Original Articles

A study to determine the association between serum ferritin levels and febrile seizures in children

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Abstract

Introduction: Febrile seizures are a common paediatric emergency. Recent studies have postulated iron deficiency in the pathogenesis of simple febrile seizures.

Objective: To determine the association between serum ferritin levels and simple febrile seizures

Method: This study was conducted at the Department of Paediatrics & Child Health, Southern Railway Head Quarters Hospital, Perambur, Chennai. Consecutive cases were selected for the study and concurrent age matched controls were selected from the same setting. Controls were selected from age matched population of children attending the outpatient department for short febrile illness without seizures. Cases and controls were selected in a 1:1 ratio. Data obtained was statistically analyzed with SPSS version 11 software.

Results: Serum ferritin (P=0.012), haemoglobin (P=0.042) and haematocrit (P=0.029) were found to be significantly lower in children with febrile seizures than controls.

(Keywords: Serum ferritin; febrile seizures)

Introduction

Febrile seizures are seizures that occur between the ages of 6 and 60 months, in the presence of fever, 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 afebrile seizures[1]. Major risk factors for recurrence of febrile seizures include age less than one year, duration of fever less than 24 hours and seizures occurring with fever of 38-39^{o}C[1]. The minor risk factors are family history of febrile seizures or epilepsy[4], developmental delay[5], complex febrile seizures, day care attendance[6,7], male gender and lower serum sodium[8]. Moreover, iron deficiency is the commonest preventable and treatable micro nutrient deficiency worldwide[9]

Objective

To determine the association between serum ferritin levels and simple febrile seizures

Method

A case control study was designed to determine the association between serum ferritin levels and simple febrile seizures. Sample size was determined based on an assumption of alpha error of 5% and power of study 80%, with prevalence of iron deficiency as 30% in controls. Cases and controls were selected in a 1:1 ratio. Simple random sampling was done. Cases were children of age group 6 months to 60 months, who presented with simple febrile seizures to the paediatric out-patient department (OPD) & Emergency Room of Southern Railway Head Quarters Hospital, Perambur, Chennai from June 2011 to June 2012. Cases comprised children who presented with a single episode of generalized tonic clonic seizures that occurred within 24 hours of onset of fever and lasted for less than 15 minutes, without any post ictal neurological deficit. Controls were selected from age matched population of children attending paediatric OPD for short febrile illness without seizures. Cases and controls were selected in a 1:1 ratio. Informed consent was obtained from legal guardians of all cases and controls. Cases with atypical febrile seizures, seizure disorders on treatment, afebrile seizures, those with clinical suspicion of central nervous system infection, neurodevelopment disorders, developmental delay, haematologic problems (thalassaemics), malignancy, rheumatologic disorders and those who were on iron supplementation were excluded

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from the study. For each case and control, a study proforma with demographic data, details of seizure episode, nature of febrile illness, family history, temperature at admission, clinical findings at presentation and initial laboratory reports including serum ferritin levels were recorded.

Iron deficiency anaemia (IDA) was defined as haemoglobin less than 11g/dl, serum ferritin less than 20 ng/ml, mean corpuscular volume (MCV) less than 70fl and mean corpuscular haemoglobin (MCH) less than 25pg/cell. Quantitative determination of ferritin in serum was done using chemiluminescence enzyme immunoassay method using a fully automatic system at the immunochemistry laboratory and complete blood count using an automated analyser in the haematology laboratory of the Hospital. Chi-square test, analysis of variance (ANOVA) test for discrete variables and t-test for continuous variables were employed using SPSS 11 for Windows. P value less than 0.05 was considered significant.

Results

Forty three cases and 43 controls were included in the study. There were 30 boys and 13 girls among cases and 23 boys and 20 girls among controls. Average duration from onset of fever to the episode of febrile seizure was 11.35±5.83 hours and average duration of seizures was 3.09±2.39 minutes. Mean age (cases 28.12±15.77 months, controls 28.02±16.50 months) and weight (cases 11.01±2.04 kg, controls 11.20±3.70 kg) were comparable among cases and controls. Twelve (27.9%) cases and 3 (7%) controls had family history of febrile seizures among first, second or third degree relatives suggesting significant (p= 0.011) association with febrile seizures. Twenty six children in the study group were detected to have IDA. IDA was more common among cases (22, 84.6%) than controls (4, 15.4%). A statistically significant difference in haemoglobin levels (cases 10.99±1.46 g/dl; controls 12.06±0.97g/dl, p=0.042), haematocrit (cases 32.41±5.36%, controls 34.39±2.38%, p=0.029) and serum ferritin levels (cases 47.98±29.22ng/ml, controls 74.07±44.67 ng/ml, p=0.012) were observed between cases and controls. In this study, majority of febrile seizures were precipitated by upper respiratory infections (26, 60.5%) followed by nonspecific viral fever (7, 16.28%) and gastroenteritis (6, 13.95%).

The baseline characteristics of the cases and controls are shown in Table 1.

Table 1: ***Baseline characteristics of cases and controls***

	Cases (n = 43)	**Controls (n = 43)**
Mean age (months)	28.12 ± 15.77	28.02 ± 16.50
Duration of fever (hours)	11.35 ± 5.83	20.19 ± 9.72
Mean duration of seizures (minutes)	3.09 ± 2.39	No seizures
Weight (kg)	11.01 ± 2.04	11.20 ± 3.70
Temperature at admission (^{0}F)	101.19 ± 11.31	99.68 ± 0.96

The haematological parameters of cases and controls are shown in Table 2.

Table 2: ***Haematological parameters of cases and controls***

	Group (N= 43)	**Mean**	**Standard deviation**	**P value**
Haemoglobin (g/dl)	Case	10.99	1.46	0.042
	Control	12.06	0.97	
Haematocrit (%)	Case	32.41	5.36	0.029
	Control	34.39	2.38	
MCHC (g/dl)	Case	33.06	1.76	0.508
	Control	35.08	2.66	
MCH (picogram/cell)	Case	24.54	2.79	0.206
	Control	26.55	8.58	
MCV (femtolitre)	Case	73.94	5.44	0.067
	Control	74.92	7.11	
Ferritin (nanograms/ml)	Case	47.98	29.22	0.012
	Control	74.07	44.67	

Discussion

Association of febrile seizures with iron deficiency was first published in an Italian study by Piscane, *et al*[10]. This was followed by more international studies[11-16]. In 2009, Hartfield[11] and colleagues, from University of Alberta, Canada reported in a retrospective study that children with febrile seizures were twice as likely to have iron deficiency as those with febrile illness alone. In this study, IDA was more prevalent among cases. Of 26 children having IDA, 22 (85%) were cases and 4 (15%) were controls. Twenty two (51%) cases had IDA. Rajwanti K *et al*[17] and Daoud *et al*[18] also reported statistically significant associations between iron deficiency and simple febrile seizures. Similar conclusions were made by Leela Kumari, *et al*[19], in children of age group 6 months to 3 years with febrile seizures. An observation in this study was the higher prevalence rate of IDA at around 30.2% in our subjects, whereas in most Western studies prevalence of IDA is around 8 to 10%. There was no statistically significant association between serum ferritin level and duration of seizures. Twelve (27.9%) cases had family history of febrile seizures, having a statistically significant association with febrile seizures in children which are in accordance with other studies worldwide. The mean corpuscular volume was 73.94±5.44 fl which was much lower than controls.

This study does have some limitations. The duration of seizures was obtained from history and no mother had actually started a stop watch when she saw her baby seizuring. Moreover, for any mother, seconds may feel like hours and minutes like centuries when she sees her baby in seizures. Approximate duration of seizures, obtained from the history, is liable to recall bias. As it is a referral hospital-based study, the prevalence of exposure and outcome variables may be different from a community setting. Serum ferritin, a nonspecific acute phase reactant, can rise in any inflammatory conditions, although both cases and controls were having fever at the time of enrolment. Cases and controls were matched for age but sex of children was not matched. Iron deficiency picture and convulsions may be seen in lead poisoning but blood lead levels could not be determined in our subjects.

Conclusion

Low serum ferritin value is a risk factor for simple febrile seizures and iron deficiency anaemia is a modifiable risk factor for simple febrile seizures in children of six months to sixty months of age.

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