

ELECTROENCEPHALOGRAPH CHANGES IN CHILDREN WITH FEBRILE SEIZURES IN ASSOCIATION WITH IRON DEFICIENCY ANEMIA.

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ABSTRACT

Introduction-It is observed that iron deficiency is related to involve in behavioural disorders, mental retardation, and impaired immune function. In children, Febrile Seizure (FS) is the most common seizure type which is not triggered by central nervous system infection or metabolic disorders. **Aim:** To study the various haematological parameters reflecting the iron deficiency anemia in the children of age group 6 month to 5 year presenting with febrile seizures. **Objectives:** 1. To determine the association between iron status and febrile seizures in children aged 6 months to 5 years. 2. To find out the correlation between the iron deficiency anemia with the febrile seizures. **Material and methods:** This prospective, case-control study enrolled total of 50 children admitted to the Pediatric department. The children were categorized into two groups: The case group: included 25 children with first attack of FS studied for EEG changes. The control group: included 25 febrile children but without seizures at the same age. Study period was from June 2017 to June 2018. Hemoglobin, mean corpuscular volume, MCH, MCHC and serum iron concentration were compared in the two groups in relation to age, sex and febrile. **Results:** The epileptiform activity was observed in 14 patients in case group with male: female ratio in males. The proportion of children with Hb < 11 g/dl was significantly higher in case group (P = >0.0001). The difference in MCV was significant in case group. The difference in Mean Serum Iron was significant in case group (P= >0.001). The common type of seizures observed were focal (84.25%), while generalized seizures were (15.75%) cases. **Conclusion:** The findings suggest that the low serum iron and presence of iron deficiency anemia can serve as a reinforcing factor for the febrile seizure in children.

Keywords Electroencephalograph, Febrile seizures, Iron deficiency anemia

No: of Tables: 04

No: of References: 19

Introduction

Febrile seizures are refer to the convulsions that occur in children between the age of 6 months to five years, with body temperature of 38°C or higher not resulting from central nervous system infection or any metabolic imbalance without any prior afebrile seizures. Simple febrile seizures are the most common type of seizure during childhood. A simple febrile seizure is a primary generalized, usually tonic-clonic attack associated with fever, lasting for a maximum of 15 min, and not recurrent within a 24-hr period. A complex febrile seizure is more prolonged (>15 min), is focal, and/or recurs within 24 hours.(1,2). The peak incidence is at the age of 18 months, and seen in 2–5% of all children.(3). The prevalence of febrile seizures in this sample was 6.4/1000 inhabitants; In the literature, it ranges from 3.5/1000 to 17/1000.(4) .It was noted that geographic discrepancy on prevalence of FS was observed in different parts of the country.

Materials and methods-This prospective, case-control study enrolled a total of 50 children admitted to the Pediatric department of KIMS University, Karad, Maharashtra. The children were categorized into two groups:-The case group: included 25 children with first attack of FS studied for EEG changes. The control group: included 25 children of febrile illness but without seizures of the same age. The study period was from June 2017 to June 2018. Hemoglobin, mean corpuscular volume, MCH, MCHC and serum iron concentration were compared

in the two groups in relation to age, sex and febrile seizures. Written informed consent was obtained from the parents of all patients for inclusion in the study. This study was approved by the Ethics Committee, KIMS University, Karad, Maharashtra. The equipments used were Brainwave 16 channel EEG machine for recording of EEG. The Nihon Kohden celltac alpha Automated Haematology Blood-analyser for haematological parameters. Biochemical serum iron were noted. Diagnostic criteria for simple FS were included as seizures associated with fever and the seizures were generalized, short duration (<15 min), no recurrence of seizures within 24 hour, child is otherwise neurologically healthy and without any neurological abnormality before and after the episode of seizures. Iron deficiency anemia--was diagnosed by peripheral blood smear study along with hematological investigations of Hb less than 11 gm/dl, Hct< 33% , MCV < 74 fl , MCH < 24 pg, MCHC < 32%, Serum Iron < 50 µg/dl . Inclusion criteria - The children aged between 6 months to 60 months were considered. They were presenting with febrile seizures including both simple and complex febrile seizures. Febrile seizures including both first episode and recurrent episodes. Exclusion criteria: Any chronic systemic illness , neuro-developmental delay , previous afebrile seizures , neurodeficits, central nervous system infections, children on iron therapy, blood transfusion were excluded.

Case selection--A control group (n = 25) was selected randomly from children

admitted for febrile illnesses without seizure, any previous history of seizure or anticonvulsant therapy. Case and control groups were comparable for birth history, age, gender, normal growth and development, family history of febrile seizures, temperature at presentation. All routine investigations like urine analysis, complete blood count, peripheral blood smear examination, radiological etc were noted. Any use of iron supplementation was noted. Age, sex, underlying illness, frequency and duration of seizures were recorded. Detail EEG

findings were recorded. Sedation were given wherever required. Statistical analysis --Data were entered and analyzed using the statistical package for the social science (SPSS). Nominal data were expressed as frequency and percentage. Numerical data were expressed as mean \pm SD and were compared using Student's *t*-test. *P* values of less than 0.05% were considered significant, and *P* values of less than 0.001% were considered highly significant. Discrete variables are expressed as counts and percentages

Table 1: Comparison of Age between two study groups.

Age group(months)	No of cases in study group	Percentage	No of cases in control group	Percentage
6-12	04	16	06	24
13-24	10	40	12	48
24-36	08	32	04	16
37-48	02	08	02	08
49-60	01	04	01	04
Total	25	100	25	100

Table-2. Gender wise distribution between two study groups

Cases with febrile seizures Study group	Cases without febrile seizures – control group	
	Male	Female
14	11	08
M:F=1.2:1		M:F=2.1:1

Table 3. Hematological parameters between two study groups

Hematological parameters	Study group	Control group	P value
Mean Haemoglobin (gm%)	9.8	11.2	<0.0001
Mean Corpuscular Volume (MCV) (fl)	72.44	81.20	0.001
Mean corpuscular haemoglobin (MCH) (pg)	20.04	28.12	0.13
Mean corpuscular haemoglobin concentration (MCHC) (gm%)	29.00	32.74	0.11
Mean Serum Iron (MSI) (mcg/dl)	44.28	51.16	<0.001

Table 4. EEG abnormalities in cases of febrile seizures .

Type of epilepsy	No. of cases	Percentage
Focal	12	84.25
Generalized	02	15.75

RESULTS:

Our study includes 50 children which were based on 25 children with FS (14 male, 11 female) and a control group of 25 children (13male, 12 female). The epileptiform activity was observed in 14 patients in case group with male: female ratio was 1.7: 1. For this study we divided age groups of 6 month - 5 yrs (Table 1.) Table 3 shows the mean values of Hb, MCV, MCHC and S Iron in case and control groups. The proportion of children with Hb < 11 g/dl was significantly higher in case group (P = 0.0001 Table 3). The difference in MCV were significant in case group (Table 3). The difference in Mean serum iron were significant in case group .(P= <0.001). The common type of seizures observed were of focal (84.25%), while generalized seizures were observed in (15.75%) cases.

DISCUSSION:

In developing countries, around 60-75% of children are affected by iron deficiency anaemia. (5) It is mainly related to nutritional deficiency of iron. Because of

association of iron deficiency anemia with later development of epilepsy it was investigated in details by various studies. Many independent risk factors like age, gender, genetic, fever, type and duration of seizure, family and developmental history, multiple seizures, iron deficiency, perinatal exposure to antiretroviral drugs etc) have been studied as potential predictors of recurrent febrile seizures. (6) Berg AT et al in 1992 stated that iron plays a critical role in the metabolism of several neurotransmitters, and in low iron status, aldehyde oxidases and monoamine are reduced.(7). In addition, Shinnar S et al stated that the expression of cytochrome C oxidase, a marker of neuronal metabolic activity, is decreased in iron deficiency. (2). In developing countries, nutrition related iron deficiency is one of the most prevalent problems, especially among infants aged between 6 and 24 months.(8,9). Many studies have clearly demonstrated the effect of iron on development, cognition, behavior and neurophysiology, and especially on brain metabolism,

neurotransmitter function and myelination(10,11).

We compared iron status in children with febrile seizures and a control group in order to determine the relationship between iron status and febrile seizures in pediatric patients in rural Western Maharashtra.

Febrile seizures broadly classified as simple febrile seizures, complex febrile seizures. Simple febrile seizure is isolated, brief, and generalized. Conversely, a complex febrile seizure is focal, multiple (more than one seizure during the febrile illness), or prolonged, lasting either more than 10 or 15 minutes.

Various factors were associated with an increased risk of febrile seizures are described, these are a first- or second-degree relative with a history of febrile seizures, attendance at day care, developmental delay, a neonatal nursery stay of more than 30 days, there was a 28% chance of experiencing at least one febrile seizure for children with two of these factors(9). They are more prone for developing various complications.

In this study, the incidence of iron-deficiency anemia in the febrile seizure group was higher than the control group. Like our results, the study of Pisacane et al reported that iron deficiency anemia is higher in case group(13).In study by Vaswani et al also, 68% of cases were iron deficient compared to 30%. (14) In the study of Sadeghzadeh et al, although anemia was not common among febrile seizure patients, iron deficiency was more frequent in these patients(15). A study by

N. ur-Rahman and Billoo on 30 children with febrile convulsion and 30 children with other febrile diseases indicated that iron-deficiency anemia in case group was significantly more common than in the control group (16).

The routine blood studies were indicated to diagnose various metabolic, infectious causes of epilepsy.(16) Such cases were not consider for this study. We considered the haematological parameters like mean values of Hb, MCV, MCHC and Serum iron in case and control groups in details. In the present study, we found no significant differences in MCH and MCHC between cases and controls. The mean Hb% in our study was 9.8 gm%. The study by Leela Kumari et al, Azhr Doud et al, showed mean Hb% was 9.4 and 10.4 respectively.(17,18). However, there was a difference between the studied groups regarding Hb, MCV and SI by Naveed-ur-Rehman, 2005 (17). Daoud et al 2002, reported that the mean level of ferritin in cases with first FS is significantly lower than that in a reference group, but the mean levels of Hb, MCV, and MCH were lower in children with first FS than in children in a control group, although the differences were not significant.(18). The electroencephalography and neuroimaging is considered in children with neurologic abnormalities on examination and in those with recurrent febrile seizures In our study focal seizures were 85.25 % and generalised seizures were 15.75%. Our study is concordance with study by Kumari PL et al, 2012.(19). The prognosis and long-term management play a vital role in reassuring

families about the good prognosis after a febrile seizure.

Conclusions: The Children should be promptly evaluated after an initial febrile seizure. Our findings suggest that a considerable percentage of children having febrile seizure suffer from iron-deficiency anemia and low serum iron. This means that low serum iron and presence of iron deficiency anemia can serve as a reinforcing factor for the febrile seizure in children.

REFERENCES

Giuseppe Capovilla et al, Recommendations for the management of febrile seizures. Ad hoc Task Force of LICE Guidelines commission. *Epilepsia* Jan 2009;50 suppl 1:2-6.

Shinnar S, Glauser TA. Febrile seizures. *Journal of Child Neurology*; 2002;suppl 1:S44-52.

Subcommittee on Febrile Seizures; American Academy of Pediatrics. Neurodiagnostic evaluation of the child with a simple febrile seizure. *Pediatrics*, 2011, 127: 389-394.

S. Al Rajeh, A. Awada, O. Bademosi, A. Ogunniyi. The prevalence of epilepsy and other seizure disorders in an Arab population: a community-based study. *Seizure*, 2001, 10 : 410-414.

Graves RC, Oehler K, Tingle LE. Febrile seizures: risks, evaluation, and prognosis.

American family physician. 2012; 85(2):149-53

Kobrinsky NL, Yager JY, Cheang MS, Yatscoff RW, Tenenbein M. Does iron deficiency raise the seizure threshold? *Journal of Child Neurology* 1995;10,(2)):105-9.

Berg AT. Febrile seizures and epilepsy: the contribution of epidemiology. *Paediatric and Perinatal Epidemiology* 1992;6:145-52.

R.F. Florentino, R.M. Guirriec. Prevalence of nutritional anemia in infancy and childhood with emphasis on developing countries .A. Stekel (Ed.), *Iron nutrition in infancy and childhood*, Raven Press ; New York: 1984. pp. 61-74.

E. DeMaeyer, M. Adiels-Tegman. The prevalence of anemia in the world .*World Health Statistics Quarterly*. 1985;38(3):302-1.

M.DeUngria, R. Rao, J.D. Wobken, M. Luciana, C.A. Nelson, M.K. Georgieff. Perinatal iron deficiency decreases cytochrome c oxidase (CytOx) activity in selected regions of neonatal rat brain. *Pediatric Research*, 2000, 48:169-176.

N. Madan, U. Rusia, M. Sikka, S. Sharma, N. Shankar. Developmental and neurophysiologic deficits in iron deficiency in children. *Indian Journal of Pediatrics*, 2011, 78 (1) 58-64.

Soheila Zareifer et al. Association between iron status and febrile seizures. *Seizure*: 2012;21,601-603.

Pisacane A, Sansor R, Impagilazzo N et al. Iron deficiency anaemia and febrile convulsion : Case control study in children under 2 years. *BMJ*. 1996; 313:343.

Vaswani R. K, Dharaskar P. G, Kulkarni S, Ghosh K. Iron Deficiency as a Risk Factor for First Febrile Seizure. *Indian Pediatr*. 2009;47:437–439.

Sadeghzadeh M, Khoshnevis P, Mahboubi E. Iron Status and Febrile Seizure-A Case Control Study in Children Less Than 3 Years. *Iran J Child Neurol*. 2012;6(4):27–31.

S S Jagtap , K C Wingker, A N Gosavi, S V Jagtap. Epilepsy – Clinico-etiological Profile at Tertiary Care Centre . *Asian Pac. J. Health Sci.*, 2017; 4(1):140-144.

Naveed-ur-Rehman AG. Billoo. Association between iron deficiency anemia and febrile seizures. *J. Coll. Phy. Surg. Pak*. 2005; 15(5):338-340.

Daoud AS, Batieha A, Abu-Ekteish F, Gharaibeh N, Ajlouni S, Hijazi S. Iron status: a possible risk factor for the first febrile seizure. *Epilepsia*; 2002;43, (7):740–3.

Kumari PL, Nair MK, Nair SM, Kailas L, Geetha S. Iron deficiency as a risk factor for simple febrile seizures-a case control study. *Indian Pediatr*. 2012;49(1):17-9.

