Research Article

Comparative Effects of Three Iron Chelation Therapies on the Quality of Life of Patients with Homozygous Transfusion-Dependent Beta-Thalassemia

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Abstract

Background:- Beta-thalassemia is a genetically inherited disorder characterized by reduced synthesis of the beta chain hemoglobin.
Treatment consists of blood transfusion and chelating therapy in a form of paranteral deferoxamine (DFO) and oral deferasirox (DFX).
Aim of the study: - to compare the quality of life, patient satisfactory adherence to the three different modalities of treatment.
Objectives:- To compare three groups of patients receiving different modalities of treatment and the effect on their daily activities .
Patients and methods:- A total of 270 patients (118)male and (152) female enrolled in the study ,their age ranging from(10.5year)-till(17year), for the period from(May 2013—till May 2014) ,
A special Questionnaire was arranged including three parts,
First was on demographic data, the second part included Wallstons health locus of control scale and the third part included the patients satisfaction.
Results:- The ratio of male to female were (1—1.3).The most common drug used was (DFX) (55.5%).Life style scale regarding ability to perform daily activity showed (90.6%) of patients on (DFX).
About patient adherence to treatment (45.3%) of (DFX) group of patients.
Conclusion:- It is concluded that optimal chelating therapy should be individualized for each patient to enhance their adherence and improve the quality of their life .

Key words : Beta-thalassemia, Iron Chelation

INTRODUCTION

Beta- thalassemia is genetically inherited disorder characterized by reduced synthesis of the beta-hemoglobin chain which in turn results in reduced synthesis of hemoglobin A (HbA). Treatment of patients with thalassemia major consists of regular blood transfusions and iron chelation therapy, which is vital to prevent excess iron deposition in the body. In Iraq there are two iron chelating agents available: deferoxamine (DFO, Desferal), an iron chelator given by infusion, and oral chelator deferasirox (DFX, Exjade) given once daily. Treatment with iron chelators has significantly increased the life expectancy of affected individuals into the third to fifth decade [1], while simultaneously decreasing the co morbidities of the disease [2].

Despite advancements in care, patients with transfusion-dependent beta-thalassemia still present complications and often suffer from psychological problems due to their lifestyle [3-5]. While the effectiveness of iron chelation therapies has been thoroughly investigated, there is limited comparative information about the benefits of the therapies on the quality of life of the patients. Furthermore, while Kirkuk is a governorate with high prevalence of beta-thalassemia, the quality of life of patients presenting with this disease and the effect

of the type of iron chelation treatment on the patient's quality of life have not been evaluated. Thus, the objective of the present study was to compare the quality of life, and satisfaction and adherence to treatment of patients with homozygous transfusion-dependent beta-thalassemia in the Kirkuk population receiving three different chelation treatments and to identify parameters affecting their quality of life.

PATIENTS AND METHODS

A total of 270 adults with (all are diagnosed as thalassemia major) transfusion-dependent homozygous beta-thalassemia attending the Thalassemia center at Kirkuk between May 2013 and May 2014 were enrolled in the study. Diagnosis with homozygous transfusion-dependent beta-thalassemia was the only criterion used for inclusion in the study. There were no exclusion criteria. The treatment modalities used are (deferoxamine IV, deferosix Exjade oral chelating drug).The scientific committee of the study and the local ethics committees of the participating hospitals approved the study. All patients were asked to answer the following three questionnaires: (i) a Wallston's health locus of control scale *Multidimensional Health Locus of Control (MHLC) Scales*, [6] (ii) questionnaire about patient satisfaction from their current therapeutic chelator with responses varying from never to always. In addition, (iii) personal data and the hematological profile of the patients were obtained in order to be able to better evaluate the quality of life of the patients enrolled in our study.

Statistical Analysis

All continuous variables are expressed as the mean ± standard deviation (SD). Comparisons of the categorical variables between the three therapies were performed by the chi square test or the Fisher test as appropriate. Differences were considered significant when the P value was <0.05. Specifically, gender, physical activity, years since diagnosis, years since chelation treatment onset, and other co morbidities were set as independent variables along with chelation treatment in order to investigate factors associated with the quality of life. Statistical analyses were performed with SPSS version 20.0 for Windows.

RESULTS

Of the 270 adult patients with homozygous transfusion-dependent beta-thalassemia that were recruited in this study, 118 were males and 152 were females (Figer1). The patients were divided into three groups based on the therapy they were receiving: the first group was receiving deferoxamine (DFO; Desferal, Novartis), the second group deferasirox (DFX; Exjade, Novartis), and the third group deferoxamine + deferasirox combination therapy. The mean age of the patients was for the DFO group, for the DFX group, and for the DFO + DFX group was recorded. The differences among the groups were not statistically significant. The demographic characteristics of the patients are shown in (Table 8). More than half of the patients (150/270) were receiving DFX, while 78 and 42 were receiving combination therapy and DFO alone, respectively (Figure 2). The majority of the patients receiving DFO (38/42) and DFO + DFX (66/78) were not involved in sports, while 68/150 of DFX patients showed a statistically significant difference (Table 1).

The disease characteristics of patients of the three groups are presented in (Table 2). There were no significant differences among the three groups between their age at the time of diagnosis and their age when DFO treatment began. When examining the co morbidities, the patients receiving DFO had significantly higher percentages of myocardial dysfunction (33.3%) and hepatic dysfunction (38.1%), while 71.4% had undergone splenectomy and 14.3% suffered from allergies (Table 10).

Results from Questionnaires

Patients completed Wallston's questionnaire pertaining to the control of their health. This questionnaire assesses five dimensions of control of one's health, "internal," "chance," "powerful others," "doctors," and "other people." According to the results of Wallston's Health Locus of Control Scale, patients only differed slightly in their belief that their doctors had control of their personal health status. The highest score was observed in the DFO group of patients compared to the DFX and DFO + DFX groups, meaning that those were the ones that felt that their doctors had greatest control over their health. There were no statistically significant differences noted among the groups for the other four dimensions.

The majority of patients felt they got benefit from receiving chelation therapy. However, when asked to rate their satisfaction with their iron chelation therapy, patients receiving DFX was more likely to respond that they did not feel restricted in terms of their activities. The differences in the means between the three groups were statistically significant. Furthermore, more patients receiving DFO responded that they were got sad by the unwanted side effects of their treatment and that the treatment negatively influenced their body and skin appearance.

Furthermore, patients receiving DFO felt that their treatment limited their ability to work, to attend school, and to perform daily activities (Table 1). Specifically,

the group receiving DFO were significantly more limited (i.e., had a higher score,) than the DFX and DFO + DFX groups .

The adherence to treatment rate was the lowest in the DFO group compared to the DFX group and the DFO + DFX group (Table 2-3). In particular, 9.5% of those receiving DFO, compared to 33.3% of those receiving DFX and 20.5% of those receiving DFO + DFX, reported that they always adhered to their treatment, while the respective percentages of those that forgot to take their treatment were 28.6%, 2.7%, and 25.6% for the DFO, DFX, and DFO + DFX groups.

The percentages of patients that felt substantial or major annoyance from the length of their treatment were 23.8% for the DFO group, 12% for the DFX group and 12.8% for the DFO + DFX group. This is in sharp contrast to the percentages of 4.8, 25.3, and 23.1% of the DFO, DFX, and DFO + DFX groups of patients that were not bothered at all from the length of their treatment (overall) (Table 4-5). In addition, more patients receiving DFO (19%) felt that their treatment was hard or very hard to receive compared to 6.7% for DFX and 5.1% for DFO + DFX. This is in contrast to 9.5%, 42.7%, and 38.2% of those receiving DFO, DFX, and DFO + DFX, respectively, that felt that receiving their therapy was easy or very easy (overall , resp.) (Table 6-7).

The three groups also differed significantly in their satisfaction to their type of therapy (infusion, oral, or combination) with the majority of patients from all the groups preferring oral therapy.

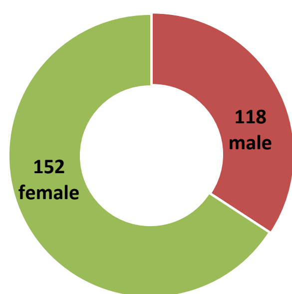

Figure 1: No. and distribution of patients according to their sex

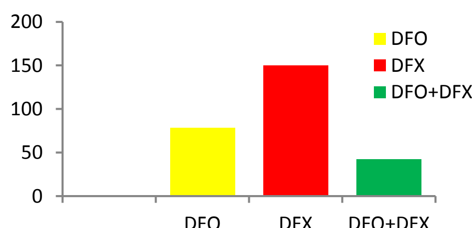

Figure 2:No. and distribution of patients according to chelation therapy.

Table 1: Effect of iron chelation therapy on the ability of the beta-thalassemia patients to perform their daily activities. A statistically significant difference was noted among the three groups. Patients receiving DFO were more limited.

DFX		DFX+DFO		DFO	
No.	%	No.	%	No.	%
2	1.33	2	2.56	38	90.47

Table 2: Adherence to treatment

DFX		DFX+DFO		DFO	
No.	%	No.	%	No.	%
50	33.33	16	20.51	4	9.52

Table 3: Forget their treatment

DFX		DFX+DFO		DFO	
No.	%	No.	%	No.	%
4	2.66	20	25.64	12	28.57

Table 4: Major annoyance from the treatment

DFX		DFX+DFO		DFO	
No.	%	No.	%	No.	%
18	12.0	13	16.66	10	23.81

Table 5: Not bothered from the treatment

DFX		DFX+DFO		DFO	
No.	%	No.	%	No.	%
38	12.0	18	23.07	2	4.76

Table 6: Hard or very hard

DFX		DFX+DFO		DFO	
No.	%	No.	%	No.	%
10	6.66	4	5.12	8	19.04

Table 7: Easy or very easy

DFX		DFX+DFO		DFO	
No.	%	No.	%	No.	%
65	43.33	30	38.46	4	9.52

Table 8: Demographic characteristics and physical activity of the patients.

		DFO	DFX	DFO+DFX	
		No(%)	No(%)	No(%)	*p**
Female		**42 (71.4)**	**80 (53.3)**	**30 (53.8)**	
Male		**36 (28.6)**	**70 (46.7)**	**12 (46.2)**	**NS**
Physical activity	**Non or low**	**16 (38.1)**	**34 (22.7)**	**6 (7.7)**	
	Moderate or high	**26 (61.9)**	**108 (72.0)**	**72 (92.3)**	**NS**
Did not answer		**0 (0.0)**	**8 (6.7)**	**0 (0)**	
Sport	**Yes**	**4 (9.5)**	**68 (90.6)**	**12 (15.4)**	
	No	**38 (90.5)**	**72 (48)**	**66 (84.6)**	**<0.001**
Did not answer		**0(0.0)**	**10(6.7)**	**0 (0.0)**	

***chi-square test.**

Table 9: Disease characteristics

	DFO	DFX	DFO + DFX	P-value*
Myocardial dysfunction	33.3%	6.7%	15.4%	0.0058
Hepatic dysfunction	38.1%	6.7%	2.6%	<0.0001
Splenectomy	71.4%	38.7%	48.7%	0.0319
Allergies	14.3%	9.3%	2.6%	0.0487

***Fisher test. DFO: deferoxamine; DFX: deferasirox; NS: not significant. P values < 0.05 indicate statistical differences between the three groups, All value are means ± SD.**

Table 10: Frequency of co morbidities or prior Splenectomy per group

	DFO	DFX	DFO+DFX	P value*
Age of disease onset ,years	2.1±2.4	2.8±4.5	2.3±4.1	NS
Age at start of DFO treatment ,years	13.1±11.1	9.0±9.6	11.1±11.6	NS
Frequency of DFO therapy, times per week	5.2±1.0	------	4.4±1.9	<0.0001
Frequency of transfusions per month	2.2±0.6	1.9±0.5	2.1±0.7	NS
Hemoglobin level prior to transfusion, g/dl	9.5±0.9	10.1±3.4	9.7±0.4	0.0208
Ferritin level up on enrolment, ng/ml	1559±1778	1738±1636	1023±944	NS

***Chi-square test. DFO: deferoxamine; DFX: deferasirox; NS: not significant. P values < 0.05 indicate statistical differences among the three groups.**

DISCUSSION

The DFO + DFX combination therapy offers a better control of serum ferritin levels, thus requiring less frequent DFO infusions [7]. It was thus not surprising that we found a decreased frequency of transfusions in the DFX group (Table 9). A higher percentage of DFO patients had co morbidities compared to the other two groups; the presence of hepatic dysfunction in patients with homozygous beta-thalassemia has been correlated with iron overload in the liver as well as to chronic hepatitis [8,9]. It is also notable that patients receiving DFX had the lowest prevalence of myocardiopathy which is in accordance with reports on the ability of DFX to prevent iron overload in the myocardium [10].

The highest rate of patient adherence to treatment was observed in the DFX patients. Adherence to therapy is the most important parameter for successful therapy. In fact low adherence of patients receiving DFO has been linked to the absence of clinical benefit [2]. Our results about satisfaction and ease of receiving their therapy matched those of previous studies, in which DFX was associated with increased satisfaction to treatment [11, 12]. Importantly, it was shown that switching chelators resulted in increased adherence, regardless of whether the patients switched from the oral to the intravenous chelator or vice versa, although the switch from DFO to DFX occurred more often [11].

According to previous studies, patients receiving DFO were more likely to suffer from depression, fatigue, dyspnea, and decreased physical functioning [13–15]. The majority of patients felt that they could participate in more activities if they were not receiving DFO [16] in accordance with the results of our study indicating that DFO limited the ability of patients to participate in sports and perform daily functions. Furthermore, long term data for safety of deferasirox (Exjade)is now available for up to five years of treatment.[17,18,19].

Conclusions

In conclusion, our study provides support for differences in the limitations of daily activities, physical activity, and quality of life among patients with transfusion-dependent beta-thalassemia depending on the type of their chelation therapy.

Furthermore, the adherence to treatment, the ease and satisfaction from their therapy. This study highlights the importance of providing beta-thalassemia patients with the optimal chelation treatment based on their individual needs, in order to decrease the presence of unwanted co morbidities and to increase the quality of life, leading to increased adherence and thus resulting in optimal clinical benefit.

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