

TO STUDY THE HEMOGLOBIN, SERUM FERRITIN, SERUM IRON, HEMATOCRIT VALUES AND PERIPHERAL BLOOD SMEAR IN CHILDREN WITH FEBRILE SEIZURE.

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Abstract

Background: To study the hemoglobin, serum ferritin, serum iron, hematocrit values and peripheral blood smear in children with febrile seizure.

Methods: Hospital based Prospective, Analytical, Case – Control study conducted on 100 patients were enrolled in the study out of which 50 were cases which were febrile convulsion patients and 50 were control who were age and weight matched children.

Results: Mean hemoglobin level was 10.37 ± 1.85 and 11.84 ± 1.69 in study and control groups respectively and this difference was found statistically highly significant ($p < 0.001$).

Conclusion: Our findings suggest that low serum iron levels and the presence of anemia can serve as strengthening factors for the FSs in children. Therefore, ID can be added to the list of risk factors for febrile convulsions. Accordingly, children with FSs are suggested to be monitored for diagnosis and treatment of IDA.

Keywords: Hemoglobin, IDA, Epilepsy.

Introduction

Due to the presence of iron in hemoglobin structure, it plays a crucial role in the transport of oxygen to different tissues such as the brain. ¹Iron deficiency (ID) reduces the metabolism of some neurotransmitters, such as monoamine and aldehyde oxidase¹. Several lines of evidence led to the hypothesis that iron may have a role in the onset of a convulsion. However, the studies carried out so far have reported conflicting results. Some studies have reported that in the patients with ID, febrile convulsion is significantly higher than that in control group ² On the contrary, some authors have concluded that the risk of FS in anemic children seems to be less than that in children without FS and that ID can be a protective mechanism against convulsions by increasing the convulsion threshold, and thus iron supplements should be given with caution to the children. Other studies have shown that ID plays no role in pediatric FS ^{2,3}

Since the relationship between IDA and FS is not yet determined, chance or other unknown factors can be considered as causes. ⁴

Materials and methods

Study design

Hospital based Prospective, Analytical, Case – Control study.

Study population

Infants and children aged between 6 months to 5 years.

Sample size

100 patients were enrolled in the study out of which 50 were cases which were febrile convulsion patients and 50 were control who were age and weight matched children.

Selection of control

The control group included the age and weight matched children suffering from a febrile illness without seizures, such as urinary tract infection, gastroenteritis and respiratory tract infection, coming to hospital.

Sampling Method

Convenience sampling

Inclusion Criteria

Children aged between 6 months to 5 years with simple/complex febrile seizures (seizure occurring in developmentally normal child in association with a febrile illness in the absence of CNS infection or any other defined cause of seizures).

Exclusion Criteria

1. Children with previous history of established non febrile seizures
2. Neurological infections (meningitis, encephalitis)
3. Hereditary metabolic disorders
4. Developmental delay
5. Children with history of birth asphyxia

6. Persistent neurological deficits

Data Collection

Demographic data, seizure details, nature of febrile illness, complete developmental history, family history of epilepsy/febrile seizures, temperature at admission, general examination, Systemic examination and nutritional status were recorded (IAP weight for age classification was used to grade protein energy malnutrition) including the final diagnosis was recorded.

Estimation of hemoglobin and hematocrit were done by auto analyzers.

Serum ferritin levels were measured using a Ferritin quantitative enzyme immunoassay test kit, which is based on a solid phase enzyme linked immunosorbent assay. The assay system utilizes one ferritin antibody for solid phase (microliter wells) immobilization and another mouse monoclonal anti-ferritin antibody in the antibody enzyme (horseradish peroxidase) conjugate solution. The test sample was allowed to react simultaneously with the antibodies, resulting in ferritin molecules being sandwiched between the solid phase and enzyme linked antibodies. After 60 min incubation at room temperature, the wells are washed with water to remove unbound labeled antibodies. A solution of Tetramethylbenzidine (TMB) is added and

incubated for 20 min, resulting in the development of a blue color. The color development is stopped with the addition of 2N Hydrochloric acid, and the color changed to yellow which is measured spectrophotometrically. At 450nm, the concentration of ferritin is directly proportion to the color intensity of the test sample.

Serum iron levels were estimated using Bathophenanthroline method, principle being Iron in the serum is present as Fe^{+3} bound to transferrin. In the assay, the proteins are precipitated and consequently the iron (Fe^{+3}) bound to ferritin is released by mild acid treatment. The iron thus released is reduced to (Fe^{+2}) by reducing agents. (Fe^{+2}) in turn reacts with Bathophenanthroline to form pink color complex whose intensity can be measured at 535 nm.

Peripheral smears were analyzed under light microscopy by a pathologist.

Data Analysis

Data was collected from eligible patients on a pre-structured pre-tested Proforma. For data analysis statistical software SPSS was used and data were analyzed with the help of frequencies, figures, proportions, measures of central tendency and appropriate statistical test.

Results**Table 1: Distribution of Cases according to peripheral smear in both groups**

Peripheral Smear	Groups				Total	
	Study		Control			
	No.	%	No.	%	No.	%
Dimorphic Anemia	2	4.0	1	2.0	3	3.0
MCHC	13	26.0	5	10.0	18	18.0
NCHC	8	16.0	8	16.0	16	16.0
NCNC	27	54.0	36	72.0	63	63.0
Total	50	100	50	100	100	100
χ^2	5.175					
P	0.159NS					

According to peripheral smear, 27(54%) and 36(72%) patients had NCNC, 13(26%) and 5(10%) had MCHC, 8(16%) each had NCHC and 2(4%) and 1(2%) had dimorphic anemia in study and control groups respectively. On applying chi square test, the difference was found statistically insignificant ($p>0.05$).

Table 2: Distribution of cases according to hemoglobin (gm%) level in both groups

Hemoglobin (gm%)	Groups				Total	
	Study		Control			
	No.	%	No.	%	No.	%
<9	13	26.0	6	12.0	19	19.0
9.1-11	13	26.0	3	6.0	16	16.0
>11	24	48.0	41	82.0	65	65.0
Total	50	100	50	100	100	100
Mean	10.37		11.84			
SD	1.85		1.69			
t	4.122					
p	<0.001HS					

Table 7 shows hemoglobin level in both study and control groups. In study group, out of total 50 patients, 24(48%) had their hemoglobin level >11 gm%, while 13(26%) each had their hemoglobin level <9 and 9.1-11 gm%.

In control group, 41(82%) patients had their hemoglobin level >11 gm% while 6(12%) and 3(6%) had their hemoglobin level <9 gm% and 9.1-11 gm% respectively.

Mean hemoglobin level was 10.37 ± 1.85 and 11.84 ± 1.69 in study and control groups respectively and this difference was found statistically highly significant ($p < 0.001$).

Table 3: Distribution of cases according to packed cell volume in both groups

PCV (%)	Groups				Total	
	Study		Control			
	No.	%	No.	%	No.	%
Abnormal (<32%)	20	40.0	7	14.0	27	27.0
Normal (32-43%)	30	60.0	43	86.0	73	73.0
Total	50	100	50	100	100	100
Mean	31.30		34.78			
SD	5.10		4.88			
t	3.482					
P	0.001					

According to packed cell volume, 20(40%) patients in study group and 7(14%) in control group had PCV within abnormal (<32%) range.

Mean PCV was $31.30 \pm 5.10\%$ and $34.78 \pm 4.88\%$ in study and control groups respectively and this difference was found statistically significant ($p < 0.01$).

Table 4: Distribution of cases according to Iron (mcg/dl) level in both groups

Iron (mcg/dl)	Groups				Total	
	Study		Control			
	No.	%	No.	%	No.	%
Abnormal (<55)	19	38.0	6	12.0	25	25.0
Normal (50-120)	31	62.0	44	88.0	75	75.0
Total	50	100	50	100	100	100
Mean	56.71		71.40			
SD	14.89		14.67			
t	4.970					
p	<0.001					

Above table shows distribution of cases according to Iron (mcg/dl) level in both groups. In study group, 19(38%) patients had abnormal (<55) range of iron while in control group only 6(12%) had abnormal range.

Mean iron was 56.71 ± 14.89 mcg/dl and 71.40 ± 14.67 mcg/dl in study and control groups respectively and this difference was found statistically highly significant ($p < 0.001$).

Table 5: Distribution of cases according to serum ferritin (ng/dl) level in both groups

Serum Ferritin (ng/dl)	Groups				Total	
	Study		Control			
	No.	%	No.	%	No.	%
Abnormal (<13)	12	24.0	2	4.0	14	14.0
Normal (13-400)	38	76.0	48	96.0	86	86.0
Total	50	100	50	100	100	100
Mean	43.46		69.37			
SD	43.30		31.31			
t	3.432					
p	=0.001					

Above table shows distribution of cases according to Serum Ferritin level in both groups. In study group, 12(24%) patients had abnormal (<13) range of serum ferritin level while in control group only 2(4%) had abnormal level.

Mean serum ferritin level was 43.46 ± 43.30 ng/dl and 69.37 ± 31.31 ng/dl in study and control groups respectively and this difference was found statistically significant ($p < 0.01$).

Discussion

Convulsions or seizures are one of the important pediatric health problems in developing and developed countries and febrile seizures are the most common seizure disorder in childhood, affecting 2% to 5% of children between the ages of 6 and 60 months¹. It is generally believed that FS is an age-dependent response of the immature brain to fever. This postulation is supported by the fact that most (80-85%) febrile seizures occur between 6 months and 3 years of age, with the peak incidence at 18 months.

According to peripheral smear, 27(54%) and 36(72%) patients had NCNC, 13(26%) and 5(10%) had MCHC, 8(16%) each had NCHC and 2(4%) and 1(2%) patients had dimorphic anemia in study and control groups respectively.

The definition of anemia varies by sex and age. The most commonly used definitions of anemia come from the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO). Anemia was defined as, when one of the following is present: Hb <11g/dl, HCT level <33%, serum iron concentration of < 22 µg/dl, Serum ferritin less than 12 microgram/dl and Peripheral smear showing Microcytic hypochromic anemia. Among the various causes of anemia, lack of sufficient iron for synthesis of hemoglobin is the most common hematologic disease of infancy and childhood. It is estimated that 30% of the global population suffers from iron-deficiency anemia, most of those affected live in developing countries. The incidence of iron deficiency anemia among children 6 months to 59 months in India is 79% and out of this 36% were mild anemic, 40% were moderately anemic and 3% suffer from severe anemia (NFHS 3 conducted in 2005-06). In the present study, mean hemoglobin level was 10.37±1.85 and 11.84±1.69 in study and control groups respectively and this difference was found statistically highly significant.

The study conducted by Kobrinsky *et al.*, found that Hb level was <11gm% in both study and control groups.

According to packed cell volume, 20(40%) patients in study group and 7(14%) in control group had PCV within abnormal (<32%) range. Mean PCV was 31.30±5.10% and 34.78±4.88% in study and control groups respectively and this difference was found statistically significant (p<0.01).

The study conducted by Naveed Ur Rehman *et al* and Billoo⁵ found hematocrit <30% more in cases as compared to controls (p=<0.01).

The serum iron concentration represents equilibrium between the iron entering and leaving the circulation. It reflects the balance between several factors, including iron absorbed, iron used for hemoglobin synthesis, iron released by red cell destruction and the size of iron stores. As a measure of iron deficiency, serum iron estimation can have some limitations because iron has a wide range of normal

values that can vary significantly with age, sex and laboratory methodology. There can be marked circadian changes (as much as 100 µg/dl during the day) in iron level. In present study, 19(38%) patients had abnormal (<55) range of iron in study group while only 6(12%) patients had abnormal iron range in control group. Mean iron was 56.71±14.89mcg/dl and 71.40±14.67mcg/dl in study and control groups respectively and this difference was found statistically highly significant (p<0.001).

Pisacane *et al*⁶ studied the serum iron level between 6-24 months of age and found low level of iron in febrile children. Bidabadi *et al*⁷ reported high serum Iron level in febrile seizure but it was statistically insignificant.

Serum ferritin is an indicator of body stores of iron. Serum ferritin is a reliable indicator which can be used to determine body stores of iron and can be repeated whenever required. A serum ferritin level below 30 µg/dl is an indicator of iron deficiency status. In the present study Mean serum ferritin level in study group was 43.46±43.30ng/dl, while in control group it was 69.37±31.31ng/dl and this difference was found statistically significant. Under steady state conditions, the serum ferritin level correlates with total body iron stores, thus the serum ferritin is the most convenient laboratory test to estimate iron stores. In study conducted by Daoud *et al*⁸ low (29.5 ±21.3 µg/dl) serum ferritin was found in children suffering from febrile seizures.

Conclusion

Our findings suggest that low serum iron levels and the presence of anemia can serve as strengthening factors for the FSs in children. Therefore, ID can be added to the list of risk factors for febrile convulsions. Accordingly, children with FSs are suggested to be monitored for diagnosis and treatment of IDA.

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