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Original Research Article

Association between serum zinc level and simple febrile seizures in children: a hospital-based study

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ABSTRACT

Background: Febrile seizures are the most common cause of convulsions in children and a frequent cause of emergency hospital admissions. There are different hypothesis about neurotransmitters and trace element (such as zinc) changes in cerebrospinal fluid and serum, which can have a role in pathogenesis of febrile convulsions. Hence we want to study this association in our set up. Objectives was to study the association between serum zinc levels and febrile seizures in childern in our set up.
Methods: This hospital based, prospective case control study was done in SKIMS Soura Srinagar, Kashmir (J and K), India for one-year period from August 2015 to July 2016. A total of 100 children aged 6 months to 6 years admitted in the hospital presenting with febrile seizures after fulfilling our inclusion and exclusion criteria were enrolled for the study. Informed consent was taken from their attendants and classified into 2 groups of 50 each. Patients with history of simple febrile seizures were taken as cases and those with fever without seizures as controls. A detailed history was taken, and complete physical examination was done on the patients and recorded on a precoded and pretested proforma. Blood was collected within 12 hours of admission and serum zinc levels were estimated. For statistical analysis, SPSS 17 program using t-test was employed. Chi-square test was performed to compare proportion between 2 or more discrete variables. $P<0.05$ was considered statistically significant.
Results: Out of 100 children enrolled, male to female ratio was 1.63:1. Majority of the children were between 6 to 12 months (36%). The clinical presentation comprised of mainly non localized fevers majority of which had clinical evidence to suggest viral etiology (60%), followed by ARI (20%), ASOM (10%), UTI (6%) and bronchiolitis (4%). Mean serum zinc level in cases was 30.96±7.93ugm/dl and in controls it was 35.95±9.25ugm/dl. Serum zinc level was found significantly low in cases of simple febrile seizures as compared to controls ($P<0.05$).
Conclusions: This study reveals that there is positive correlation between low serum zinc levels and febrile convulsions.

Keywords: Febrile convulsions, GABA, Serum zinc, Zinc supplementation

INTRODUCTION

Febrile seizures (FS) are the most common form of convulsion in children which occurs in 2 to 5% of children aged between 6 months to 60 months.[1] As per the definition of the American Academy of Pediatrics, FS occur in the absence of central nervous system infection, metabolic disorders and history of febrile seizures.[2] FS occurs because the electrical system of the brain has not been adequately evolved so as to struggle against the stress of body temperature increases.[3] Zinc is one of the important element that plays a vital role in the treatment and prevention of neurological disorders.[4] Zinc modulates

the activity of glutamic acid decarboxylase, the rate limiting enzyme in the synthesis of gamma-aminobutyric acid (GABA), which is a major inhibitory neurotransmitter.[5] It complements the inhibitory effects of calcium on the excitatory N-methyl-d-aspartate receptors which become activated when a patient develops low levels of zinc and induce an epileptic discharge in children with high fever.[6] Various studies have reported the low serum zinc level in children with febrile seizures.[7-11]

The present study intends to estimate the serum zinc level in children with febrile seizures and acute febrile illness without seizure and to correlate the serum zinc level with simple febrile seizures in our set up.

METHODS

This hospital based prospective case control study was conducted in SKIMS Soura Srinagar, Kashmir (J and K), India for one year period from August 2015 to July 2016. A total of 100 children, 50 each in case and control group i.e. children with febrile seizure (case group) and febrile children without seizures (control group) were included. Informed consent was obtained from the parents or guardians. A detailed history was obtained including age, sex, socioeconomic status, duration of fever before onset of seizures, duration of seizures, consanguinity, family history of epilepsy, family history of febrile seizures and consanguinity. Complete physical examination of the child was performed with weight, height, head circumference and mid arm circumference to emphasis that there is no evidence of malnutrition.

Inclusion criteria

Children aged between 6 months to 5 years with Febrile seizures.

Exclusion criteria

- Children who had mental retardation
- Atypical convulsion / Seizure disorder
- On medications (Antiepileptic drugs)
- Chronic diseases
- Malnutrition
- Central nervous system infection
- Children on zinc supplementation, or with diarrheal disease.

The sample for zinc estimation was drawn within 24 hours of admission of patient in both the groups. The sample was centrifuged for 3-4 minutes at 3,000-4,000 rpm, serum thus obtained and preserved in sterile deionized vial. Estimation of serum zinc was done within 6 hours of collection using colorimetric test kits, with 2-(5-bromo-2-pyridylazo)-5-(N-propyl-N-sulphopropylamino) phenol as the reagent.

The cut off value for hypozincemia was taken as 65µgm/dl as per the World Health Organization (WHO) recommendation.[12] Data was analyzed using SPSS version 17.0. The difference in mean among the groups was assessed by ANOVA and t-test was used to analyze inter group difference. A p- value less than 0.05 was taken as statistically significant.

RESULTS

The study group consisted of 50 cases and 50 controls. Majority of the cases were between 6 to 12 months (36%). Very few children were in the upper age group i.e. between 2 to 3 years (16%), 3 to 4 years (8%) and between 4 to 5 years (6%) as shown in Table 1.

Table 1: Age group distribution of group A and group B.

Age group (months)	Group A (cases) = 50		Group B (controls) = 50	
	No.	%	No.	%
6-12	18	36%	14	28%
13-24	17	34%	19	38%
25-36	8	16%	12	24%
37-48	4	8%	3	6%
49-60	3	6%	2	4%

There were 31 (62%) males and 19 (38%) females among cases with male female ratio of 1.63:1 as shown in Table 2.

Table 2: Gender distribution of group A and group B.

Gender	Group A (cases) n = 50		Group B (controls) n = 50	
	No.	%	No.	%
Male	31	62%	29	58%
Female	19	38%	21	42%
Total	50	100%	50	100%

Table 3: Distribution of diagnosis in group A and group B.

Diagnosis	Group A (cases)		Group B (controls)	
	No.	%	No.	%
Non localised fever (viral)	30	60%	23	46%
ARI (Acute respiratory infections)	10	20%	21	42%
ASOM (Acute suppurative otitis media)	5	10%	3	6%
UTI (Urinary tract infection)	3	6%	2	4%
Bronchiolitis	2	4%	1	2%
Total	50	100%	50	100%

Among the cases, fever was triggered by non-localised fever (viral) in 30 (60%) followed by respiratory tract infection in 10 (20%), ASOM in 5 (10%), UTI in 3 (6%), bronchiolitis in 2 (4%) cases as shown in Table 3.

Table 4: Comparison of mean serum zinc level between group A and group B.

Variables	Serum zinc level (ugm/dl)	Mean difference	P-value
Group A	30.76±7.93	-5.23	<0.05
Group B	35.95±9.25		

Table 4 represents the mean serum zinc level in the both groups. Mean serum zinc level was -5.23ugm/dl less in cases of simple febrile seizure as compared to controls (P<0.005).

Table 5: Comparison of zinc deficiency among group A and group B.

Zinc level	Group A		Group B		Total	
	No.	%	No.	%	No.	%
<65µgm/dI	30	60%	17	34%	47	47%
>65µgm/dI	20	40%	33	66%	53	53%
Total	50	100%	50	100%	100	100%

Table 5 represents the number of patients in both groups with bio-chemical hypozincemia and shows that 30 (60%) of the cases and 17 (34%) of the controls had bio-chemical hypozincemia (P= 0.001).

DISCUSSION

Febrile seizure is the most common disorder in childhood with good prognosis. There are different hypothesis about changes in trace elements and neurotransmitters in biological fluids which can have a role in pathogenesis of febrile seizures.[13] Zinc is an essential micronutrient required for the normal function and development of the central nervous system.[4] Males predominated in present study with male female ratio of 1.63:1. This was similar to the gender ratio ranging from (1.4-1.7):1 as reported by other studies.[7,8,14-19] Family history of seizures was present in 10%, 7% had history of simple febrile seizures in the first degree relatives and 3% had history of epilepsy in family; while among 3% patient with family history of epilepsy 2% had history in first degree and 1% had history in second degree relative. Similar findings were reported by Guzman et al whom reported family history in 10% of patients.[20] However, Kumari, Margaretha and Kafadar reported family history in 44.4%, 48%, 26% of patients respectively.[8,18,21] The clinical presentation comprised of mainly non-localized fevers majority of which had clinical evidence to suggest viral etiology (60%), followed by ARI (20%), ASOM (10%), UTI (6%) and bronchiolitis (4%). Margaretha and Günduz have reported ARI as most common cause.[8,22]

Majority of the authors who have correlated serum zinc level with simple febrile seizure have studied this correlation by compairing mean serum zinc level between cases and controls, while few others studied this correlation by determining the number of patients having hypozincemia in subject population. Also, the hypothesis proposed by Izumit (hypozincemia during fever triggers febrile seizure) is consistent with our results.[23] Hypozincemia was present in majority of the patients (60%), though no statistically significant difference was found in the mean age, gender distribution, physical parameters, and nutritional status between the patients of hypozincemia and normal zinc level. Mahyar et al, also reported the similar findings.[17] In the present study, significant difference of -5.23µg/dl was obtained in mean serum zinc level in cases as compared to controls. Similar findings have been reported by other studies.[3,7-11,14-17,19]

The present study also did not reveal any significant difference in mean serum zinc level in relation to age groups or gender as reported by several other studies.[15,18,19] Hypozincemia was observed to be more frequent in children with simple febrile seizures in the present study.

CONCLUSION

Authors observed significant lower serum zinc level in children with febrile seizures in comparison with febrile children without seizures and also in children with lower serum zinc levels, prolonged seizures were observed. Hence children with low serum zinc levels are more prone to get febrile seizures than children with normal serum zinc levels. However further prospective case control studies with large number of cases are required to establish the correlation between serum zinc and febrile convulsion.

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