Original Article

The Relation between Left Ventricular Function and Serum Ferritin in Major B-Thalassemia

Montazare Lotfe Elahi S MD[1], Hashemi A MD[2], Behjati SM MD[3], Zaolfaghari F BSc[4], Dehghani A BSc[4,] Akhavane ghalibaf M MD[5], beigomi M MD[1]

1- Shahid Sadoughi University of Medical Sciences and Health Services, Yazd, Iran
2-Department of Pediatrics, Hematology, Oncology and Genetics Research Center, Shahid Sadoughi University of Medical Sciences and Health Services, Yazd, Iran
3- Department of Pediatrics, Shahid Sadoughi University of Medical Sciences and Health Services, Yazd, Iran
4- Hematology, Oncology and Genetics Research Center, Shahid Sadoughi University of Medical Sciences and Health Services, Yazd, Iran
5- Pediateric, Shahid Sadoughi University of Medical Sciences and Health Services, Yazd, Iran

Received: 10 March 2011
Accepted: 20 July 2011

Abstract

Objective

Cardiac dysfunction is a major cause of death in patients with beta thalassemia. In these patients, repeated blood transfusion, ineffective erythropoiesis and increased gastrointestinal iron absorption lead to iron overload in the body and this induced heart failure. Left ventricular ejection fraction was measured in major beta thalassemia (β-Th) patients to detect the relation of serum ferritin level and left ventricular systolic function.

Materials and Methods

The present prospective study evaluated 75 patients with β-thalassemia (39 female, 36 male) aged one to 44 years old. They were treated with desferal 5 days a week for at least six months. For this study they treated by desferal 7 days a week. Left ventricular ejection fraction and serum ferritin were measured before and after intervention, and they were compared for the best treatment.

Results

The mean ejection fraction was 60.45% and 62.9% before and after aggressive therapy, which difference was significant. Serum ferritin level also was reduced after intervention. Difference between mean ferritin before and after intervention was 49.984. Serum ferritin showed negative correlation with left ventricular function.

Conclusion

Lower serum ferritin concentration with aggressive therapy was associated with better left ventricular function.

Keywords

β- thalassemia, ejection fraction, ferritin

Corresponding Author

Azam sadat Hashemi, Pediatric Hematologist & Oncologist, Assistant professor – Hematology oncology and Genetics Research Center, Shahid Sadoughi university of medical sciences and health services, Yazd- Iran
Email:dr_a_hashemi@yahoo.com

[Downloaded from ijpho.ssu.ac.ir on 2024-03-29]

Introduction

Major thalassemia will remain to be the one of the major health problem for at least the next few decades, particularly in developing countries (1). Thalassemias are a group of genetic disorders caused by unbalanced synthesis of alpha and non-alpha chains of globins due to impaired globin genes. Clinical characteristics of the major thalassemia are ineffective erythropoiesis and hemolytic anemia with microcytic hypochromic erythrocytes. Deposition of iron in heart myocytes causes severe disruption of their normal sarcomere structure, leading to a substantial loss of myofibrils, z-bands, and intercalated discs. Ultrastructural examination of myocytes of these patients revealed the presence of disrupted myocytes showing loss of myofibers, dense nuclei, and a variable number of pleomorphic electron dense cytoplasmic granules (2). Therefore cardiac disorders related to ventricular failure are the most frequent causes of death in this syndrome (4, 5, 6, 7).

At present, a common method to detect heart failure in these patients is measurement of the left ventricular ejection fraction (LVEF) through M-mode echocardiography (3).

Materials and Methods

This prospective study evaluated 75 major β-thalassemia patients (39 female,36 male) with a mean age of 29.12 years (1-44y). They followed in the outpatient service of thalassemia unit of Shahid Sadoughi hospital. Known beta thalassemia major patients with at least 10 units of blood transfusion, irrespective of their age and sex were included in this study. Patients who had blood transfusion less than 10 units were excluded. The patients were treated usually with despheral 5days a week. In aggressive therapy they received despheral 7 days a week for sixmonths. Serum ferritin was evaluated before and after aggressive therapy. M-mode echocardiography also was done to evaluate left ventricular function by ejection fraction before and after intervention. Echocardiography was performed by a pediatric cardiologist. Ejection fraction was estimated from the parasternal long-axis M-mode measurement according to Serum ferritin and ejection fraction were compared before and after aggressive therapy. Inaddition, the relation between systolic function changes, age (patients<10 and >10 years old) and sex were evaluated. None of the patients were excluded in this stage. All statistical analyzes were performed in SPSS statistical program (version 16 for windows) and T-test exact test was used.

Results

Mean of the ejection fraction was 62.9% after six months aggressive therapy, which was 60.45% before intervention. Difference between mean ferritin was 49.984 () before and after aggressive therapy. Both changes were significantly different (Pvalue#0.00 and Pvalue=0.001 respectively). Serum ferritin showed negative correlation with left ventricular ejection fraction .The patients with the highest serum ferritin had the lowest ejection fraction and left ventricular function. Mean changes of systolic function in male and female were 1.83, 2.46. However no significant difference was found (Pvalue=0.681) between them. Mean changes of systolic function in patients younger than 10 years old were 2.43 and in patients older than10 years old were 1.89 (Pvalue=0.725), but no significant difference was found. Mean ferritin before intervention in women was higher, and it was reduced after aggressive therapy. Sixty nine point four percent of male and 69.2% of female used deferoxamine regularly and 30.6% of male and 30.9% of female used it irregularly, but no significant difference was found.

[Downloaded from ijpho.ssu.ac.ir on 2024-03-29]

Discussion

Major beta thalassemia is a genetic disorder in which there is a progressive iron overload in various organs, leading to death in early adulthood. This iron overload occurs as a result of increased intestinal absorption and frequent blood transfusion needed in these patients (8).

Cardiac muscle is one of the organs affected by iron overload. Cardiac biopsies revealed the presence of disrupted myocytes showing loss of myofibers, dense nuclei, and a variable number of pleomorphic electron dense (9). Left ventricular involvement was reported. Necropsy studies showed that both ventricles are equally affected with hypertrophy and myocyte disruption (10). The results obtained from this study revealed that treatment with depheral from 5 to 7 days increased left ventricular ejection fraction (60.45% to 62.9%).

Previous studies documented the relation between left ventricular function and iron chelation. In 1998 Mariotti et al performed a study to evaluate the impact of therapy on subclinical cardiac dysfunction in phlebotomized ex-thalassemia major patients. They found that with complete phlebotomy program; indices of contracture and diastolic function were normal (11). Moreover, Anderson et al confirmed that siderotic heart failure is often reversible with intravenous iron chelation with desferioxamine (12). Although Yapark et al in 1998 and Ashena et al. in 2007 did not find any statistically significant relationship between serum ferritin concentration and systolic and diastolic indices (3,13). Telfer et al monitored liver function and serum ferritin level to predict the complications of iron overload in thalassemia patients. They demonstrated that the clinical end point of death or cardiac failure was significantly associated with increasing iron load (14).

Waldes-Cruz et al demonstrated abnormalities of left ventricular systolic and diastolic function even in asymptomatic children with β thalassaemia, using computer assisted echo studies (15). Borow et al reported an abnormal left ventricular end systolic pressure/dimension relation in asymptomatic young adults with β thalassaemia, showing normal indices of global systolic performance (16). Others have reported early cardiac dysfunction in asymptomatic β thalassaemic patients with chronic iron overload, using stress radionuclide angiography. The stress induced alterations of left ventricular systolic performance showed a correlation with the total amount of blood transfusion in these patients. Even in patients with few blood units transfusion, an abnormal response of the left ventricular ejection fraction to exercise was found, while the hemoglobin concentration was not predictive of left ventricular performance (17). Moreover, in asymptomatic patients with β thalassaemia submitted to an aggressive iron chelation regimen, a decrease in serum ferritin was associated with an increase in the left ventricular ejection fraction during stress test (18).

In our study, we found a weak but significant correlation between left ventricular ejection fraction and serum ferritin concentration. Patients with a higher ferritin level had a lower ejection fraction than patients with a lower ferritin concentration.

In 1994 Olivieri etal Found that the cardiovascular prognosis in thalassaemic patients was excellent if serum ferritin concentrations were maintained below 2500 ng/ml (26). This value has been considered a “safe” concentration (19). Our study also demonstrated the importance of a low ferritin level for the preservation of left ventricular function. The higher mean age of our patients confirmed a significant improvement of the treatment and lower ferritin concentration in this population. We suggest that a serum ferritin value of less than 1000 ng/ml should be considered the ideal goal of any therapeutic schedule. The value of early starting this therapeutic approach and maintaining good compliance has been documented before (19, 20).

This study showed negative relation between left ventricular function and serum ferritin, which suggested to try to decrease serum ferritin by aggressive therapy.

[Downloaded from ijpho.ssu.ac.ir on 2024-03-29]

Acknowledgment
We appreciate contribution of Pediatric award of shahid Sadoughi hospital.

Conflict of interest
None

Refrences
1. Nadeem I, Khalid H, Muhammad Y, Samina A. Ferritin Levels in Patients of Beta Thalassaemia Major. International Journal of Pathology; 2004; 2(2):71-74.
2. Hamdy AM, Zein El-Abdin MY, Abdel-Hafez MA. Right ventricular function in patients with beta thalassemia: relation to serum ferritin level. Echocardiography. 2007;24(8):795-801.
3. Ashena Z, Ghafurian S, Ehsani MA. The relation between left ventricular diastolic indices and serum ferritin in thalassemia major. Pediatr Hematol Oncol. 2007;24(1):3-14.
4. Engle MA. Cardiac involvement in Cooley's anemia. Ann NY Acad Sci.1969;119:694–702.
5. Hahalis G, Monalis AS, Gerasimidou I, et al. Right ventricular diastolic function in beta-thalassemia major: echocardiographic and clinical correlates. Am Heart J. 2001;141:428–434.
6. Orkin SH, Nathan DG. The thalassemias, In: Nathan DG, Orkin SH, Insburg DG, Look AT. eds. Hematology of Infancy and Childhood, ed 6. Philadelphia: WB Saunders;2003:888.
7. Favillis S, De Simone L, Mori F, et al. The cardiac changes in thalassemia major: their assessment by Doppler echocardiography. G Ital Cardiol. 1993;23:1195–1200.
8. Fosburg MT, Nathan DG: Treatment of Cooley's anemia. Blood 1990;76:435–444.
9. Kyriacou K, Michaelides Y, Senkus R, et al: Ultrastructural pathology of the heart in patients with β-thalassemia major. Ultrastruct Pathol 2000;24:75–81.
10. Hahalis G, Manolis AS, Apostolopoulos D, et al: Right ventricular cardiomyopathy in beta-thalassemia major. Eur Heart J 2002;23:147–156
11. Mariotti E, Angelucci E, Agostini A, Baronciani D, Sgarbi E, Lucarelli G. Evaluation of cardiac status in iron-loaded thalassaemia patients following bone marrow transplantation: improvement in cardiac function during reduction in body iron burden. Br J Haematol. 1998;103:916–921.
12. Anderson LJ, Westwood MA, Holden S, et al. Myocardial iron clearance during reversal of siderotic cardiomyopathy with intravenous desferrioxamine: a prospective study using T2* Cardiovascular magnetic resonance. Br J Haematol. 2004;127:348–355.
13. Yaprak I, Aksit S, Ozturk C, Bakiler AR, Dorak C, Turker M. Left ventricular diastolic abnormalities in children with beta-thalassemia major: a Doppler echocardiographic study. Turk Pediatr.1998;40:201–209.
14. Telfer PT, Prestcott E, Holden S, et al: Hepatic iron concentration combined with long-term monitoring of serum ferritin to predict complications of iron overload in thalassaemia major. Br J Haematol 2000;110:971–977.
15. Valdes Cruz LM, Reinecke C, Rutkowski M, et al. Preclinical abnormal segmental cardiac manifestations of thalassemia major in children ontransfusion-chelation therapy: echocardiographic alterations of left ventricular posterior wall contraction and relaxation pattern. Am Heart J 1982;103:505–11.
16. Borow KM, Propper R, Bierman FZ, et al. The left ventricular end-systolic pressure–dimension relation in patients with thalassemia major.Circulation 1982;66:980–5.
17. Leon MB, Borer JS, Bacharach SL, et al. Detection of early cardiac dysfunction in patients with severe b-thalassemia and chronic iron overload. N Engl J Med 1979;301: 1143–8.
18. Aldouri MA, Wonke B, Hoffbrand AV, et al. High incidence of cardiomyopathy in b-thalassemia patients receiving regular transfusion and iron chelation reversal intensified chelation. Acta Haematol 1990;84:113–17.
19. Olivieri NF, Nathan DG, MacMillan JH, et al. Survival in medically treated patients with homozygous beta-thalassemia. N Engl J Med 1994;331: 574–8.
20. Wolfe L, Olivieri NF, Sallan D et al. Prevention of cardiac disease by subcutaneous deferoxamine in patients with thalassemia major. N Engl J Med 1985;312: 1600–3.

[Downloaded from ijpho.ssu.ac.ir on 2024-03-29]