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Relationships between serum electrolytes and febrile seizure

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Abstract

Background: Febrile seizures as a seizure occurring in febrile children between the ages of 6 and 60 months who do not have an intracranial infection, metabolic disturbance, or history of afebrile seizures. The mechanism of seizure activity is altered in hyponatremia, due to deficiency of sodium ion, more calcium ion influx, and generation of repetitive action potential which will cause repetitive seizure initiation. Our study to assess the effect of serum electrolyte (Na^+ , k^+ , Ca^{+2}) in children with febrile convulsion.

Patients and Method: A case-control study was conducted from 1 st of October 2017 till 31th of January 2018 and involved 60 children aged 6 months to 6 years, divided into 30 cases with febrile convulsion and the other 30 were normal children (control). Cases and control were collected from pediatric floor and pediatric emergency unit in Al-Imamain Al-Kadhimin teaching hospital. The information taking from the case sheets.

Results: We found serum electrolyte disturbance Na is decreased (66.7%), K^+ is increased (16.7%) and Ca^{+2} is decreased (6.7%) respectively. most common age group affected <2 y (36.6%). Complex seizure associated with (Na^+ , K^+ , Ca^{+2}) disturbance. Family history and status epilepticus more common in complex group (26.6%).

Conclusion: There is significant association between serum electrolyte (Na^+ , K^+ , Ca^{+2}) level and febrile convulsion.

Keywords: Fever, convulsion, febrile

Introduction

The American Academy of Pediatrics (AAP) has announced a standard definition of febrile seizures as a seizure occurring in febrile children between the ages of 6 and 60 months who do not have an intracranial infection, metabolic disturbance, or history of afebrile seizures^[1]. Simple FS have an age range classically described as 6 to 60 months. The peak incidence is usually in the second year of life. FS are prevalent in up to 5% of children, with the overall incidence estimated to be 460/100,000 in the age group of 0- 4 years^[2]. Most FS are simple; however, up to 30% might have some complex features^[3]. 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. In fact, a positive family history of FS in first degree relative is observed in up to 40% of patients^[4]. Gender distribution has been studied in the literature. One previous study found a mild male predominance^[5]. but this has not been supported by other literature reviews. Seasonal variation with regard to seizure incidence has not yet been fully understood. Studies have shown that FS tend to occur more in the winter months and are more common in the evening^[6]. The underlying pathophysiological explanations for these observations remain obscure^[7, 8]. FS can be seen in multiple family members and there is evidence of genetic and environmental causes. A positive family history of FS can be found in 25-40% of cases when a child present with a FS^[9-11]. The number of FS a child has affects the risk of a sibling experiencing a FS^[12]. Significantly higher concordance rates are seen for FS in monozygotic twins as compared to dizygotic twins in multiple twin registries^[13]. The two most consistently identified risk factors for developing febrile seizures are the height of the temperature and a positive family history in first-degree relatives^[14, 15, 16]. Febrile seizures are classified as simple or complex based on duration, physical characteristics, and recurrence patterns. A self-limited, short (< 15 minutes), generalized, tonic-clonic seizure that does not recur within the same illness and is not associated with post-ictal pathology is classified as a simple febrile seizure (SFS).

Febrile seizures that do not meet all criteria for SFS are classified as complex febrile seizures

(CFS). A prolonged febrile seizure (PFS) is a complex seizure that lasts longer than 15 minutes, and a febrile seizure that continues longer than 30 minutes is classified as febrile status epilepticus (FSE) [17]. FSE accounts for 5% to 9% of all febrile seizures [18, 19] and 25% of all episodes of status epilepticus occurring in children [14, 20]. In the second year of life, two-thirds of all cases of status epilepticus are FSE, FSE is considered a medical emergency [21]. Prolonged febrile seizures in childhood are known to have adverse physiologic consequences, including increased cerebral metabolic demand and systemic changes such as hypoxia, hypoglycemia, and arterial hypotension. Genetic factors appear to play a role when epilepsy develops after febrile seizures. Temporal lobe seizures are more likely to begin early but remit permanently if a first-degree relative had a febrile seizure [22]. Collectively, children with complex febrile seizures can be said to have a small but identifiable risk for later epilepsy, based on genetic, developmental and acquired factors. If these children develop persistent temporal lobe seizures, they are likely to continue to experience seizures in later life, Seizure activity can begin in a very discrete region of cortex and then spread to neighboring regions,

there is a seizure initiation phase and a seizure propagation phase [23].

Initiation phase is characterized by two concurrent events in an aggregate of neurons [24].

1. High-frequency bursts of action potentials and
2. Hypersynchronization.

The bursting activity is caused by a relatively long-lasting depolarization of the neuronal membrane due to the influx of extracellular calcium, which leads to the opening of voltage-dependent sodium channels which leads to an influx of sodium [24]. In the case of hyponatremia due to deficiency of sodium ion, more calcium ion influx, and generation of repetitive action potential which will cause repetitive seizure initiation. Fever plays an important role in causing disturbances in fluid and electrolyte imbalance. Hyponatremia has been thought to enhance the susceptibility to seizures associated with febrile illness in childhood. Sodium levels are lower in those children with complicated convulsions in comparison with those having simple convulsions. the sodium concentrations are lowest in children with repeated seizures compared with children having simple or other complicated types of febrile seizures such as focal seizures. Seizures lasting longer than 15 min during febrile convulsions have been studied serum potassium levels showed no significant differences between patient groups. However, calcium levels and osmolarity significantly lower than control groups. The electrolytic modification of overall hyponatremia is probably due to the syndrome of inappropriate antidiuretic hormone may have a role in short-term relapses of febrile convulsions. Hypernatremia has been documented in some children with high fever, without seizures, it may be that Hyponatremia in predisposed subjects lowers the threshold of neuromuscular excitability [25-28].

Aim of study: To assess the effect of serum electrolyte

disturbance (Na^+ , k^+ , Ca^{+2}) in children with febrile convulsion.

Patient and Methods: A case-control study was conducted from the 1st of October 2017 till 31 of January 2018 and involved 60 children aged 6 months to 6 years, divided into 30 cases with febrile convulsion and the other 30 were normal children (control). Cases and control were collected from pediatric floor and pediatric emergency unit in Al-Imamain Al-Kadhimin teaching hospital. History was taken from parents involving information about gender, first or recurrence, type FC it's simple or complex, have status epileptics or not, family history, FC remit (spontaneously or only with intervention), response to treatment, investigation (brain image, EEG, CSF), according to type of seizure we divided to two groups simple and complex groups. serum electrolyte normal limits (S.Na = 135-150mEq/L, S.K = 3.6-5.5mmol/L, S.Ca=9-11mg/L), according to kit from (ABBOTT) company in America.

Exclusion Criteria

- 1- Children with signs of meningitis.
- 2- Children with developmental delay.
- 3- Children with neurologic disorders.

Statistical analysis: The IBM SPSS software program version 24, was used for all computerized statistical analysis. The results were expressed as frequencies and percentages. Variables were compared by using Chi-square χ^2 tests. *P*-value equal or less than 0.05 was considered to be statistically significant and > 0.001 was highly significant.

Results: Among cases group, there were 14 boys (23.3%) and 16 girls (26.3%). The male to female ratio was 1:1.14. According to serum electrolyte results in patient group shows the S.Na⁺ is significant decreased (66.7%) (0%) F.C and control, while in S.K⁺ is increased (16.7%) (0%) and S.Ca is decreased (6.7%) (0%) respectively.

According to the relationship between age of children and type of febrile seizure. The study shows the common age in F.S is less than 2 years 11(36.6%), as shown in table (1).

Table 1: Relationship between Age of child and type of seizure

Child Age (in months)	Type of Seizures		
	Simple No (%)	Complex No (%)	Total No (%)
<1y	2 (6.7%)	5 (16.6%)	7 (23.3%)
1y to < 2y	5 (16.7%)	6 (20%)	11 (36.6%)
2y to < 3y	0 (0%)	5 (16.6%)	5 (16.7%)
3y to < 4y	2 (6.7%)	0 (0%)	2 (6.7%)
4y to 5y	2 (6.7%)	3 (10%)	5 (16.7%)
Total	11 (36.7%)	19 (63.6%)	30

Serum electrolyte disturbance assessment we found Na was more common in patient with complex F.S than simple F.S (46.7%), (20%) respectively while S.K (16.7%), (0%) and Ca (6.7%), (0%) between complex and simple in type as shown in table 2.

Table 2: Relationship between Serum Electrolytes and Type of febrile Seizure

S. Electrolytes Level		Type of Seizure			
		Simple freq. (%)	Complex freq. (%)	Total No (%)	P-Value
Na+ Value	Normal	5 (16.7%)	5 (16.7%)	10 (33.3%)	0.284
	Decreased	6 (20%)	14 (46.7%)	20 (66.7%)	
K+ Value	Normal	11 (36.7%)	14 (46.7%)	25 (83.3%)	0.062
	Increased	0 (0%)	5 (16.7%)	5 (16.7%)	
Ca + value	Normal	11 (36.7%)	17 (56.6%)	28 (93.3%)	0.265
	Decreased	0 (0%)	2 (6.7%)	2 (6.7%)	
Total		11 (36.7%)	19 (63.3%)	30 (100%)	0.144

Status epileptics seen more common in complex group than simple (26.6%) (3.3%) respectively, as shown in table (3).

Table 3: Relationship between status epileptics and type of febrile seizure

Status Epileptics	Type of seizures		p- value
	Simple No (%)	Complex No (%)	
Yes	1 (3.3%)	8 (26.6%)	0.057
No	10 (33.3%)	11 (36.7%)	
Total	11 (36.7%)	19 (63.3%)	

*P-value if less than 0.05 significant

Family history was positive in patient with complex F.C 8 (26.6%) than simple F.C 3 (10%), as shown in table (4).

Table 4: Relationship between family history and type of febrile seizure

Family history	Type of seizures		p-value
	Simple No (%)	Complex No (%)	
Yes	3 (10%)	8 (26.6%)	<0.417
No	8 (26.7%)	11 (36.6%)	
Total	11 (36.7%)	19 (63.3%)	

Treatment is indicated in complex F.S simple F.S (50%), (6.7%) respectively.

Discussion

Regarding to male to female ratio 1:1.14 was almost equal which not agreed with Kulandaivel M [29], due to our sample small in size. There is significant disturbance in serum electrolyte (Na, K, Ca) which agree with HUGEN CA study (52%) [28]. The current study shows common age was < 2 years (36.6%) which agree Kulandaivel M study [29]. According to type of febrile convulsion the study shows S.Na decreased complex convulsion (46.7%) than simple convulsion (20%) which agree with the Kulandaivel M study was (92.4%), (32.8%) respectively [29] While S.K was increased with complex convulsion (16.7%) which disagree with study Hugen CA due to our sample different in mass and short period of study, and S.Ca was decreased with complex convulsion (6.5%) and p value was not significant which disagree with the study of Usha Kiran, *et al.* study was p value significant (p=0.0001) [30], due to our sample small in size. Regarding to relationship between status epileptics and type of febrile convulsion we see the complex type mostly affected (26.6%) which this agree with Nishiyama M, *et al.* Study [31]. Family history positive in the complex seizure than in simple (26.6%) which agree with Shrestha D, *et al.* study (40%) [8]. Specific anticonvulsant treatment use for complex F.C (50%) which agree with Patel AD, *et al.* study [32].

Conclusion

1. There is significant association between serum electrolyte (Na⁺, K⁺, Ca⁺²) level and febrile convulsion.

2. Positive family history and Status epileptics see more common in children with complex febrile seizure.

Recommendation

1. Specific anticonvulsant treatment is indicted to the complex febrile seizure specially who have positive family history and statues epilpticus.
2. Long follow-up with patient with febrile convulsion include growth and development and school preforms.

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