic factors, metabolic disturbances like hyponatremia. The present study conducted on 100 children, 50 subjects with febrile seizures and 50 without febrile seizures to find out the association of serum sodium, serum potassium and serum chloride in febrile seizures and comparing them with the children of the same age group with fever but no seizures.

In the present study, demographic parameters (ex: gender, age) were studied. In this study, 41 (82 %) out of 50 in the febrile seizure group had simple febrile seizures, remaining 9 (18 %) children presented with atypical febrile seizures (as per the definition). Sadlier et al [13], stated that typical febrile convulsions are more common than atypical febrile convulsions. In their study it was found that, 87 % of the children had simple febrile seizures and 13 % had atypical febrile seizures.

In this study, 19 (38 %) children are under 1 year of age, 15 (30 %) children are between 1-2 years of age, 9 (18 %) children are between 2-3 years of age, 5 (10 %) constitute 3-4 years of age and remaining 2 (4 %) children are between 4 to 5 years of age. The age distribution observed in various other studies showed the same pattern as in this study. The male preponderance observed in this study has also been reported in other studies. Majority of the children are males 32 (64 %) and 18 (36 %) children are females. Osaghae et al [14], stated in their study that, although febrile seizure is common in children less than 60 months of age, it is more frequent in those less than 24 months of age accounting for 64(40.3 %) with overall male to female ratio of 1.6:1. Taylor et al [15], in his study stated that the incidence of febrile convulsions is more in male children than in female children as he opined that the comparatively earlier maturation of the female brain could provide protection against potential triggers such as fever.

In the present study, majority of the children, 21 children had URTI (42 %) as the probable focus of fever in febrile seizures, 12 (24 %) children had viral pyrexia, 6 children (12 %) had diarrhoeal diseases, 4 % had ASOM and 8 % had no focus for fever. Amongst those with no febrile seizures also majority had URTI (32 %), 18 % had no focus. The findings of our study are in the line of published literature. Kaputu Kalala et al [16], in their study stated that upper respiratory tract infections were the most often implicated provoking factors, occurring in 69.5 % of patients.

Serum sodium

In this study, 66 % of the febrile seizure group had normal serum sodium levels and 34 % of children had low serum sodium levels. Amongst the other study group with no febrile seizure, no child had abnormal serum sodium levels. This depicts there is some predisposition to a febrile seizure for patients with hyponatremia at the time of febrile illness. 11 (64.7%) children had loe sodium levels who had repeat seizure episodes within same febrile period compared to 6 (35.3%) children who had repeated seizure episodes within same febrile period but with normal sodium levels. The sodium concentrations were lowest in children with repeated seizures compared with children having simple ($p < 0.01$) or other complicated types of Febrile seizures. This again emphasizes that children with hyponatremia have a certain risk of developing a repeat episode. In a study by Al Rubae et al [17], low levels of serum sodium were observed in cases group when compared to control group while no significant difference between serum potassium levels of two groups. In another study, Hugen et al [18], studied that the mean serum sodium levels of children with recurrent seizures are significantly lower than the mean serum sodium levels of children with a single seizure. In a study by Hawas et al [19], concluded that changes in sodium and potassium levels could have a role in the development of simple febrile seizure. In a study by Maksikharan A et al [20], they found no significant difference in mean serum sodium levels between 276 patients with single febrile seizures and those in whom febrile seizures recurred within 24 hours. This knowledge may be of practical value in deciding whether to admit the child or allow it to return home and in advising parents of the risk of a repeat seizure.

On the other hand, Kenney et al [21], have shown that routine measurements of biochemical tests are not necessary in febrile seizures. These investigators have shown that measurement of serum electrolytes may result in a very low number of abnormal findings, particularly in children with febrile seizures.

Serum potassium

In living organisms, the functions of sodium and potassium are quite different. In the present study, serum potassium levels were observed in the two groups and there is no statistically significant difference observed among the two groups. Amongst 50 subjects, only 1 % children had potassium level abnormal, 49 (98 %) had normal values. 1 % of those with no febrile seizures had abnormal values and 98 % had normal. P value was 0.315 which is non-significant. Akbayram et al [22], in their study, obtained that Calcium and potassium concentrations in the FS group were lower than their levels in the control group, On the other hand, Al-Rubae et al [17], in their study, showed that low levels of serum sodium were observed in FS patients when compared to other group while no significant difference in potassium level between patient and control. There is no statistically significant difference in potassium levels between two groups.

Serum chloride

Number of subjects with febrile seizures with abnormal chloride levels in our study was 1 (2 %), while number of children having normal values were 49 (98 %). The group with no febrile seizures and

abnormal chloride values were 1 (2 %), normal values were 49 (98 %). P value is 1.00 which is non-significant. There are very few studies on serum levels of chloride in febrile seizures. Stoini et al [23], studied Serum sodium, chloride and potassium concentrations in children with febrile seizures and found no significant differences in above concentrations in children with typical, recurrent and atypical febrile seizures (P > 0.05).

Conclusions

The estimation of serum electrolytes is essential for the rationale understanding of pathogenesis and management of febrile seizures. The association between serum electrolyte changes and incident febrile seizures suggest that alteration in serum electrolytes is likely to play a clinically significant role in causing seizures in patients with febrile seizures. Therefore, routine measurement of serum electrolytes, especially sodium is warranted in subject with febrile seizures. However, as there are certain limitations in the present study in terms of population size and different materials and methods, more studies are required to study the association of serum electrolytes in febrile seizures.

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