

Evaluation of safety and efficacy of Deferoxamine compared with deferasirox in transfusion dependent beta thalassemia patients: a single center retrospective study

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Abstract

Purpose: The primary cause of mortality and morbidity in thalassemia major is iron overload. The objective of this study was to compare the safety and efficacy of deferoxamine and deferasirox in transfusion dependent beta thalassemia patients. **Methods:** A retrospective observational study was conducted among 178 patients. Patients were divided into two groups, deferoxamine group (90 patients) and deferasirox group (88 patients). Standardized data collection form was used to collect data. Clinical and demographic characteristics of patients were recorded by checking medical records. The collected data was analyzed using SPSS software. **Findings:** It was revealed that both drugs, deferoxamine and deferasirox were effective and safe in transfusion dependent beta thalassemic patients. Both are efficacious in reducing serum ferritin level. Their laboratory parameters were within clinically accepted range. **Conclusion:** Deferoxamine and deferasirox treatment have equal efficacy and safety for transfusion dependent beta thalassemia population. Therefore, oral deferasirox is recommended for more compliance and convenience.

Keywords: Iron chelators; Iron overload; Thalassemia; Safety; Efficacy.

INTRODUCTION

Thalassemia is a genetic blood disorder, caused by mutation in globin chains (alpha and beta) of hemoglobin [1]. Globally, approximately 7% population has defected hemoglobin gene and about 300 000 – 500 000 babies are carrier of haemoglobinopathies (β -thalassemia, α -thalassemia, and sickle cell disease) [2]. Around 5000 children are born with beta (β) thalassemia every year in Pakistan with 5-8% carrier rate [3]. Such people requires frequent blood transfusion which resulted in accumulation of iron with subsequent organ damage and death [4, 5]. Patients with iron overload need iron chelation therapy for improvement with iron chelators (deferiprone, deferasirox, or deferoxamine) [6, 7].

Deferoxamine (DFO), a naturally occurring trihydroxamic acid produced by *Streptomyces pilosus*, is an iron chelating agent

administered as intramuscularly [8], intravenously [9] or subcutaneously [10] and considered as standard therapy for iron overload worldwide in patients with transfusion dependent β -thalassemia [11, 12]. But DFO treatment over 8 to 12 hours daily is a burdensome regimen and can leads to poor compliance, reduced efficacy, bad quality of life and some other risks like skin rash and heart failure [13-16].

Deferasirox (DFX) is an oral iron chelating agent with efficacy, tolerability and safety in preventing iron accumulation due to blood transfusion in patients (above 2 years) with β thalassemia major [17]. Preclinical and clinical data has demonstrated its positive effect in reducing liver and cardiac iron [18-20]. However, a study indicated that it causes transient acute renal insufficiency [21].

There is limited research in Pakistan high lightening the comparison between DFO and DFX in terms of safety and

efficacy. Therefore, this study was conducted to compare the safety and effectiveness of DFO and DFX in patients with blood transfusion-dependent β -thalassemia major.

METHODS

A retrospective observational study was conducted over a 6-month period among children and adolescents with Thalassemia. The ethical approval for the study was granted by review board on human research of University College of Pharmacy, Punjab University Lahore, Pakistan. Participants in the study were selected based on the inclusion and exclusion criteria. Sample size was calculated using Cochran formula for prevalence [22].

Patients, aged 5 years and above, diagnosed with β -thalassemia major with current serum ferritin higher than 1000 ng/ml were included as well as patients with a lifetime history of at least 20 units of red cell transfusions and received at least ≥ 10 units/year of red blood cells transfusions. Patients were excluded if they were participating in any clinical trial or receiving an investigational drug. Those patients who were suffering from co-morbid clinical conditions were also excluded. Standardized data collection form was used to collect data from 178 patients. Patients were divided into two groups (DFO and DFX group). We recorded basic demographics (e.g., gender, age, payment,

etc.), and clinical information (e.g., diagnosis, Hb level, complications, serum ferritin level, iron chelation treatment etc.) of patients in a clinical record form. Efficacy of the chelation was assessed by change in serum ferritin. Safety was evaluated by clinical and laboratory monitoring of adverse effects, including complete blood count, serum creatinine and blood urea. Gastrointestinal disorders (nausea, vomiting, diarrhea and abdominal pain.), local skin reactions (hardness, swelling, redness, and soreness), and other symptoms were also checked. Six cycles of treatment were evaluated and compared.

All the data collected was analyzed by using SPSS (Statistical Package for the Social Sciences) program. $P < 0.05$ was considered as statistically significant.

RESULTS

Demographics characteristics of all Patients are presented in the Table 1. Data of 178 patient's was analyzed. 90 patients were taking DFO as iron chelating agent whereas DFX was given to 88 patients for iron overload treatment. Majority of the patients getting DFO and DFX treatment were male and resident of rural area. It was found that 98.3% were dependent on guardians and belonged to very low socioeconomic class with monthly income less than 20,000 PKR. More than half (56.7) of the participants have family history of thalassemia.

Table 1: Demographics characteristics of study population

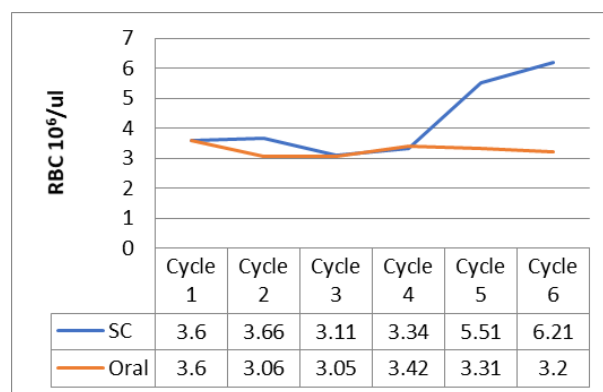
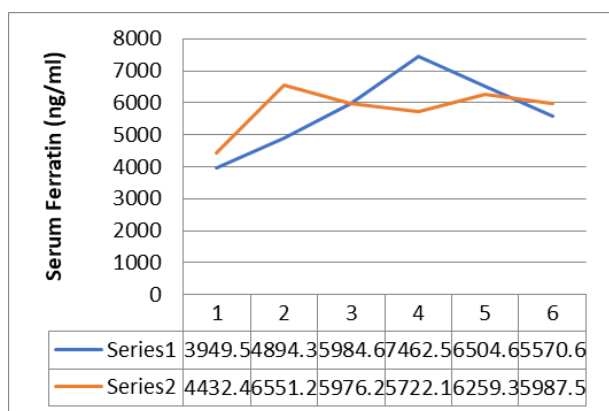
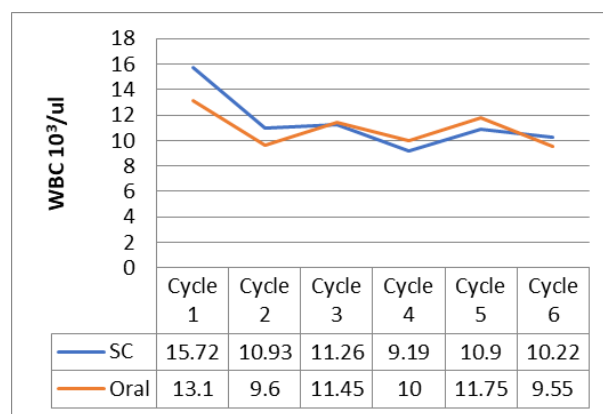
Parameters		Deferoxamine N (%)	Deferasirox N (%)	Total N (%)	P-value
Gender	Male	55 (61.1)	60 (68.2)	115 (64.6)	0.350
	Female	35 (38.9)	28 (31.8)	63 (35.4)	
Locality	Rural	49 (54.4)	65 (73.9)	114 (64.0)	0.008
	Urban	41 (45.6)	23 (26.1)	64 (36.0)	
Income source	Self	0 (0.0)	4 (4.5)	4 (2.2)	0.121
	Dependent	89 (100)	85 (96.6)	174 (98.3)	
Annual income	<20K	87 (97.8)	84 (95.5)	171 (96.6)	0.444
	>20K	3 (3.3)	4 (4.5)	7 (3.9)	
Family history	Yes	52 (57.8)	49 (55.7)	101 (56.7)	0.880
	No	38 (42.2)	39 (44.3)	77 (43.3)	

Table 2: Comparison of lab values of treatment groups (DFO and DFX)

Lab Values	Deferoxamine						Deferasirox					
	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6
Serum ferritin(ng/ml)	3949.53±2 412.608	4894.27±2 665.128*	5984.59 ±2627.5 81	7462. 47±8 446.2 37	6504. 61±5 443.3 66	5570 .57± 2591 .836	4432 .37±1 864.7 23	6551 .22± 3957 .098 *	5976 .19± 2946 .356	5722 .10± 3075 .170	6259 .33± 6570 .789	5987 .48± 3516 .486
WBC's(10 ³ /ul)	15.72±13.0 89	10.93±10. 209	11.26±9 .277	9.19± 6.684	10.90 ±11.1 93	10.2 2±6. 048	13.10 ±17.2 08	9.60 ±8.2 54	11.4 5±12 .626	10.0 0±7. 372	11.7 5±13 .307	9.55 ±5.0 19
RBC's(10 ⁶ /ul)	3.60±0.645	3.66±4.36 1	3.11±0 .654	3.34± 1.126	5.51± 19.69 5	16.2 1±62 .981	3.60 ±1.7 53	3.06 ±0.6 42	3.05 ±0.8 06	3.42 ±0.8 41	3.31 ±0.6 12	3.20 ±0.5 24

Platelets(10^3 /ul)	381.14±173.380	257.63±153.404	264.47±142.504	308.59±379.770	261.61±138.044	333.54±364.437	312.24±270.779	288.78±170.961	253.33±121.089	286.70±144.436	252.01±119.112	271.01±173.057
LFT(ALT)	113.23±53.148	106.14±69.762**	74.53±41.872	65.21±47.999	74.09±45.543	67.56±44.082	116.39±69.302	71.22±58.8**	80.77±54.413	80.16±49.493	62.37±47.477	61.81±39.110
LFT(AST)	120.57±112.343	102.72±62.792**	71.25±44.385	59.33±41.507	75.40±62.111	75.13±42.015	82.06±51.049	62.41±38.208**	74.97±46.877	66.42±28.215	52.62±27.867	76.54±43.610
LFT(ALP)	333.18±176.546	320.00±151.744	397.93±153.826	384.39±165.447	366.32±159.210	344.00±157.443	370.03±155.829	351.02±159.197	380.03±168.936	405.14±133.393	347.85±153.445	447.00±28706.6
RFT(Urea)	30.25±9.915*	26.87±9.709	26.76±6.888	32.40±6.840	21.83±6.090**	23.47±14.237	24.73±9.609*	27.46±11.017	24.70±6.812	29.90±14.956	28.15±4.120**	31.83±11.325
RFT(Creatinine)	2.42±8.138	0.52±0.355	0.52±0.361	0.43±0.124	0.41±0.193	0.58±0.344	0.51±0.228	0.52±0.246	0.46±0.221	0.48±0.217	0.46±0.206	0.52±0.317

Table 2 represents the comparison of clinical values of six cycles of treatment with DFO and DFX. Serum ferritin level in DFO group increased significantly but dropped at last cycles. On the other hand, DFX treatment showed fluctuation in serum ferritin level. White blood cells, Platelets, Alanine aminotransferase (ALT) and Aspartate aminotransferase (AST) values decreased in both DFO and DFX group with the passage of time. However, alkaline phosphatase (ALP) and creatinine increased in both treatment groups. Red blood cells count elevated with DFO treatment while declined with DFX. Urea level decreased by DFO in each cycle while increased by DFX. The graphical presentation of comparison of two groups (DFO and DFX) is shown in Fig 1.



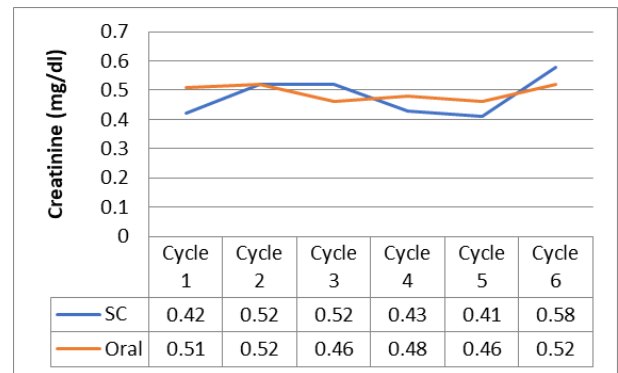
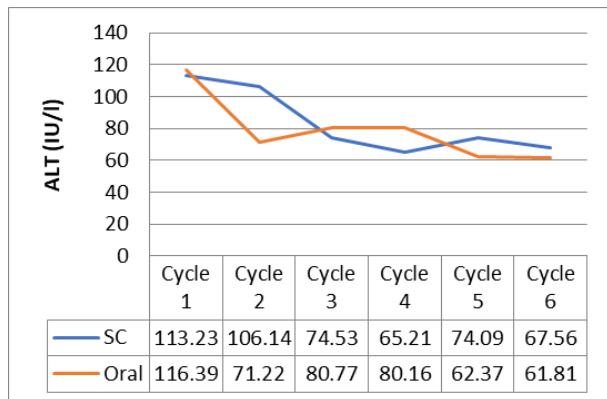
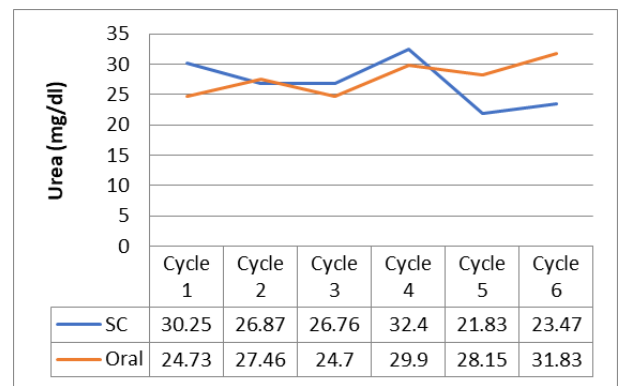
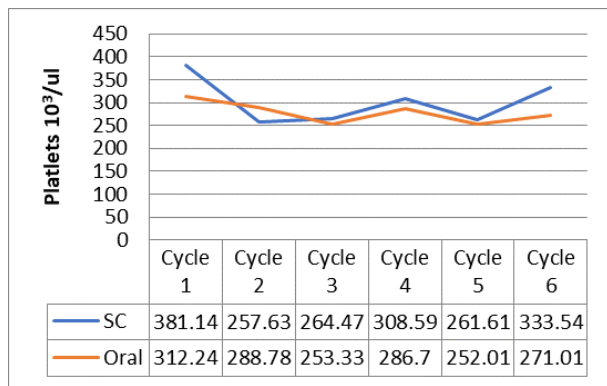
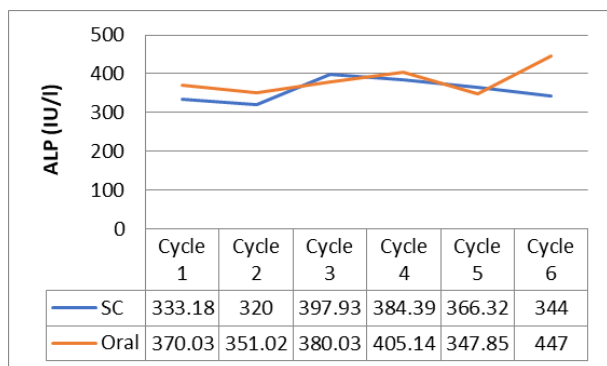
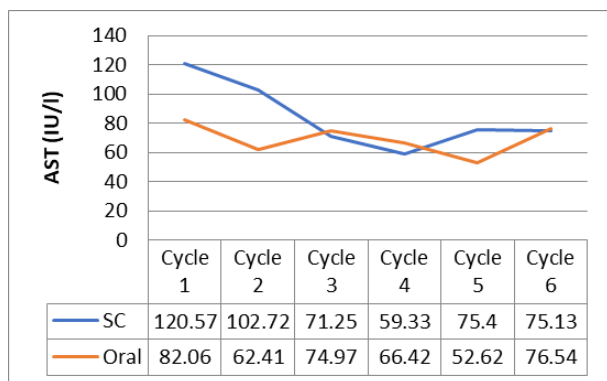


Figure 1: Comparison of clinical parameters of DFO and DFX



DISCUSSION

This study was conducted to compare the safety and efficacy of two iron chelators, DFO and DFX. Thalassemia is a major health and economic trouble in the Mediterranean region, with iron overload becoming major cause of mortality. Therefore, iron chelation is required to reduce the burden of iron with fewer side effects [23]. β -thalassemia is very common in Pakistan and only few get bone marrow transplantation as treatment [24].

In our study, proportion of male was high. This finding was observed in other studies as well [25-27]. Based on our literature review, previously available limited data shows that thalassemia is prevalent in rural areas as compared to urban [28-30]. Our study reported the same results. Previous studies showed that consanguineous marriage is major risk of hereditary diseases [30, 31]. It was also observed in this study that more than half of participants have thalassemia in their family history.

As in previous studies [32], this study also revealed that changes in serum ferritin concentration was similar for DFO and DFX. Both are effective in reducing serum ferritin level [33-35].

In terms of safety profile, DFO and DFX showed same results. Consistent with the findings from previous studies [32, 35-38] it was observed from laboratory parameter that both treatments are safe.

Our study did not report any serious adverse effects to either drug. DFO and DFX showed difference in RBCs and blood urea level, but the levels were within clinically accepted range. Serum creatinine, serum transaminases (ALT, AST, and ALP), WBCs, and platelets counts were same. Therefore, both treatments have same safety profile. In terms of comparable efficacy and safety of DFO and DFX, studies [39-41] identified that oral preparation are more compliant and convenient to be taken on long term basis.

CONCLUSION

In conclusion, we found that both DFO and DFX treatment are safe and effective in beta thalassaemic patients. The oral DFX is suggested due to its more compliance and convenience.

Conflict of Interest

Authors do not have any conflict of interest

Grants

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Authors Contributions

Narjis Batool, collected the data, assisted in preparation of the manuscript and interpretations of the factual materials.

Sadia Yasmeen, collected the data and coordinated the activities on this project and helped in the analysis of the results.

Rabia Anwar, collected the data and coordinated the activities on this project and helped in the analysis of the results.

Zikria Saleem, is the head of the project. He organized the team for the smooth running of this project by coordinating all the members.

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