

RESEARCH ARTICLE

RELATIONSHIP BETWEEN IRON DEFICIENCY ANEMIA AND FEBRILE SEIZURES

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Abstract

Objective

Febrile seizure is the most common convulsive disorder in childhood. The role of iron in metabolism of neurotransmitters and carrying oxygen to the brain suggests the possibility of a relationship between iron deficiency anemia and febrile seizures.

The aim of this study was to investigate the relationship between iron deficiency anemia and febrile seizures.

Materials & Methods

This case - control study was performed on 132 cases and 88 controls, aged 9 months to 5 years, from July 2007 to June 2009 in Baqiyatallah Hospital. Patients were selected using simple random sampling. The case group included children with first febrile seizure (core temperature over 38.5°C during seizure) without a central nervous system infection or an acute brain insult. The control group included children suffering from a febrile illness without seizure. Iron deficiency anemia was defined with one of these laboratory indexes: 1) Hemoglobin (Hb) <10.5mg/dl 2) Plasma ferritin <12ng/dl 3) Mean corpuscular volume (MCV) <70 fl. The data collected from patients were analyzed with SPSS.13 software.

Results

Low plasma ferritin was found in 35 cases (26.5%) compared to 26 controls (29.5%), low Hb level was found in 4 cases (3%) compared to 6 controls (6.8%) and low MCV was found in 5 cases (3.8%) compared to 6 controls (6.8%). There was no significant difference in plasma ferritin, Hb level and MCV indices between the two groups.

Conclusion

Considering the above-mentioned results, there is no relationship between iron deficiency anemia and febrile seizures.

Keywords: Iron deficiency anemia, febrile seizures, Children

Introduction

Febrile convulsion is the most common convulsive disorder in children which occurs in 2-5 % of them (1). This seizure happens in children aged between 6 months and 5 years, with a core temperature higher than 38 °C without a central nervous system infection or an acute brain insult (2).

Iron deficiency is one of the most common nutrition-related problems in the world, with an appraised 5 billion people (including the human infants especially between 6 and 24 months of age) so afflicted. In developing countries, 46–66% of the

children under the age of four are anemic, half having iron deficiency anemia (3 , 4).

Considering the age prevalence of iron deficiency anemia and febrile convulsions which are the same, the role of iron in the metabolism of neurotransmitters (such as GABA and serotonin) and some enzymes (such as monoaminoxidase and aldehydoxidase), the function of hemoglobin in conveying oxygen to the brain, and since fever can exacerbate symptoms that result from anemia, a relationship between iron deficiency anemia and febrile convulsions is probable (5 , 6 , 7).

Kobrinisky et al deduced that iron deficiency might have a protective effect on febrile convulsions (8). Piscane et al believed that in patients with iron deficiency anemia, there was a notably higher incidence of febrile convulsions compared to the control group (9). Daoud et al reported that plasma ferritin in the first episode of febrile convulsions was significantly lower than the control group (10). Hartfield et al showed that children with febrile convulsions were nearly twice as likely to be iron deficient as those with febrile sickness merely (11). Considering the conflicting results of the previous studies, we designed this case-control study to evaluate the relationship between iron deficiency anemia and febrile convulsions.

Materials & Methods

This case - control study was performed on 132 cases and 88 controls, aged 9 months to 5 years, from July 2007 to June 2009 in Baqiyatallah Hospital (a referral hospital in Tehran). Patients were selected through simple random sampling. The case group included children with first

febrile seizure (core temperature over 38.5°C during seizure) without a central nervous system infection or an acute brain insult. The control group included children suffering from a febrile illness without seizure such as urinary tract infection, gastroenteritis and respiratory tract infection. Controls and cases were age- and sex-matched. Exclusion criteria were previous history of seizures, developmental delay and neurological deficits. Hemoglobin (Hb), mean corpuscular volume (MCV) and plasma ferritin (PF) were measured for all children in the hospital laboratory. Anemia was defined when one of the following was present: Hb<10.5mg/dl, plasma ferritin<12ng/dl and MCV<70 fl. The collected data were analyzed with SPSS 13 software. Descriptive analysis was used to describe, mean and standard deviation, chi-square for comparing qualitative data, independent T-Test for quantitative data and odds ratio for comparing risks in each group. Statistical significance was set at P < 0.05.

Results

Of these 220 subjects, 132 patients were in the case group and 88 patients were in the control group.

Frequency of the patients based on age and gender is shown in table 1. There was no significant difference in age and gender between cases and controls.

Frequency distribution of iron deficiency anemia according to plasma ferritin, Hb level and MCV indices are shown in table 2. There was no significant difference in plasma ferritin, HB level and MCV indices between cases and controls.

Table 1. Frequency distribution of patients based on age and gender

character	No.	Average age ± (SD)	Gender male No.	Gender male %	Gender female No.	Gender female %
Cases	132	39 ± 15.92	81	61.4	51	36.6
Controls	88	35.1 ± 15.35	47	53.4	41	46.6

Table 2. Frequency distribution of patients with iron deficiency anemia according to plasma ferritin, Hb and MCV indices

Character	Cases	Controls
Patients with decreased HB		
No.	4	6
%	3	6.8
P.value	0.241	0.241
Patients with decreased plasma ferritin;		
No.	35	26
%	26.5	29.5
P.value	0.623	0.623
Patients with decreased MCV;		
No.	5	6
%	3.8	6.8
P.value	0.312	0.312

Discussion

Considering the above-mentioned results, it seems that there is no relationship between iron deficiency anemia and febrile seizures. The results of previous studies are controversial; some of them concluded that iron deficiency anemia caused intensification of febrile seizures, others mentioned protective effects of iron deficiency against febrile seizures and the remaining confirmed our results.

Pisacane et al., in a case-control study of 293 controls and 146 patients aged 6 to 24 months, showed a significantly higher rate of iron deficiency anemia in patient with febrile seizures as compared to controls (9), while Daoud et al.(10) in a similar study on 75 patients and 75 controls, concluded that only a low plasma ferritin level was correlated with febrile seizure, but there was no significant difference in hemoglobin and MCV. Kobrinsky et al., (8) in a case-control study of 25 cases and 26 controls, described that anemia increased the threshold for febrile seizure and that lack of iron might protect against the development of febrile convulsions. Naveed-ur-Rehman(12) declared that plasma ferritin level was significantly depleted in cases compared to controls and suggested that iron deficient children were

more vulnerable to febrile convulsions. Bidabadi et al. (13) suggested that iron deficiency anemia was less frequent among cases with febrile seizures, as compared to the controls. Abaskhanian et al (14), in a cases-control study of 100 cases and 100 controls, reported that the incidence of febrile seizure was lower in cases with iron deficiency anemia but the difference was not significant. Asadi-Pooya et al (15) conducted a case-control study on 96 cases and 106 controls and stated that there was no significant difference in the means of hemoglobin, hematocrit, MCV, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration (MCHC) and platelet count between cases and controls. Also, the study showed no relationship between epilepsy and RBC indices. However, this study was performed on epileptic children while we studied children with febrile seizures.

Vaswani et al (16) performed a cases-control study on 50 cases and 50 controls and concluded that the mean serum ferritin level was significantly diminished in cases compared with controls, so iron deficiency might be a possible risk factor for febrile convulsion in children. A large retrospective case-control study of 361 patients and 390 controls which was performed by Hartfield et al

(11) showed that children with febrile convulsions were nearly twice as likely to be iron deficient compared to those with febrile sickness merely. His study suggested that screening for iron deficiency should be regarded in children presenting with febrile convulsions.

In the present study, no relationship was found between iron deficiency anemia and febrile seizures in children aged between 9 months and 5 years. Thus, performing screening tests for recognizing children who suffer from iron deficiency anemia and treating them to prevent febrile seizures is controversial and to some extent depends on the expert's views and patient's conditions.

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References

1. Aicardi J. Febrile convulsion in epilepsy in children. 5th ed, Lippincot, William & Wilkins 2004; P. 220-34.
2. Wolf PS, Shinnar S. Febrile seizures in current management in child neurology. 2nd ed, London: Hamilton; 2002. P. 960-96.
3. DeMaeyer E, Adiels-Tegman M. The prevalence of anemia in the world. *World Health Stat Q* 1985;38:302-16.
4. Stoltzfus R. Defining iron-deficiency anemia in public health terms: a time for reflection. *J Nutr* 2001;131(2S-2):565S-7S.
5. Harris R. Iron deficiency anaemia: does it really matter? *Occasional Review, paediatrics and child health* 2007;17(4):143.
6. Parks YA, Wharton BA. Iron deficiency and the brain. *Acta Paediatr Scand* 1989; S5 (suppl 361):71-7.
7. Weatherall DJ, Clegg JB. The thalassaemia syndromes. 4th ed. London: Blackwell Science; 2001. P. 192,231.
8. Kobrinsky NI, Yager JY, Cheang Ms, Yatscoff RW, Tenenbein M. Does iron deficiency raise the seizure threshold? *J Child Neurol* 1995; 10(2): 105-9.
9. Pisacane A, Sansone R, Impagliazzo N, Coppola A, Ronaldo P, D'Apuzzo A, Tregrossi C. Iron deficiency anaemia and febrile convulsions: case-control study in children under 2 years. *BMJ* 1996; 313(7153):343.
10. 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.
11. Hartfield DS, Tan J, Yager JY, Rosychuk RJ, Spady D, Haines C, et al. The association between iron deficiency and febrile seizures in childhood. *Clin Pediatr (Phila)* 2009; 48(4): 420-6.
12. Naveed-ur-Rehman, Billoo AG. Association between iron deficiency anemia and febrile seizures. *J coll Physicians Surg Pak* 2005 Jun;15(6):338-40.
13. Bidabadi E, Mashouf M. Association between iron deficiency anemia and first febrile convulsion. A case-control study. *Seizure* 2009;18(5):347-351 .
14. Abaskhanian A, Vahid Shahi K, Parvinnejad N. The Association between iron deficiency and the first episode of febrile seizure. *J Babol Univ Med Sci* 2009; 11(3): 32-36.
15. Asadi-Pooya AA, Ghetmiri E. Red blood cell indices in children with idiopathic epilepsy: A case-control study. *Clinical Neurology and Neurosurgery* 2006;108(6):614-615 .
16. Vaswani M, Dharaskar P G, Kulkarni S, Ghosh K. Iron Deficiency as a Risk Factor for First Febrile Seizure . *Indian paediatrics j* 2009 ; 3:1-3 .