

Serum Sodium Level in Febrile Seizure - Does It Predict Seizure Recurrence within 24 Hours?

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ABSTRACT

Background: Febrile seizure is the most common convulsive event in children younger than 60 months and often recurs within the first twenty four hours. It has been observed that children with recurrent febrile seizure have lower serum sodium levels.

Objective: To ascertain the role of serum sodium level as a predictor of seizure recurrence within the same febrile illness.

Materials & Methods: 60 children admitted for febrile seizure between 6 months to 60 months were included in the study. An age and sex matched group of 60 children with fever but no convulsions were the controls. Serum sodium levels were evaluated in all children. Children with seizures were further divided in two groups based on serum sodium level into Group A with serum sodium level <135 mEq/L and Group B with serum sodium level >135 mEq/L. Both these group were followed for next 24 hour for recurrence of seizure.

Results: Although we did not found any significant difference in the mean serum sodium levels between children with febrile seizures and controls (138.73 ± 5.45 mEq/L & 139.73 ± 4.65 mEq/L respectively) with p value >0.05 but there were significantly higher mean number of seizures (2.17 ± 0.95) in cases having serum sodium level less than 135 mEq/L than cases having serum sodium level more than 135 mEq/L (1.45 ± 0.82) within the case group with p value <0.01.

Conclusion: Serum sodium level can assist in predicting the risk of recurrence within the same febrile episode although there appear to be no significant association of low serum sodium level and its predisposition to occurrence of initial febrile seizure episode.

Key words: Febrile seizure, serum sodium levels.

INTRODUCTION

Febrile seizures are the most common form of childhood seizures. [1] The American Academy of Pediatrics (AAP) defines febrile seizure as a seizure occurring in a febrile child between the ages of 6 and 60 months who do not have an intracranial infection, metabolic disturbance, or history of afebrile seizure. [1] The Simple febrile seizure is single, generalized seizure that

lasts less than 15 minutes in children from six months to five years old, and occurs more commonly in some families. [1-3]

Cumulative incidence of febrile seizure in Western Europe and the USA is reported to be 2-5% based on population studies but it varies in rest of the world between 5-10% in India to 8.8% in Japan and 14% in Guam. [4-5]

Febrile seizures recur in approximately thirty percent of those experiencing a first episode, in fifty percent of those having two or more episodes and in fifty percent of infants who are less than one year old at initial febrile episode. [6-7]

Probability of having another febrile seizure episode is major risk. One of the most frequently asked question by parents is the probability of another convulsion during the same febrile episode. The most consistent risk factor reported is family history of febrile seizure and onset of first episode less than 18 months of age. Peak temperature and the duration of fever prior to seizure are two other definite risk factors for recurrence of febrile seizure. The chance of recurrence is low if peak temperature is high and recurrence chance is high if there is shorter duration of recognized fever. [8-10] Children with multiple risk factors have the highest risk of recurrence.

Controversies exist regarding the role of relative hyponatremia in prediction of febrile seizure recurrence within first 24 hours. In an American study of 175 patients, findings showed no difference between serum sodium levels of the simple febrile seizure group and the recurrent simple febrile seizure group; [11] they did however show a statistically significant difference in serum sodium levels of the afebrile and febrile groups, in that the serum sodium levels of the latter were lower than those of the former. In an another study no significant difference was observed in the serum sodium levels between the simple febrile seizure and the simple febrile seizure with recurrence groups, [12] however a significant relative hyponatremia was observed in the simple febrile seizure group as compared to the afebrile seizure control group. At the same time, some researchers found the serum sodium level to be lower in children with recurrent convulsion within the same febrile illness reporting this as minor risk factors for recurrence of seizure in same febrile episode. [13-18]

With this background and considering the importance of pediatric

febrile seizures and their possible recurrence, we performed a prospective case –control observational study to assess the role of serum sodium levels in predicting the recurrence of seizure within the same febrile episode.

MATERIALS AND METHODS

Subjects:

This prospective case –control observational study was conducted in a tertiary care pediatric hospital attached with SMS medical college, Jaipur from April 2013 to March 2014. Total 120 children aged between 6months to 5 years were included in the study. As case group, 60 children with seizures associated with fever (axillary temperature $>38^{\circ}\text{C}/100.4^{\circ}\text{F}$) were taken along with 60 age matched febrile controls without convulsion. Children having signs of neurological infections (meningitis, encephalitis), neuro-developmental delay, known neurological disorder, gastroenteritis or inadequate fluid intake and dyselectrolytemia other than hyponatremia were excluded from the study.

Intervention

A detailed clinical history and clinical examination was done in all cases. Complete blood count (CBC), Peripheral blood smears (PBF), blood culture & sensitivity, urine & stool routine and microscopy along with culture & sensitivity were done accordingly. CSF was done in all children < 18 months of age and in those who are having undue or unexplained drowsiness or irritability.

Serum sodium levels were done in all cases at the time of admission using peripheral venous sample by the Insight Electrolyte Analyzer (Fully Automated Analyzer) in our institute's laboratory. A serum sodium level of less than 135mEq/L was taken as cut off value to label as hyponatremia.

Based on serum sodium level, case group was further subdivided into Group A with serum sodium level less than 135mEq/L and Group B with serum sodium level equal or more than 135mEq/L. Children under both

these groups were then followed up in the In-Patient Department during the next 24 hour for any seizure recurrence.

Sample size and statistical analysis:

Based on previous study [18] expecting the difference in the mean serum sodium levels between children having fever with single seizure episode and recurrent seizure episodes to be 3.9 ± 3.8 mEq/L and assuming the power of test to be 80% and alpha error of 0.05, the sample size was calculated to be minimum 50 subjects in group. A 20% extra was taken in both groups.

All data were recorded and analyzed using IBM SPSS statistics, ver. 20 for windows. Quantitative data were standardized as mean and standard deviation. Qualitative data were expressed as percentage and proportion. The fisher's exact (two tailed), Chi-square test and Z-score were performed to analyze differences

in proportions of categorical variables between two or more groups. Mann-Whitney (Wilcoxon) W-test was used to compare medians. The p value less than 0.05 were taken as statistically significant.

RESULTS

There were 60 febrile children with seizures in our study. The mean age was $29.4(+16.9)$ months consisting of 38 boys (63.3%) & 22 (33.6%) girls. Among the 60 febrile controls without seizures, the mean age was $25.5(+16.24)$ months with 37(61.6%) boys and 23(38.3%) girls. Out of 60 cases of febrile seizures 18(30%) have simple febrile seizures & 42 (70%) had complex febrile seizures.

There was no significant difference in the mean serum sodium levels between children with febrile seizures (138.73 ± 5.45 mEq/l) and controls (139.73 ± 4.65 mEq/L) with p value > 0.05. (Table 1)

Table 1- Mean Serum Sodium Level in Case and Control Groups

Group	Total Number	Mean Serum Sodium Level (mEq/L)	SD	P value
Febrile Seizure	60	138.73	5.45	P value >0.05 (Not Significant)
Febrile children with no seizure	60	139.73	4.65	

Out of 60 febrile seizures cases, 18 (30%) had hyponatremia (Group A) & rest 42 (70%) were having serum sodium level >135 mEq/l (Group B). We found that 66.66% (12 out 18) children with febrile seizures who had hyponatremia (Group A) developed seizure recurrence within 24

hours while only 28.57% (12 out of 42) children with febrile seizure who had serum sodium level >135mEq/L (group B) developed recurrence within 24 hours. This was statistically significant (P value<0.01) (Table 2).

Table 2- Distribution of Cases according to Serum Sodium Level and Recurrence of Seizures

Serum Sodium Levels	Total Number	Recurrence of Seizure	No Recurrence of Seizure	P value
Group A (<135mEq/L)	18	12 (66.66%)	6 (33.33%)	<0.01 (Significant)
Group B (>135mEq/L)	42	12 (28.57%)	30 (71.42%)	

$\chi^2=7.620, df=1$

We also found that mean number of seizure episodes were significantly higher (2.17 ± 0.95) in cases having serum sodium

level <135mEq/L (Group A) than in cases having serum sodium level >135mEq/L (Group-B) (Table 3)

Table 3- Mean Episode of Seizures according to Serum Sodium Level

Serum Sodium Levels	Mean Seizure episodes	SD	P value
Group A (<135mEq/L)	2.17	0.95	<0.01 (Significant)
Group B (>135mEq/L)	1.45	0.82	

DISCUSSION

In our prospective study, serum sodium level <135mEq/L was there in 30%

(18 out of 60 children) of cases with febrile seizures. This is comparable to the incidence of 18-35% found in other studies.

[19-20] There was no significant difference between the mean serum sodium of children with febrile seizure and controls. This is opposite to the results of other studies. [11-12] This difference in observation may be due to the fact that their controls group consisted of children with afebrile seizures and not febrile children without seizure as was ours.

In our study, total 24 out of 60 (40%) developed recurrence of seizures while Berg AT et al., [10] Razieh fallah et al., [21] Heydarian et al., [12] Youssef A et al. [22] and Hugen CA et al. [15] observed 14.6%, 18%, 18.79%, 25.51% and 28% respectively in their studies. The difference of higher proportion of recurrent febrile seizure in our study could be possibly due to different inclusion criteria in different studies as well as wide variation in the sample size. Heydarian et al. [12] included only simple febrile seizure as the case subjects while Razieh fallah et al. [21] divided their cases into categories of Simple, Repeated (multiple) & Recurrent febrile seizure.

Although we observed no statistically significant difference in mean serum sodium levels of febrile children with seizure & febrile children with no seizures but there was statistically significant difference in serum sodium level of children with recurrent febrile seizure as compared to children with single febrile seizure. These results have been supported by works of Kirivanta T et al., [13] Millichap JG et al., [14] Hugen CA et al., [15] Offringa M et al., [16] Park SY et al. [17] and latest by Jayashree Nadkarni et al. [18] in 2011. However no such difference was noted by two other studies. [11-12] Difference in number of patients included these studies along with specific genetic predisposition can be the cause of such difference as number of patients included in both of these studies were larger than ours.

In our study, we again divided the children with febrile seizures (Case Group) to Group A (Serum Sodium level <135mEq/L) and Group B (Serum Sodium level >135mEq/L) and followed them for next 24 hours for recurrence of seizures.

There was clear cut more episodes of recurrent seizure in Group A than Group B.

CONCLUSION

Based on finding of our study, we conclude that serum sodium level can assist in predicting the risk of recurrence within the same febrile episode although there appear to be no significant association of serum sodium and its predisposition to occurrence of initial febrile seizure episode. So measurement of electrolytes should not be performed for the sole purpose of identifying the cause of a simple febrile seizure as recommended by AAP CPG 2011 guidelines. [1]

Conflict of Interest: None.

CONTRIBUTIONS DETAIL:

Dr. Ghanshyam swami- participated in study design, manuscript preparation along with interpretation of data.

Dr. Kusum Devpura- participated in analysis and interpretation of data.

Dr. Varun Meena - participated in acquisition of data.

Dr. Luvdeep Dogra- participated in concept, design and critical review.

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