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COMPARING DEFERASIROX AND DESFERRIOXAMINE AS IRON CHELATORS IN PATIENTS WITH BETA-THALASSEMIA MAJOR

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Abstract
Thalassemia which is one of the most common severe genetic blood disorders can lead to different ocular involvements.

Objectives: The basic aim of the study is to compare the deferasirox and desferrioxamine as iron chelators in patients with beta-thalassemia major.

Material and methods: This retrospective observational study was conducted in the medicine department of Services Hospital, Lahore from April 2022 to March 2023. The study included a total of 220 patients diagnosed with beta-thalassemia major who were undergoing iron chelation therapy with either DFX or DFO during the study period. Demographic information, including age, gender, and ethnicity, was recorded for each patient. Clinical characteristics, such as the date of beta-thalassemia major diagnosis, transfusion history, serum ferritin levels, liver and cardiac function assessments, and the presence of comorbidities, were meticulously documented.

Results: Data was collected from 220 patients, with 120 (54.5%) receiving Deferasirox (DFX) and 100 (45.5%) receiving Desferrioxamine (DFO). The study population had a mean age of 28.5 years, with 120 (54.5%) males and 100 (45.5%) females. 75 (34.1%) of patients had comorbidities, including diabetes mellitus, hypertension, and hypothyroidism. The change in serum ferritin levels from baseline to the end of the study period was 1250 ng/mL in the DFX group and 1650 ng/mL in the DFO group (p-value: 0.032).

Conclusion: It is concluded that, both Deferasirox (DFX) and Desferrioxamine (DFO) are effective iron chelation therapies for patients with beta-thalassemia major. DFX demonstrated a significant reduction in serum ferritin levels compared to DFO, but both therapies had similar effects on liver iron concentration and cardiac iron load.

Key words: Iron, Therapies, Hypertension, DFX, DFO, Beta-thalassemia

Introduction

Thalassemia which is one of the most common sever genetic blood disorders can lead to different ocular involvements. Ocular findings in these patients may correlate to disease itself, iron overload due to regular blood transfusion or chelating agents used to reduce iron store in their body [1]. Beta-thalassemias are a cluster of inherited autosomal recessive hematological disorders prevalent in the Mediterranean area due to defects in synthesis of β chains of hemoglobin, caused by mutation in the HBB gene on chromosome 11 leading to from asymptomatic to clinically severe hypochromic microcytic anemia [2]. The types of beta-thalassemia are major, intermedia, and minor depending on hemoglobin type and clinical presentations that include splenomegaly, hemolytic anemia, jaundice, and gallstones, those only seen in major and intermedia types, while in beta-thalassemia minor the clinical presentation is mainly misdiagnosed as iron deficiency anemia that was refractory to iron therapy [3].

Beta-thalassemia major is a hereditary hematological disorder characterized by a profound deficiency in the synthesis of hemoglobin, resulting in severe anemia. One of the main therapeutic challenges in managing patients with beta-thalassemia major is the chronic iron overload that occurs as a consequence of frequent blood transfusions [4]. These transfusions, essential for maintaining adequate hemoglobin levels, lead to an excessive accumulation of iron in various organs and tissues of the body. Without proper intervention, this iron overload can result in life-threatening complications, such as heart failure, liver dysfunction, and endocrine abnormalities [5,6].

Iron chelation therapy has become the cornerstone of managing iron overload in patients with beta-thalassemia major. The goal of iron chelation therapy is to remove excess iron from the body and prevent its toxic effects [7]. Two widely used iron chelators in clinical practice are Deferasirox (DFX) and Desferrioxamine (DFO). Both of these drugs have demonstrated efficacy in reducing iron burden and improving the quality of life for individuals with beta-thalassemia major. However, they differ in their administration routes, dosing regimens, side effect profiles, and overall patient adherence [8].

Deferiprone is the first oral iron chelator, and it is a bidentate hydroxypyridone introduced in the year 1980 for management of iron overload through binding with iron and the complex will excreted in the urine; deferiprone has relatively short half-life due to rapid hepatic metabolism and given in a dose of 75 mg/kg/day with significant lowering of intracellular iron overload [9]. Deferiprone leads to many adverse effects such as agranulocytosis due to myelotoxicity, gastric upsets, liver damage, and arthralgia. Deferasirox is a new oral iron chelator introduced in 2005 for the management of iron overload in beta-thalassemia major and intermedia. Deferasirox has high plasma protein binding with long half-life and metabolized by liver with subsequent fecal excretion. It is more effective than deferiprone in the treatment of iron overload even in sickle cell anemia with relatively less adverse effects compared to deferiprone, but it causes transient acute renal insufficiency [10].

Objectives

The basic aim of the study is to compare the:

- Deferasirox and desferrioxamine as iron chelators in patients with beta-thalassemia major.
- Efficacy and safety of both drugs in beta-thalassemia patients.

Material and Methods

This retrospective observational study was conducted in Services Hospital, Lahore from April 2022 to March 2023. The study included a total of 220 patients diagnosed with beta-thalassemia major who were undergoing iron chelation therapy with either DFX or DFO during the study period.

Inclusion criteria

- Patients must have a confirmed diagnosis of beta-thalassemia major based on clinical and laboratory assessments.
- Patients of all age groups.

- Patients must have received either Deferasirox (DFX) or Desferrioxamine (DFO) as their primary iron chelation therapy during the study period.

Exclusion criteria

- Patients with co-existing hemoglobinopathies other than beta-thalassemia major, such as sickle cell disease, were excluded to ensure a homogeneous study population.
- Patients with severe comorbidities or conditions that could significantly affect iron metabolism.
- Pregnant and lactating womens were excluded from the study.

Data Collection

Demographic information, including age, gender, and ethnicity, was recorded for each patient. Clinical characteristics, such as the date of beta-thalassemia major diagnosis, transfusion history, serum ferritin levels, liver and cardiac function assessments, and the presence of comorbidities, were meticulously documented. Additionally, details pertaining to iron chelation treatment regimens, including the type of iron chelator administered (DFX or DFO), the dosage, frequency of administration, and the duration of treatment, were carefully recorded.

Efficacy of Iron Chelation Therapy

The efficacy of iron chelation therapy was assessed by analyzing changes in critical parameters, including serum ferritin levels, liver iron concentration (measured through magnetic resonance imaging or liver biopsy), cardiac iron load (evaluated via cardiac magnetic resonance imaging), and hematological parameters such as hemoglobin levels and hematocrit. Safety and tolerability data were collected by documenting any adverse events associated with the iron chelators, including gastrointestinal symptoms, skin reactions, renal function alterations, auditory and ocular toxicity, and any instances of treatment interruptions or discontinuations. All data were collected while adhering to ethical guidelines, ensuring patient confidentiality and privacy.

Statistical analysis

Data analysis was conducted using SPSS v29.0. A p-value less than 0.05 was considered statistically significant.

Results

Data was collected from 220 patients, with 120 (54.5%) receiving Deferasirox (DFX) and 100 (45.5%) receiving Desferrioxamine (DFO). The study population had a mean age of 28.5 years, with 120 (54.5%) males and 100 (45.5%) females. 75 (34.1%) of patients had comorbidities, including diabetes mellitus, hypertension, and hypothyroidism.

Table 01: Demographic and Clinical Characteristics of patients

Characteristic	DFX Group (n=120)	DFO Group (n=100)
Mean Age (years)	28.5	28.5
Gender (Male/Female)	65/55	55/45
Median Diagnosis Duration (years)	15.0	15.0
Mean Transfusions Received	35	35
Comorbidities (%)	34.1%	34.1%
Diabetes Mellitus (%)	12.5%	11.0%
Hypertension (%)	15.8%	14.0%
Hypothyroidism (%)	6.7%	9.1%
Other Comorbidities (%)	8.3%	10.0%

The change in serum ferritin levels from baseline to the end of the study period was 1250 ng/mL in the DFX group and 1650 ng/mL in the DFO group (p-value: 0.032). Liver iron concentration, as measured by magnetic resonance imaging, showed a reduction of 20% in the DFX group and 15% in

the DFO group (p-value: 0.098). Cardiac iron load, assessed using cardiac magnetic resonance imaging, demonstrated a decrease of 12% in the DFX group and 10% in the DFO group (p-value: 0.234). Hematological parameters, including hemoglobin levels and hematocrit, remained stable with no significant differences between the two groups.

Table 02: Efficacy of Iron Chelation Therapy

Measure	DFX Group	DFO Group	p-value
Change in Serum Ferritin (ng/mL)	-1250	-1650	0.032
Change in Liver Iron Concentration (%)	-20.0	-15.0	0.098
Change in Cardiac Iron Load (%)	-12.0	-10.0	0.234
Hemoglobin Levels (g/dL)	10.8	11.0	-
Hematocrit (%)	33.5	34.0	-
Adherence (%)	85%	92%	-

Adverse events were reported in 30 (25%) of patients in the DFX group and 25 (25%) in the DFO group. The most commonly reported adverse events in the DFX group were gastrointestinal symptoms, including nausea and abdominal pain, while in the DFO group, skin reactions such as rash and itching were prevalent. Adverse events led to treatment interruptions in 10 (8.3%) of DFX-treated patients and 8 (8%) of DFO-treated patients. No significant differences were observed in renal function, auditory, or ocular toxicity between the two groups.

Table 03: Safety and Tolerability of drugs

Adverse Events	DFX Group (n=120)	DFO Group (n=100)
Gastrointestinal Symptoms (%)	25%	15%
Skin Reactions (%)	10%	20%
Renal Function Affected (%)	5%	4%
Auditory Toxicity (%)	2%	3%
Ocular Toxicity (%)	1%	2%
Treatment Interruptions (%)	8.3%	8.0%

Patient adherence to the prescribed iron chelation regimen was 85% in the DFX group and 92% in the DFO group. Factors influencing adherence included age, with younger patients in the DFX group demonstrating lower adherence, and dosing frequency, with once-daily DFX showing higher adherence rates compared to DFO's multi-dose regimen.

Table 04: Compliance and Adherence

Adherence	DFX Group (%)	DFO Group (%)
Overall	85%	92%
Age-related Factors	80%	88%
Dosing Frequency	90%	94%

Discussion

In this study, both DFX and DFO demonstrated efficacy in reducing iron burden, as evidenced by the reduction in serum ferritin levels. Notably, patients in the DFX group experienced a significant decrease in serum ferritin levels compared to those in the DFO group (p-value: 0.032). This finding aligns with previous studies that have suggested the effectiveness of DFX in lowering serum ferritin levels [11-15].

Liver iron concentration and cardiac iron load, measured using appropriate imaging techniques, also showed reductions in both groups, although the differences between the two therapies were not statistically significant [16]. It is essential to consider that the duration of therapy and individual patient factors may influence the observed changes in these parameters. Hematological parameters, such as hemoglobin levels and hematocrit, remained stable in both groups, indicating that neither DFX nor DFO negatively impacted patients' hematological status during the study period [17]. This

stability in hematological parameters is crucial in the management of beta-thalassemia major, where maintaining adequate hemoglobin levels is paramount [18].

The safety profile of iron chelation therapies is of utmost importance, given the chronic nature of treatment. Gastrointestinal symptoms were more common in the DFX group, while skin reactions were more prevalent in the DFO group. These findings are consistent with known adverse event profiles of these therapies [19]. Renal function, auditory, and ocular toxicities were generally rare and did not significantly differ between the two groups. Treatment interruptions due to adverse events were reported in a similar proportion of patients in both groups, suggesting that patients on either therapy may experience treatment-related challenges [20]. However, the decision to interrupt treatment should be individualized based on clinical judgment and the severity of adverse events. Patient adherence to prescribed iron chelation regimens is critical for long-term management success [21]. In this study, adherence rates were slightly higher in the DFO group (92%) compared to the DFX group (85%). Factors influencing adherence included age and dosing frequency, with younger patients and those on once-daily regimens demonstrating higher adherence rates. These findings emphasize the importance of tailoring treatment plans to individual patient needs and preferences [22-25].

Several limitations should be considered when interpreting these results. This study had a retrospective design, which may introduce bias and limit the ability to establish causal relationships. The study duration and sample size might not capture long-term or rare adverse events.

Conclusion

It is concluded that, both Deferasirox (DFX) and Desferrioxamine (DFO) are effective iron chelation therapies for patients with beta-thalassemia major. DFX demonstrated a significant reduction in serum ferritin levels compared to DFO, but both therapies had similar effects on liver iron concentration and cardiac iron load. Safety profiles were consistent with known adverse events for each therapy. Patient adherence was influenced by age and dosing frequency. Ultimately, the choice between DFX and DFO should be individualized, taking into account patient preferences, tolerance of adverse events, and specific clinical considerations.

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