

FEBRILE SEIZURE IN THALASSEMIC PATIENTS

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Abstract

Objective

Febrile seizure is the most common seizure disorder in children. Its pathophysiology is not fully understood yet; however, some risk factors have been cited for it. Iron is one of these influential elements and is involved in the metabolism of some neurotransmitters which are reduced in iron-deficiency anemia and also increases the sensitivity of neural cells during a febrile episode. The present study aimed to determine the rate of febrile seizure in thalassemic patients and to compare it with the corresponding rate in the normal population.

Materials & Methods

This descriptive cross-sectional study was conducted on 766 patients with thalassemia major. They were all older than 6 months and were referred to Dastghaib Cooly's Clinic, affiliated to Shiraz University of Medical Sciences, from Oct 2006 to May 2007, and 766 normal and healthy children as the control group. Questionnaires containing demographic data and past history of febrile seizure, age of febrile seizure, number of episodes, hospitalization, and related family history were prepared and filled through interviewing the parents.

Results

Febrile seizure was detected in 7 cases of the patient group (0.9%) versus 18 cases (2.3%) of the control group. The frequency of febrile seizure in the controls was 2.5 times more than that in the thalassemia group, which was statistically significant ($P < 0.05$).

Conclusion

This study showed a lower rate of febrile convulsion in thalassemic patients compared to the control group. Accordingly, it could be suggested that high iron storage is a protective factor against febrile convulsion.

Keywords: seizure, febrile, thalassemia, convulsion

Introduction

Febrile seizure is the most common seizure disorder in children and its prevalence rate among young children is 2-5% (1, 2). Its pathophysiology is not fully understood yet; however, some risk factors have been cited for it (3, 4). Several studies have shown that iron level may play a role in its occurrence (5-11).

Iron is an influential element in central nervous system functioning. Its deficiency is associated with neurologic complications such as cognitive behavioral changes

(12), developmental delay (13), breath holding episodes, stroke and pseudotumor cerebri (14). Iron deficiency during pregnancy induces some changes in dendritic structures of neural cells (7). It is involved in the metabolism of some neurotransmitters including monoamine and aldehyde oxidase, which are reduced in iron-deficiency anemia (9, 12, 14, 15) and increases the neural cells sensitivity during a febrile episode (7).

Iron deficiency is a nutritional issue in the world today, particularly in developing nations. It is estimated that about 5 billion cases are affected by it (16). The disorder is very common in 6- to 24-month old infants. In developing countries, about 44-66% of the children younger than 4 years are anemic; of which half is iron deficiency anemia (10, 17). According to the World Health Organization (WHO) statistics, the rate is estimated to be 20% in Iran (16).

There have been some studies on the role of plasma iron level in febrile seizure but the results are not unanimous. Some studies demonstrate the protective role of it while others do not (5-11, 18, 19). Table 1 presents different accounts on the relationship between iron level and febrile seizure.

The plasma iron level is high in moderate to severe thalassemic cases. Thus, if iron plays a protective role in febrile seizure, its incidence is expected to be lower in thalassemic patients compared to healthy individuals. To our knowledge, only one study that was carried out in Thailand supported this expectation (18). The present study aimed to determine the rate of febrile seizures in thalassemic patients and compare it with the corresponding rate in the normal population.

Materials & Methods

This descriptive cross-sectional study was conducted on 766 patients with thalassemia major who were older than 6 month and were referred to Dastghaib Cooly's Clinic, affiliated with Shiraz University of Medical Sciences, Iran, from Oct 2006 to May 2007.

The patients were selected based on the prevalence of febrile seizure in the community (2-5%) and its rate among the thalassemia patients (1%) (1), error level of 0.5 and power of 80%. The control group consisted of 766 normal and healthy children at the pediatric clinics

of the same hospital. Attempts were made to select controls with similar sex and age distribution as the cases. Written informed consents were obtained from the parents and the study protocol was approved by the ethics committee of the university.

Questionnaires containing demographic data and past history of febrile seizure, age of febrile seizure, number of episodes, hospitalization, and corresponding family history were prepared and filled. Questions regarding the history of afebrile seizure and its etiology and family history of epilepsy were also included. It is worth noting that all such data were collected through interviewing the parents and guardians. To avoid bias, just one child from each family was randomly selected & interviewed about. To confirm febrile seizure, the medical records of those suspected of it were reviewed. Chi-square test was used to statistically compare the two groups.

Exclusion criteria were history of brain lesions such as brain tumor, abscess or cyst, mental retardation, intracerebral hemorrhage, hypoparathyroidism and afebrile seizure.

Febrile seizure is defined as a convulsion that occurs within the ages of 6 months to 5 years and is associated with a fever and a temperature over 38.5°C, with no evidence indicating cerebral infection of any other etiology. The child in such conditions is neurologically healthy (1, 20).

Results

The study population consisted of 2 groups of 766 thalassemia major patients (group I, cases) and 766 normal children (group II, controls).

The mean age of the cases and the controls was 16.4 years & 15.5 years, respectively. One hundred and fifty (19.6%) patients in group I were under 5 years of age. Regarding gender, 49.8% and 49.2% of the cases and controls were female, respectively. Sixty two percent of the cases and 52% of the controls were from urban areas. Based on the completed questionnaires, 12 cases were diagnosed with febrile seizure, of whom 7 had a history of hospitalization. After interviewing the parents of the 12 cases for the second time and reviewing the medical records of the 7 cases, it was revealed that one case had afebrile seizure, 2 cases had Shigella infection

with convulsion and 2 cases had just chills rather than convulsion. These 5 cases were excluded from the study. Therefore, the real number of cases with febrile seizure was 7 which accounted for 0.9% of the thalassemia patients.

The details are presented in table 2. Three cases in this group had a family history of febrile seizure.

Out of 766 controls, 20 had febrile seizure, and there was one case of meningitis and one case of shigellosis which were excluded from the study. Therefore, there were 18 cases (2.3%) of febrile seizure in the control group. Also, 12 cases (1.5%) had a family history of febrile seizure in the same group (Table 3).

The frequency of febrile seizure in the controls was 2.5 times more than that in the thalassemia group, which was statistically significant ($P < 0.05$) (Table 3).

Discussion

This study showed a lower rate of febrile convulsion in thalassemic patients compared to the control group. In other words, it could be said that high iron storage might probably act as a protective factor against febrile convulsion.

These results of this study are consistent with the results of a previous study performed by Auvicha in Thailand (18). They reviewed 430 patients with β -thalassemia. Three of them had febrile convulsion and the rate of febrile convulsion was 4.4 times less than the normal population.

Also, Hartfiel showed that the rate of Iron deficiency anemia in patients with febrile convulsion was two times less than its rate in febrile patients without convulsion (5).

In another study by Dauod, it was shown that serum ferritin was significantly lower in cases with febrile convulsion compared to individuals in the control group (9).

It is estimated that the prevalence of Iron deficiency anemia is 23-33% in developing countries (10). According to WHO studies in Iran, this rate is 20% among Iranian children (17).

The present study showed that a positive family history of febrile convulsion was less frequently found in

thalassemic patients compared to the control group. This might be due to the high incidence of thalassemia minor and intermedia in families with thalassemic patients. Consequently, the level of serum iron is higher among such families and therefore, the rate of febrile seizure is lower.

Considering the role of iron in cerebral neurotransmitter metabolism and its effect on the activities of central nervous system in neonates and children, it can be suggested that febrile seizure and serum iron level are negatively correlated.

One of the main limitations of this study was that parents did not have a correct understanding of febrile seizure; therefore, we tried to describe seizure, febrile seizure & its differential diagnoses for them before interview and data collection.

Another limitation was incomplete or lack of medical records, so the only way to evaluate the obtained data was through interviewing the parents which could result in insufficient data. On the other hand, there were no data on the serum iron and ferritin levels at the time of febrile seizure. It was assumed that serum iron and ferritin levels were high in thalassemic patients. Obviously, the results would be more reliable if those data were available.

Taking into account the prevalence of iron deficiency anemia in children and its relationship with febrile seizure, as shown in the present and similar previously studies, it could be suggested that iron supplement and treatment of iron deficiency anemia could reduce the corresponding incidence. Considering the fact that iron deficiency can serve as a risk factor of febrile seizure, screening for the deficiency in children is advisable to prevent recurrent convulsive attacks and the consequent associated neurological complications.

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References

1. Haslom RHA. Febrile seizures. In: Behrman RE, Kleigman RM, Jenson HB, editors. Nelson text

- book of pediatric. 18th ed. Philadelphia: WB. Saunders company; 2007. P.2457-58.
2. Aicardi J. Febrile convulsion in epilepsy children. In: Engel J, Timothy A, Pedley, Aicardi J, Dichter MA, editors. *Epilepsy: a comprehensive textbook*. Volume 3. 2th ed. Lippincot: William & Wilkins; 2008. P659-64.
 3. Shinnar S. Febrile seizure. In: Swaiman KF, Ashwal S, Ferriero DM, editors. *Pediatric neurology principles and practice*. 4th ed. Mosby; 2006. P1079-86.
 4. Huang CC, Wang ST, Chang YC, Huang MC, Tsai JJ. Risk factors for a first febrile convulsion in children: a population study in southern Taiwan. *Epilepsia* 1999; 40(6):719-25
 5. Hartfield DS, Tan J, Yager JY, Rosychuk RJ, Spady D, Haines C, Craig WR. The association between iron deficiency and febrile seizures in childhood. *Clinical Pediatrics* 2009; 48(4):420-26.
 6. Pisacane A, Sansone R, Impagliazzo N, Coppola A, Rolando P, D'Apuzzo A, Tregrossi C. Iron deficiency anaemia and febrile convulsions: case-control study in children under 2 years. *BMJ* 1996; 313(7053):343.
 7. Kobrinsky NL, Yager JY, Cheang MS, Yatscoff RW, Tenenbein M. Does iron deficiency raise the seizure threshold? *J Child Neurol* 1995; 10(2):105-9.
 8. Im S, Ah JK, Choi BJ, Lee IG, Whang KT. The relationship between iron deficiency anemia and febrile seizure. *J Korean Child Neurol soc* 2003; 11(1):55-60.
 9. 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.
 10. Naveed-ur-R, Billoo AG. Association between iron deficiency anemia and febrile seizures. *J Coll Physicians Surg Pak* 2005; 15(6):338-40.
 11. Bidabadi E, Mashouf M. Association between iron deficiency anemia and first febrile convulsion: A case-control study. *Seizure* 2009; 18(5):347-51.
 12. Beard LJ, Connor JR. Iron status and neural functioning. *Ann Rev Neut* 2003; 23:41-58.
 13. Argulo-kinzler RM, Peirano P, Lin E, Algarin C, Garrido M, Lozoff B. Twenty-four-hour motor activity in human infants with and without iron deficiency anemia. *Early Human Development* 2002; 70:85-101
 14. Gosh K. Non Hematological effects of iron deficiency: A Perspective. *Indian J Med Sci* 2006; 60: 30-37.
 15. Yager JY, Hartfield DS. Neurologic manifestations of iron deficiency in childhood. *Pediatr Neurol* 2002; 27(2):85-92.
 16. Stoltzfus RJ, Mullany L, Black RE. Iron deficiency anemia. In: Ezzati M, Lopez AD, Rodgers A, Christopher JL, editors. *Comparative quantification of health risks: global and regional burden of disease attributable to selected major risk factors*. Volume 1 Geneva: World Health Organization; 2004. P.163-209.
 17. Freire W. Strategies of the Pan American Health Organization–World Health. Organization for the control of iron deficiency in Latin America. *Nutr Rev* 1997; 55:183-8.
 18. Auvichayapat P, Auvichayapat N, Jedsrisuparp A, Thinkhamrop B, Siroj S, Piyakulmala T, Paholpak S, Wattanatorn J. Incidence of febrile seizures in thalassemic patients. *J Med Assoc Thai* 2004; 87(8):970-3.
 19. 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.
 20. Wolf PS, Shinnar S. Febrile seizure. In: Bernard LM, editors. *Current management in child neurology*. 3th ed. Hamilton: London; 2005. P.83-8.