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SHORT COMMUNICATION

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Evaluation of Iron Chelation Therapy in Adults with Beta-Thalassemia Major in Hilla City

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Abstract

Background: People with thalassemia can have too much iron in their bodies. This overload can come from the disease itself or from regular blood transfusions. Excess iron can harm the heart, liver, and endocrine system.
Objectives: This study aims to show how effective Deferasirox therapy is in lowering iron levels in thalassemia patients.
Materials and Methods: We enrolled 30 patients and a healthy control group from November 2022, to February 2023. The participants were gathered from the maternity hospital's Department of Genetic Diseases in Babylon Province, Iraq. The patients were newly diagnosed, and the data included the sex of the patients—male and female—aged between 18 and 35 years, with a total of 20 patients. We collected data related to serum calcium and serum ferritin from medical records in the maternity hospital's Department of Genetic Diseases. The control group included 10 healthy men and women from the general population who visited the hospital and do not have beta thalassemia major. We analyzed serum ferritin and serum calcium levels.
Results: We found a significant increase in serum ferritin in patients before and after blood transfusions in beta thalassemia major when compared to healthy controls. We also observed a significant decrease in serum calcium in patients before and after blood transfusions in beta-thalassemia major compared to healthy controls.
Conclusion: The treatment for removing excess iron from the body is effective. However, the repeated blood transfusions for patients reduce the effectiveness of Deferasirox in promoting iron excretion.

Keywords: Thalassemia, Iron chelation, Desferrioxamine, Ferritin

1. Introduction

Thalassemia is a group of inherited hemoglobin disorders characterized by a multi-genetic condition that includes alpha thalassemia, beta-thalassemia, delta beta-thalassemia, and others. It is a hereditary disease, meaning that at least one parent must carry the disorder. For a child to be affected, they must inherit one abnormal gene from each parent. The disorder is caused by a genetic mutation or the deletion of key segments of certain genes. Molecular defects in the beta-globin gene cluster on chromosome 11 and the alpha-globin gene cluster on chromosome 16 lead to problems with hemoglobin production [1].

People with thalassemia can experience iron overload in their bodies. This can occur due to the disease itself or from frequent blood transfusions. Excess iron can damage the heart, liver, and endocrine system, which includes glands that produce hormones essential for various body functions. This damage is marked by excessive iron deposits [2]. Without proper iron chelation therapy, nearly all patients with beta-thalassemia can reach dangerously high iron levels. Even with chelation therapy, repeated blood transfusions can still cause iron overload, leading to increased reactive oxygen species in the body. This oxidative stress may damage parathyroid glands and other organs, potentially resulting in hypoparathyroidism and hypocalcemia [2].

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Calcium and phosphate are crucial minerals for maintaining strong bones. They also play vital roles in muscle function, nerve signaling, and the secretion of various glands. Parathyroid hormone is the main hormone that regulates calcium levels in the body [3].

Chelation therapy is a treatment that removes excess iron caused by regular blood transfusions. It is important because high iron levels can harm organs. The medications used in chelation therapy are called chelating agents. There are three chelating agents currently available:

- Desferrioxamine (DFO) – delivered through a pump that slowly infuses the medicine via a needle into the skin over 8 to 12 hours, five or six times a week.
- Deferiprone (DFP) – taken as a tablet or liquid three times a day; it can be used with DFO to reduce the number of infusions needed.
- Deferasirox (DFX)– taken once a day as a tablet that dissolves in a drink. Each medication has its own pros and cons [4].

Chelating drugs can vary in their ability to eliminate iron and may help treat various iron metabolism disorders, including beta-thalassemia and other types of thalassemia not dependent on transfusions. Evaluating the risks and benefits of the chosen therapy is essential, taking into account individual differences, as well as the long-term effectiveness, safety, and cost of the chelating medication.

Deferasirox (DFX/DFRA) has shown effectiveness in increasing fecal iron excretion without significantly affecting urinary iron levels. It can also lower liver iron and serum ferritin levels in some patients when taken at recommended doses of 10 to 30 mg/kg/day. Doses of 10 to 40 mg/kg have been linked to a steady rise in iron excretion, although doses of 20 mg/kg may not be sufficient to create a negative iron balance in many patients. Most patients respond better to 40 mg/kg of deferasirox, achieving an average iron excretion rate of 28 mg/day per 50 kg of body weight [5].

Currently, millions of patients with transfusion-related iron overload use DFX/DFRA. Recent studies indicate that DFRA is relatively effective, well-tolerated, and safe, offering hope for improved treatment options [6]. However, there are concerns about acute renal failure and other serious side effects such as diarrhea, nausea, constipation, abdominal pain, skin rashes, and increased serum creatinine levels from prolonged use of DFX/DFRA. Its effectiveness is also questioned since it may not achieve a negative iron balance or eliminate excessive cardiovascular iron [7].

2. Materials and methods

2.1. Subjects and study design

A total number of patients and a healthy control group (subjects) were enrolled in this study during the period (22/11/2022) to (15/2/2023). The data were collected from the maternity hospital, Department of Genetic Diseases, when they attended the hospital for treatment. The total number of patients and the healthy control group in this study is [30] samples.

2.2. Patients group (β thalassemia major patients)

The patients included in this study were newly diagnosed, and a set of data included both the sex of the patients (male and female) whose ages ranged between (18 – 35) years, and the number of patients was [20], where the data related to serum calcium and serum ferritin analyzes that we obtained from the medical record in a hospital in the maternity hospital Department of Genetic Diseases.

2.3. Healthy control group

The control group in this study included ten mature males and females selected of them from general population, specifically females and males who came to the hospital as patients relatives and medical staff.Only themales and females who not have thalassemia were selected to participate in this study, their age ranged between (18 – 35) years, number of healthy control group was [10] and free from any disease.

2.4. Methods

The data on serum ferritin and serum calcium measurements were collected from medical records in the maternity hospital's Department of Genetic Diseases. In patients with thalassemia, serum ferritin levels are high, while serum calcium levels are low.

Blood samples were taken from patients with β thalassemia major and a healthy control group using a disposable syringe. We collected five milliliters (ml) of blood from each participant through venipuncture, then slowly pushed it into gel disposable tubes. The blood in the gel tube was allowed to clot at room temperature for 30 minutes. Next, we centrifuged the samples for 10 to 15 minutes at 3000 rpm and separated the serum into several 0.5 ml Eppendorf tubes. We used these tubes to measure serum ferritin and serum calcium, and then stored them at –20 °C until analysis. We used specific chemicals and standard kits

from various sources to evaluate parameters such as ferritin and calcium.

For biochemical parameter investigation, we measured serum ferritin concentration using a sandwich immunodetection method. Detector antibodies in a buffer bind to antigens in the sample, forming antigen-antibody complexes. These complexes then migrate onto a nitrocellulose matrix and are captured by immobilized streptavidin on a test strip. A higher number of antigens in the sample results in more antigen-antibody complexes, leading to a stronger fluorescence signal from detector antibodies. This signal is processed by the AFIAS instrument (Biotech Company) to display the serum ferritin concentration in the sample.

To measure serum calcium concentration, we used the CPC (O-Cresol Phthalein Complexone) method developed by Moorehead and Briggs. This method determines total calcium concentration in serum, plasma, or urine. In an alkaline solution, CPC reacts with calcium to form a dark-red colored complex. The absorbance measured at 570 nm is proportional to the amount of calcium in the specimen.

2.5. Ethical approval

A local ethics committee examined and approved the study protocol, subject information, and consent form in accordance with 22/11/23, dated June 2, 2023.

2.6. Statistical analysis

Data were processed and analyzed with the statistical package SPSS version 23.

Results are expressed as (mean ± SD), paired t-test was used to assess differences, and Independent –samples T test was used between patients and controls. P value below 0.05 was considered statistically significant.

3. Results

3.1. Serum ferritin levels before and after blood transfusion in patients with ßthalassemia major

In (Table 1) the mean values and SD (Standard Deviation) for serum ferritin and serum calcium of the patient group before blood transfusion were 3486.925 ± 2510.787 Nanogram /milliliter (ng/ml) and the mean value of the patient group after blood transfusion which was 4408.470 ± 2943.5002 ng/ml. There was ahighly significant increase in the patient group after blood transfusion compared with the before blood transfusion group ($p < 0.000$).

Table 1. Mean values of serum ferritin and Serum calcium of the patients group before and after blood transfusion with ßthalassemia major.

	M ± SD		
Parameters	Before blood transfusion	After blood transfusion	P-value
Ferritin ng/ml	3486.925 ± 2510.787	4408.470 ± 2943.5002	0.000***
Calcium mg/dl	2.21295 ± 0.8299	2.1550 ± 0.5835	0.6

*** p-value < 0.000 was high significant in serum ferritin and Non-significant in serum calcium.

Table 2. Mean values of serum ferritin and serum calcium of thepatient group before blood transfusion and healthy control group.

	M ± SD		
Parameters	Before blood transfusion	Control	P-value
Ferritin ng/ml	3486.925 ± 2510.787	76.200 ± 20.865	0.000***
Calcium mg/dl	2.2195 ± 0.8299	9.3400 ± 0.8195	0.000***

*** p-value < 0.000 was high significant.

The mean values and SD for serum calcium of the patient group before blood transfusion was 2.21295 ± 0.8299 milligram /deciliter (mg/dl) and the mean value of the patient group after blood transfusion was 2.1550 ± 0.5835 mg/dl. There was non-significant in the patient group before compare with after blood transfusion group ($p < 0.6$).

3.2. Serum ferritin and serum calcium before blood transfusion in patients with ßthalassemia major and healthy control

In (Table 2) the mean values and SD for serum ferritin of the patient group before blood transfusion were 3486.925 ± 2510.787 ng/ml and the mean value of the healthy control group was 76.200 ± 20.865 ng/ml. There was a highly significant increase in the patient group before blood transfusion compared with the healthy control group ($p < 0.000$).

The mean values and SD for serum calcium of the patient group before blood transfusion were 2.2195 ± 0.8299 mg/dl and the mean value of the healthy control group was 9.3400 ± 0.8195 mg/dl. There was a highly significant increase in the healthy control group compared with the patient group before blood transfusion ($p < 0.000$).

3.3. Serum ferritin and serum calcium after blood transfusion in patients with ßthalassemia major and healthy control

In (Table 3) the mean values and SD for serum ferritin of the patient group after blood transfusion were 4408. 470 ± 2943.500 ng/ml and the mean value of

Table 3. Mean values of serum ferritin and serum calcium of thepatient group after blood transfusion and healthy control group.

Parameters	M ± SD		P-value
	After blood transfusion	Control	
ferritin ng/ml	4408. 470 ± 2943.500	76.200 ± 20.865	0.000***
Calcium Mg/dl	2.155 ± 0.584	9.3400 ± 0.8195	0.000***

*** p-value < 0.000 was high significant.

the healthy control group was 76.200 ± 20.865 ng/ml. There was a highly significant increase in the patient group after blood transfusion compared with the healthy control group ($p < 0.000$).

The mean values and SD for serum calcium of the patient group after blood transfusion were 2.155 ± 0.584 mg/dl and the mean value of the control group was 9.3400 ± 0.8195 mg/dl. There was a highly significant decrease in the patient group after blood transfusion compared with the healthy control group ($p < 0.000$).

4. Discussion

The current study examines the effectiveness of chelation therapy to remove excess iron in patients with beta thalassemia major. It also looks at some biochemical parameters, such as serum ferritin and serum calcium, before and after blood transfusions in these patients [8].

Biochemical studies of serum ferritin before and after blood transfusions in patients with beta thalassemia major showed high levels of serum ferritin. Table 1 indicates a significant increase in the patient group after blood transfusion compared to before ($p < 0.000$). This finding aligns with other research, which found that frequent blood transfusions lead to increased iron levels. Excess iron can damage the heart, liver, and endocrine system, which includes glands that produce hormones regulating various processes in the body. This damage shows up as excess iron deposits if adequate iron chelation therapy is not given [9].

For serum ferritin levels before blood transfusions, the study again showed high levels in patients with beta thalassemia major. Table 2 presents a significant increase in serum ferritin in the patient group before transfusion compared to the healthy control group ($p < 0.000$). This finding matches other studies [10] that report hyper-transfusion has improved the life expectancy of thalassemia patients over the years; however, iron overload remains an unavoidable complication due to the high number of blood transfusions. Many studies conclude that liver cirrhosis is linked to high serum ferritin levels [11, 12].

After blood transfusions, serum ferritin levels in patients with beta thalassemia major remained high. Table 3 shows a significant increase in the patient group after blood transfusion compared to the healthy control group ($p < 0.000$). This research found that the iron levels in the human body come mainly from dietary consumption rather than iron excretion [13]. The body removes iron at a very slow rate, and the amount of iron in feces matches dietary intake. However, situations like blood transfusions in beta thalassemia major can suppress hepcidin production, leading to iron overload [13].

The study also addressed serum calcium levels before and after blood transfusions in patients with beta thalassemia major. It found low serum calcium in these patients. Table 1 shows no significant difference in serum calcium levels in patients before transfusion compared to after ($p < 0.6$).

For serum calcium between patients before blood transfusion and healthy controls, the study showed that serum calcium levels were significantly lower in transfusion-dependent beta thalassemia patients. Table 1 highlights a significant increase in the healthy control group compared to the patient group before transfusion ($p < 0.000$). This finding corresponds with other research that noted complications from blood transfusion therapy due to iron deposits in the parathyroid glands [14]. It has also been reported that asymptomatic hypocalcemia is common and may go unnoticed for some time unless specifically checked.

After blood transfusions, serum calcium levels in patients with beta thalassemia major remained significantly lower than in healthy controls [15]. Table 1 illustrates a significant increase in the healthy control group compared to patients after transfusion ($p < 0.000$). This finding aligns with other studies suggesting that damage to the parathyroid glands in transfusion-dependent beta thalassemia may result from oxidative stress caused by iron overload. Excess iron from repeated blood transfusions deposits in various organs, including the parathyroid glands, leading to decreased serum calcium levels [16, 17]. The average serum calcium level was significantly lower in transfusion-dependent beta thalassemia patients compared to controls. Some researchers have reported similar observations [18, 19]. However, some studies found no change in serum calcium levels in beta thalassemia patients, possibly due to differences in nutritional status among study groups [20].

5. Conclusion

It is noted that the treatment used to remove excess iron from the body is effective, but the repeated blood transfusion process for patients leads to a lack of effectiveness of treatment (Deferasirox) in iron excretion. As for calcium, it is excreted with iron excretion.

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Conflicts of interest

The author declare these no conflict of interest.

References

1. Marengo-Rowe AJ. The thalassemias and related disorders. In Baylor university medical center proceedings. 2007;20(1):27–31, Taylor & Francis.
2. Cianciulli P. Treatment of iron overload in thalassemia. Pediatric endocrinology reviews: PER. 2008;6:208–13.
3. Al Kenani AKT, Al Mamory BHM, Al Obaidi AFH. Iron-deficiency anemia as a risk factor for the first simple febrile convulsion. Medical Journal of Babylon. 2022;19(3):372–378. doi: 10.4103/MJBL.MJBL_42_22.
4. Jeon US. Kidney and calcium homeostasis. Electrolytes & Blood Pressure: E & BP. 2008;6(2):68.
5. Beto JA. The role of calcium in human aging. Clinical nutrition research. 2015;4(1):1.
6. Nisbet-Brown E, Olivieri NF, Giardina PJ. Effectiveness and safety of ICL670 in iron-loaded patients with thalassaemia: A randomised, double-blind, placebo-controlled, dose-escalation trial. Lancet (London, England). 2003;361:1597–1602. doi: 10.1016/S01406736(03)13309-0.
7. Nick H, Acklin P, Lattmann R, *et al.* Development of tridentate iron chelators: From desferrithiocin to ICL670. Curr Med Chem. 2003;10:1065–1076. doi: 10.1016/S0140-6736(03)13309-0.
8. Taher AT, Porter J, Viprakasit V. Deferasirox reduces iron overload signififi- cantly in nontransfusion-dependent thalassemia: 1-year results from a prospective, randomized, double-blind, placebo-controlled study. Blood. 2012;120:970–977. doi: 10.1182/blood-2012-02-412692.
9. Keberle H. The biochemistry of desferrioxamine and its relation to iron metabolism. Ann N Y Acad Sci. 1964;119:758–768. doi: 10.1111/j.1749-6632.1965.tb54077.x.
10. Cianciulli P. Treatment of iron overload in thalassemia. Pediatr Endocrinol Rev. 2008;6(Suppl 1):208–13.
11. Riaz H, Riaz T, Khan MU, Aziz S, Ullah F, Rehman A, *et al.* Serum ferritin levels, socio-demographic factors and desferrioxamine therapy in multi-transfused thalassemia major patients at a government tertiary care hospital of Karachi, Pakistan. BMC research notes. 2011;4:1–5.
12. Knovich MA, Storey JA, Coffman LG, Torti SV, Torti FM. Ferritin for the clinician. Blood Rev. 2009;23:95–104. doi: 10.1016/j.blre.2008.08.00.
13. Mercadante CJ, Prajapati M, Parmar JH, Conboy HL, Dash ME, Pettiglio MA, *et al.* Gastrointestinal iron excretion and reversal of iron excess in a mouse model of inherited iron excess. Haematologica. 2019;104(4):678.
14. De-Sanctis V, Vullo C, Bagni B, Chiccoli L. Hypoparathyroidism in beta thalassemia major: Clinical and laboratory observations in 24 patients. Acta Haematol. 1992;88:105–8.
15. Costin G, Kogut MD, Hyman CB, Ortega JA. Endocrine abnormalities in thalassemia major: Gertrude Costin, MD; Maurice D, et.al. American Journal of Diseases of Children. 1979;133(5):497–502.
16. Hershko C. Pathogenesis and management of iron toxicity in thalassemia. Annals of the New York Academy of Sciences. 2010;1202(1):1–9.
17. Alshammary AA-M, Al-Fetlawi SS, Aljanabi ZA. Role of carotid ultrasound in the evaluation of atherosclerotic changes in beta thalassemia major patients. Medical Journal of Babylon. 2022;19(3):476–481. doi: 10.4103/MJBL.MJBL_89_22.
18. Hamidieh AA, Moradbeag B, Pasha FA, Jalili M, Hadjibabaie M, Keshavarznia M. High prevalence of hypoparathyroidism in patients with beta-thalassemia major. International Journal of Hematology-Oncology and Stem Cell Research. 2009: 17–20.
19. Patne A, Hisalkar PJ, Gaikwad SB, Karnik A. Evaluation of HPT markers in â thalassemia major patients. Indian J Appl Res. 2014;4(1):389–390.
20. Mahachoklertwattana P, Sirikulchayanonta V, Chuansumrit A, Karnsombat P, Choubtum L, Sriphrapradang A, *et al.* Bone histomorphometry in children and adolescents with β-thalassemia disease: Iron-associated focal osteomalacia. The Journal of Clinical Endocrinology & Metabolism. 2003;88(8):3966–72.