Letter to the Editor

Compliance with Deferoxamine Therapy among Transfusion-Dependent β-Thalassemia Patients in Nineveh Province, Northern Iraq

Dear Editor,

β-Thalassemia is an inherited blood disorder, where there is an impaired hemoglobin (Hb). A synthesis caused by genetically deficient or absent synthesis of β-globin chains. This problem results in a series of pathophysiological changes that may range from a simple mild anemia (β-thalassemia minor) to a complex life-threatening condition (β-thalassemia major). The latter is a serious condition characterized by severe anemia that appears early in life (from the sixth month to the first year) with consecutive hypoxia, growth retardation, and bone marrow hyperplasia.[1]

This condition requires urgent treatment with a regular blood transfusion program every 4–6 weeks to correct anemia and related symptoms. Unfortunately, repeated blood transfusion will add other problems to these patients, the most important is iron overload.[2]

The human body cannot effectively excrete iron, so the excess iron from transfused blood accumulates to reach toxic levels and is then precipitated in the tissues and other body organs, leading to organ malfunction. The outcome of iron overload and toxicity is serious organ damage with overall adverse influences on vital body functions, including cardiac, respiratory, endocrine, hepatic, and renal functions.[2] Accordingly, this necessitates the use of an iron chelating agent.

Deferoxamine is the first effective iron-chelating agent used since the 1960s. It has a high affinity and selectivity to iron and binds to it in a ratio of 1:1 forming a complex that is, excreted by urine or bile.[3]

Deferoxamine has exhibited high efficiency in reducing mortality and morbidity of transfusion-dependent thalassemia patients.[4] However, deferoxamine has poor oral bioavailability and should be administered by subcutaneous infusion (8–12 h overnight) for 5–7 days per week or by intravenous infusion (24 h infusion).[3]

Although it is safe, compliance with deferoxamine therapy is a frequent problem that may lead to iron overload effects upon any inconvenient and improper use of the drug.[4] The present study is directed to examine the state of compliance with deferoxamine therapy in transfusion-dependent β-thalassemia patients in Nineveh Province, Northern Iraq.

The present study had approval from the regional research committee of the Mosul Health Administration, and the scientific research committee of the College of Pharmacy, University of Mosul, Iraq.

A total of 40 transfusion-dependent β-thalassemia patients aged 4–20 years, who are attending the Thalassemia Center at Ibn-Alatheer Teaching Hospital in Mosul, Nineveh, Iraq, were enrolled in this study. The study was conducted over the period from December 4, 2022, to April 1, 2023.

The patients were diagnosed with β-thalassemia major based on Hb variant testing by high-performance liquid chromatography. The patients were divided into two groups according to the degree of compliance with deferoxamine treatment as an iron chelating therapy. This subdivision depended on the history of deferoxamine treatment as follows:

- *Good compliance*: A total of 19 patients with regular use of deferoxamine therapy, that is, using a subcutaneous infusion of deferoxamine at a dose of 40 mg/kg/day for 10–12 h intervals daily, 5 days a week.
- *Poor compliance*: A total of 21 patients with irregular use of deferoxamine therapy (i.e., not fulfilling the criteria of good compliance).

About 5 mL of venous blood was collected from each individual in plain tubes. The tubes were placed in a water bath at 37°C for 15 min for blood clotting to take place. Serum samples were obtained by centrifugation at 4000 rpm for 10 min. The serum was placed in 1 mL Eppendorf tubes and frozen at −20°C for subsequent analyses.

Serum ferritin was measured automatically by an enzyme-linked fluorescent immunoassay method using a kit supplied by Biomerieux, France, and the Vidas machine (Biomerieux).

Standard statistical methods were used to determine the mean and the standard deviation of the studied variables. The unpaired Student's *t* test was used to compare variables of the two compliance/age groups. Statistical significance was considered to be present at $P < 0.05$.

Table 1: Comparison of serum ferritin levels by age of patients.

Parameters	Mean ± standard deviation		*P* value
	<10 years old *N* = 20	≥10 years old *N* = 20	
Serum ferritin (ng/mL)	3644.52 ± 1341	6558.91 ± 2343.26	0.0001**

**significant at $P \leq 0.05$

Table 2: Comparison between patients according to their compliance with deferoxamine therapy

Parameters	Mean ± standard deviation		*P* value
	Good compliance *N* = 19	Poor compliance *N* = 21	
Age (years)	8.9 ± 5.4	11.2 ± 5.2	NS
Age at starting DFO	2.7 ± 0.8	3.5 ± 0.9	0.014*
Years on DFO	6.4 ± 5.16	7.8 ± 5	NS
Serum ferritin (ng/mL)	3427.74 ± 1422.8	6373.93 ± 2201.8	0.000**

DFO: deferoxamine

**Significant at $P \leq 0.05$

The comparison between the two age subgroups of patients revealed a significant increase in the level of serum ferritin in the older age subgroup (≥10 years old) [Table 1]. Moreover, when the patients were compared according to their compliance with deferoxamine therapy, there was a significant increase in the mean serum ferritin level in the poor compliance group. In addition, the mean age at starting deferoxamine therapy was also significantly higher among those with poor compliance [Table 2].

The results of the present study revealed a significant increase ($P < 0.01$) in the mean level of serum ferritin in all comparisons performed whether by age of patients or the degree of their compliance to deferoxamine therapy. It was clear that transfusion-dependent β-thalassemic patients exhibited significantly high levels of serum ferritin [Tables 1 and 2], which is a common finding due to ineffective erythropoiesis (with increased gastrointestinal iron absorption) and repeated blood transfusions that consequently causes iron accumulation and iron overload.[5] It has been found that serum ferritin levels positively correlate to the number of transfused blood units in transfusion-dependent thalassemia patients.[5] Deferoxamine is an effective drug in reducing serum ferritin levels when administered properly.[4]

However, the mean level of serum ferritin was significantly elevated in the older age subgroup of patients despite using deferoxamine [Table 1]. The higher serum ferritin levels among older age thalassemic patients were also revealed by Younus *et al.*[6] However, in the current study, this finding may be related to improper use or poor compliance to deferoxamine.

A significantly higher mean level of serum ferritin ($P < 0.01$) was noticed in poor compliance patients when compared to those with good compliance [Table 2]. It seems that the regular use of deferoxamine helped reduce the mean level of serum ferritin, although it was still high. This indicates that blood transfusion-dependent β-thalassemia patients have to be very well adapted to the use of deferoxamine to get the required benefits of reducing iron overload.[7]

Following our findings, other researchers such as Sharan and Gomber,[7] and Meabed *et al.*[8] have also concluded that poor compliance and/or inadequate dosage of deferoxamine in addition to the delayed initiation of iron chelating therapy, were all significant factors in the development of failure of response to deferoxamine therapy in thalassemic patients on regular blood transfusion.

The use of deferoxamine is an effective medicine in reducing serum ferritin levels when used in the proper doses and method of administration. The state of poor compliance to deferoxamine was encountered in more than 50% of the patients enrolled in the present study. Poor compliance has led to reduced efficacy of the drug as indicated by the elevated mean level of serum ferritin.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

Ahmed Yahya Dallal Bashi[1], Zaid Muwafaq Younus[2], Muzahim Saeed Younis Al-Hamdani[3]

[1]Department of Pharmacy, Al-Noor University College, Mosul, Iraq, [2]Department of Pharmacognosy, College of Pharmacy, University of Mosul, Mosul, Iraq, [3]Thalassemia Center of Mosul, Ibn Al-Atheer Teaching Hospital, Nineveh Health General Office, Mosul, Iraq

Address for correspondence: Dr. Ahmed Yahya Dallal Bashi, Department of Pharmacy, Al-Noor University College, Mosul, Iraq.
E-mail: ahmed.yahya50@alnoor.edu.iq, ahmed_dallalbashi@yahoo.com

Submission: 21-Jul-2023 **Accepted:** 15-Sep-2024 **Published:** 21-Nov-2024

References

1. Saud IA, Majid LM. Relation of immunoglobulin level and white blood cell count with frequency of infection in splenectomized and non-splenectomized B thalassemia major patients. Med J Babylon 2023;20:264-7.
2. Taher AT, Saliba AN. Iron overload in thalassemia: Different organs at different rates. Hematol Am Soc Hematol Educ Program 2017;2017:265-71.
3. Bellotti D, Remelli M. Deferoxamine B: A natural, excellent and versatile metal chelator. Molecules 2021;26:3255.
4. Rashid M, Karimi M. Compliance of deferoxamine injection in beta-thalassemia major patients in Iran. Transf Med (Oxford, England) 2012;22:104-7.
5. Dallal Bashi AY. Is the total number of blood transfusion in β-thalassemia major patients can be used to assess their serum ferritin levels? Tikrit J Pharm Sci 2013;9:30-6.

6. Younus ZM, Alhially YAH, Dallal Bashi AY. Evaluation of conventional renal function tests in β-thalassemia major patients in Nineveh Province. Tikrit J Pharm Sci 2012;8:6-14.
7. Sharan S, Gomber S. Comparison of compliance, convenience, satisfaction and life disturbances among transfusion-dependent beta-thalassemic children on iron chelation therapy: An observational and cross-sectional study. Int J Contemp Med 2019;7:26-31.
8. Meabed MH, Mohamed OH, Ali AA. Iron chelation therapy in beta thalassemia. Med J Cairo Univ 2022;90:633-9.

Access this article online

Quick Response Code:

Website: https://journals.lww.com/mjby

DOI: 10.4103/MJBL.MJBL_1053_23

How to cite this article: Bashi AYD, Younus ZM, Al-Hamdani MSY. Compliance with deferoxamine therapy among transfusion-dependent β-thalassemia patients in Nineveh Province, Northern Iraq. Med J Babylon 2024;21:S315-7.