Adherence and Satisfaction of Deferasiroxversus Deferoxamine in Transfusion-Dependent Beta-Thalassemia

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Abstract

Objectives: The present study was aimed to compare the adherence and satisfaction with deferoxamine (Desferal®) versus deferasirox (Exjade®), a novel oral iron chelator, in patients with transfusion-dependent beta-thalassemia.

Patients and Methods: In this cross-sectional, single-center study, 108 homozygous βthalassemia major patients aged between 3-21 years old were enrolled. They were on regular blood transfusions and iron chelators (either deferoxamine or deferasirox) for about three months. Another fifty-six apparently healthy non-thalassemic subjects were enrolled as a control group. **Results:** Adherence and satisfaction wereassessed byusing a simplequestionnaire establishedduring an interviewwithpatientsortheirparents.The serumferritin level was measuredbythe ELISAmethod**.**

Our findings showed that adherence and satisfaction in the deferasirox group were more than that with deferoxamine group patients. Serum ferritin level in the deferasirox group was significantly lower than in the deferoxamine group at ($p<0.001$). while the control group was significantly lower than both patients groups at ($p<0.001$). Patients on deferasirox had lower adverse effects than the deferoxamine group since deferoxamine produce irritation and pain at the injection site for the patients.

Conclusion: Our findings concluded that deferasirox is an effective iron chelator as deferoxamine but with better adherence and satisfaction than deferoxamine. Deferasirox can be used as a preferred iron chelator therapy in iron-overload patients with beta-thalassemia.

Key Words: *BetaThalassemia, Satisfaction, adherence, Iron Chelators, Deferoxamine, Deferasirox.*

Introduction

Beta-thalassemia may be a severe inherited blood disease that has been known to be caused by a mutation within the β-globin gene resulting in the excessive destruction of red blood cells1,2. it's been estimated that over 42000 newborns are suffering from β-thalassemia per annum worldwide. Without transfusion, β- Cooley's anemia causes death amongst infected children before the age of three years old 2. Thalassemia may be a disease status during which patients need continuous control and management, regular blood transfusions can prevent death and reduce mortality. However, excessive iron accumulated from transfused red blood cells can cause organ failure3,4. Therefore, iron chelation treatment is important to scale back the iron store within the body and improve the long-term survival rate of patients with thalassemia, which is taken into account important adjuvant therapy.4

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Currently, the most iron chelators available for clinical use in Iraq are deferoxamine and deferasirox. Deferoxamine, which needs routine intravenous or subcutaneous injections from 5 to 7 days weekly, has been considered a typical therapy for hemochromatosis over the past four decades.However, the treatment with deferoxamine for about 8 to 12 hours daily may lead to poor compliance and a few negative impacts like skin rash, hematological toxicity, and heart problems 5-7.

Deferasirox, a once-daily oral iron chelator, was introduced in 2005 as first-line therapy for patients over 2 years aged with chronic hemochromatosis thanks to blood transfusions5. Although Deferasirox has some mild adverse events, some studies indicated that it's a positive effect on lowering liver iron and producing high patient compliance8,9,10.

Similar to normal individuals, Thalassemic patients should have normal life status, however, continuous transfusion, iron chelation, and clinic visits have an excellent psychological impact leading to rejection of taking their medical management at the proper way, which assessed by satisfaction and compliance.

The present study was aimed to match the satisfaction and adherence with the deferoxamine group versus the deferasirox group. to verify the efficacy of both chelators; serum ferritin was also measured to match patients groups and with the control group.

Materials and Methods

A cross-sectional, single-center investigation study was carried out with the cooperation of the medical staff of Thalassemic Center of Ibn Al-Atheer Teaching Hospital in Nineveh Province, Mosul, Iraq. Ethical clearance was obtained from the Research Board Committee after approval of the protocol.

One hundred and eight patients of 3 to 21 years old of age with a diagnosis of β-thalassemia and having a chronic iron overload from regular blood transfusions as assessed by serum ferritin of > 600 ng/ml were divided into, firstly deferoxamine group treated by 20-50 mg/kg/day (n = 54, 30 male & 24 female) with age mean (13.2±4.03 years), second deferasirox group treated by 10-30 mg/kg/day (n = 54, 31 male & 23 female) with age mean (9.65±3.32 years), and the third control group of apparently health subject (n = 56, 36 male & 20 female) with age means (11.8±5.3 years). In this study satisfaction and adherence was assessed by using a questionnaire which usually done during an interview and reporting notes for each patient

Informed consent was taken from the patients or their relatives, a questionnaire regarding the personal and treatment details was obtained as name, age, sex, frequency of transfusion, type of chelation used, satisfaction, and adherence.

Patient compliance depended on the patient's use of deferoxamine. Five to seven times/week were regarded as compliance, while for Deferasirox patients, six to seven times/week were regarded as compliance. The iron overload was assessed by serum ferritin determination by using Ferritin AccuBind® ELISA - Monobind Inc. (Lake Forest, California, USA) commercial kit, depending on

Chemwell 2910 fully automated devices for enzyme-linked assay methods.

Data are presented as mean ± S.D. and were analyzed by using one way ANOVA test and nonpaired t-test were used to compare between the groups. RResults were considered statistically significant at $p \leq 0.05$. The correlation was done using Pearson and spearman's rho depending on the type of data (parametric or nonparametric).

Results

Table 1 shows that patients treated with deferasirox significantly were more satisfied in comparison with those treated with deferoxamine (90.7% vs 66.7%, respectively). Among patients who had previously taken deferoxamine then received deferasirox before the study 77% were reported a preference for deferasirox than deferoxamine.

The proportion of patients' compliance was greater in those receiving deferasirox than in those receiving deferoxamine (90.7% vs 61.1%), as shown in Table 1.

In this study serum ferritin levels within and between groups shows a wide range of variation.

There is a significant difference ($p<0.001$) in the serum level of ferritin between the deferoxamine group

(3891.2±1845.6 ng/ml) as compared with the deferasirox group (2212±1485 ng/ml).

Also, there are high significant variations ($p<0.001$) in each of the deferoxamine group and deferasirox group when compared with the Control group with (26.4±19.7 ng/ml) as shown in Table 2. The importance of adherence can be determined by serum ferritin level mean for all patients (N=108, 3051±1868 ng/ml) and when grouped as adherence patients (N=82,2620.4±1713.2 ng/ml) and non-compliance patients (N=26, 4411.6±1704 ng/ml), a significant difference ($p<0.001$) presented as shown in Figure 1.

Figure 2 represents the distribution of ferritin level data frequency for non- adhered patients that appear after the mean of all patients (3051ng/ml) especially for deferoxamine treated patients, while the distribution for compliance patients before the mean of all patient especially for deferasirox treated patients.

By determining correlations for all patients' data (N=108), the Pearson correlation showed a significant positive correlation ($p<0.01$) between age and ferritin level ($r = 0.374$), and negative correlation ($p<0.01$) between serum ferritin level and adherence ($r = -0.412$). Moreover, there is a significant positive correlation ($p<0.01$) between compliance and satisfaction ($r = 0.342$) by using Spearman's rho correlation (nonparametric correlation) these correlations are shown in Table 3.

Table 1. Percentage of satisfaction and adherence for deferoxamine and deferasirox

	Parameters	Deferoxamine Group (N=54)	DeferasiroxGroup (N=54)
Satisfaction	Satisfied	66.7%	90.7%
	Non Satisfied	33.3%	9.3%
adherence	adhered	61.1%	90.7%
	Non adhered	38.9%	9.3%

Table 2. Comparison of serum ferritin between deferoxamine group and deferasirox group and each group with controls group

Parameters	Control Group	Deferoxamine	Deferasirox Group
Serum ferritin Level	26.4±19.7	3891±1845a	2212±1485b,c

a $p<0.001$ vs control; b $p<0.001$ vs control; c $p<0.001$ vs deferoxamine group

Table 3. Relationship between studied parameters for all patients

Correlations R value p-value				
Serum ferritin level	**Age**	**N=108**	**r = 0.374**	**p<0.01**
Serum ferritin level	Adherance	N=108	r = -0.412	p<0.01
Adherance	Satisfaction	N=108	r = 0.342	p<0.01

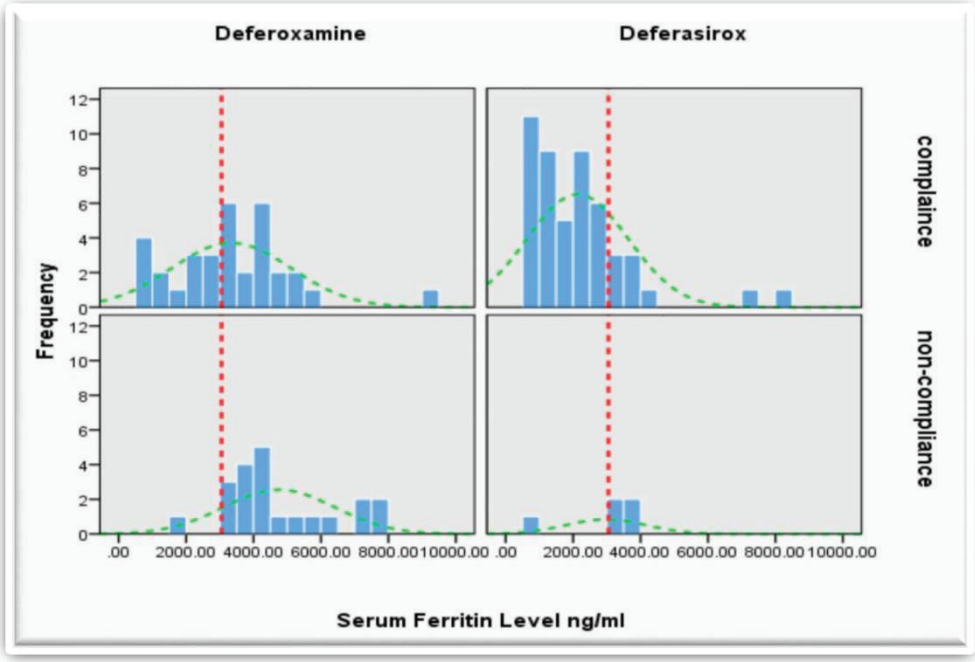

Figure 1. Frequency of Distribution of serum ferritin level among cmplianed and non-complianed patients for deferoxamine group and deferasirox group

Discussion

Iron chelators act by removing transiently available (labile) iron pools, either in plasma or within cells, because cellular storage iron (present as ferritin and hemosiderin) are not directly accessible for chelation11-13. Chelate iron is derived from two main sources: (a) iron released from macrophages after the catabolism of red cells and (b) iron released within cells after the catabolism of cellular ferritin and hemosiderin. For transfusion-dependent thalassemia major patients, it is important to choose an appropriate iron chelator to reduce iron burden in the body to prolong and improve the quality of life [14,15.]

This study showed that Deferasirox had a rational better satisfaction and compliance than deferoxamine, especially for younger ages. Some older ages prefer deferoxamine because they are adapted on deferoxamine as part of their life or they cannot tolerate deferasirox. From another view no one of the chelation has very satisfied chelator due to limitation of normal life, so patients opinions about deferoxamine come from problem of subcutaneous injection for long period (8-12 hours per day) with painful and ulceration at injection sites, these agree with (Rofail et al, 2009) who showed administration of deferoxamine slow subcutaneous infusion negatively impacts on satisfaction which was shown to be a determinant of adherence[16]. While Deferasirox has taken orally as an effervescent tablet once daily is more suitable, but have the problem of bitter taste with slight large particle size cause irritation to the larynx and induce nausea, that agrees with (Trachtenberg et al, 2011) when showed patients with poor adherence to Deferasirox noted stomach pain and bad taste [17]. Deferasirox is preferable by 77% of patients who had previously been treated with deferoxamine. The reasons for preferring Deferasirox were, more convenient to be taken, less disruptive to their day or their sleep, and to their families, that mentioned by (Cappellini et al,2007)[5].

Serum ferritin is used as an indirect measure of iron overload, it is not an accurate assessment but gives a fairly good idea of iron overload [18,19]. In this study, serum ferritin at the Deferasirox group was lower than the deferoxamine group.

Pennel et al, (2014) when compared between deferoxamine versus Deferasirox showed a small difference of serum ferritin level means at the end their study 3129 ng/ml versus 3375 ng/ml respectively [20], that

disagree with the present study which had significant means variation p<0.001 between groups 3891 ng/ml versus 2212 ng/ml respectively these may be due to more compliance for Deferasirox than deferoxamine that leads to decrease ferritin level more than non-compliance while the result of this study agree with (Bashir and Sadoon, 2010) as they concluded that serum ferritin is higher in an older patient, the higher rate of blood transfusion and poor compliance [21].

Also (Mahmoud and Aziz, 2012) showed significant variations p<0.001 between serum ferritin levels of patients on deferoxamine and patients on Deferasirox and also for good compliance and poor compliance[22].

Improved satisfaction and convenience of a once-daily oral dose of Deferasirox compared to deferoxamine has been shown in other studies10,23 which may be translated into increased compliance as showed in this study that leads to improving health outcomes and quality of life.

The minor adverse effects with ease of use of deferoxamine or Deferasirox act as a choice factor for patients to determine satisfaction and compliance that in turn decrease ferritin level and consequently decrease complications, morbidity, and mortality.

Conclusion

It has been concluded that deferasirox is an effective iron chelator as deferoxamine but with a better satisfaction and compliance and lowered serum ferritin level than that of deferoxamine, in mild to moderate iron overloaded patients.

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