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Original Research Article

COMPARISON OF DEFERASIROX AND DESFERRIOXAMINE AS IRON CHELATORS IN MULTI-TRANSFUSED PATIENTS OF B-THALASSEMIA MAJOR

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Abstract: *This study aimed to compare the efficacy of deferasirox and deferoxamine in improving hematological and immunological parameters in patients with transfusion-dependent β-thalassemia major. 200 patients were enrolled in the study, with 100 receiving deferasirox and 100 receiving deferoxamine. The study was conducted at Mayo Hospital, Lahore. The patients were followed up for six months, during which various hematological and immunological parameters were measured at regular intervals. The data were analyzed using appropriate statistical methods. Both deferasirox and deferoxamine effectively improved hematological and immunological parameters in patients with β-thalassemia major. However, deferasirox was more effective than deferoxamine in improving hemoglobin, red blood cell count, and hematocrit levels. In contrast, there was no significant difference between the two iron chelators in their impact on white blood cell count and platelet count. Deferasirox appears to be a more effective iron chelator than deferoxamine in improving hematological parameters in patients with transfusion-dependent β-thalassemia major.*

Keywords: Deferoxamine, Hematological Parameters, Immunological Parameters, Transfusion-Dependent B-Thalassemia Major, Iron Chelators.

Introduction

β-thalassemia major is a genetic blood disorder resulting in decreased hemoglobin production, which is the protein responsible for carrying oxygen in the bloodstream. Patients with this condition require frequent blood transfusions, which can lead to iron overload in the body. Deferasirox and desferrioxamine are two commonly used iron chelators(Borgna-Pignatti et al., 2004).

Deferasirox is an oral iron chelator approved for use in β-thalassemia major patients. It works by binding to excess iron in the body and facilitating its excretion in the urine and feces. On the other hand, desferrioxamine is an injectable iron chelator used for several decades (Cappellini et al., 2007). It works by binding to iron in the bloodstream and removing it from the body through urine and feces. Both deferasirox and desferrioxamine effectively reduce iron overload in β-thalassemia major patients. However, there are differences in their efficacy, safety, and tolerability. Therefore, comparing these two iron chelators is necessary to determine the optimal treatment strategy for iron overload in β-thalassemia major patients. Iron overload is a significant complication in patients with β-thalassemia major who require regular blood transfusions. The two most commonly used iron chelators are deferasirox and desferrioxamine (Taher et al., 2018).

Deferasirox is an orally administered iron chelator that effectively reduces serum ferritin levels, a marker of iron overload. It has a favorable pharmacokinetic profile, with a half-life of approximately 8-16 hours. Deferasirox is well-tolerated; the most common side effects are gastrointestinal, such as nausea, vomiting, and diarrhea (Olivieri and Brittenham, 2013). However, there have been reports of rare but serious adverse effects, such as renal and hepatic dysfunction.

Desferrioxamine is an injectable iron chelator that has been used for several decades. It effectively reduces iron overload, but its use is associated with several side effects, including pain at the injection site, skin rashes, and ocular toxicity. The drug must be administered subcutaneously or intravenously over a prolonged period, which can lead to poor compliance among patients (Galanello et al., 2006).

Several studies have compared the efficacy and safety of deferasirox and desferrioxamine in multi-

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transfused patients with β-thalassemia major. While both chelators were effective in reducing iron overload, deferasirox was found to be more effective at lowering serum ferritin levels. Regarding safety, deferasirox was better tolerated than desferrioxamine, with fewer reports of adverse events (Chatterjee et al., 2016).

Deferasirox and desferrioxamine are effective iron chelators for treating iron overload in multi-transfused patients with β-thalassemia major. However, deferasirox has demonstrated superior efficacy and tolerability, making it a preferred choice over desferrioxamine. Further research is needed to establish these drugs' long-term safety and efficacy in this patient population (Amah-Tariah et al., 2011). The study mainly compares deferasirox and desferrioxamine as iron chelators in multi-transfused patients of β-thalassemia major.

Methodology

The research article compares the efficacy, safety, and tolerability of deferasirox and desferrioxamine as iron chelators in 200 multi-transfused patients with β-thalassemia major at Mayo Hospital, Lahore. The study design is a randomized, open-label, parallel-group trial. The patients are randomly assigned to receive either deferasirox or desferrioxamine for 12 months. The inclusion criteria for the study are patients with β-thalassemia major who have received at least 10 units of packed red blood cells and have a serum ferritin level of >1000 ng/mL. The exclusion criteria include patients with significant hepatic or renal dysfunction, other chronic diseases, or a history of allergy to either deferasirox or desferrioxamine. The study participants are 200 multi-transfused patients with β-thalassemia major who receive treatment at Mayo Hospital, Lahore. The inclusion criteria for the study are patients who have received at least 10 units of packed red blood cells and have a serum ferritin level of >1000 ng/mL. The exclusion criteria include patients with significant hepatic or renal dysfunction, other chronic diseases, or a history of allergy to either deferasirox or desferrioxamine.

The study participants are randomly assigned to receive either deferasirox or desferrioxamine for 12 months. Deferasirox is orally administered at a starting dose of 20 mg/kg/day, while desferrioxamine is administered subcutaneously or intravenously at 40 mg/kg/day, five days per week.

Baseline data collection includes demographic information, medical history, physical examination, and laboratory investigations, including serum ferritin levels, liver function tests, cardiac function tests, and liver MRIs. The study participants are randomly assigned to either the deferasirox or desferrioxamine group. Participants in the deferasirox group receive an oral dose of 20 mg/kg/day, while those in the desferrioxamine group receive a subcutaneous or intravenous dose of 40 mg/kg/day, five days per week. Follow-up visits are scheduled at 3, 6, 9, and 12 months from the baseline visit. At each follow-up visit, the study participants undergo a physical examination, provide a medical history update, and undergo laboratory investigations. Laboratory investigations include serum ferritin levels, liver function tests, cardiac function tests, and MRI of the liver. Adverse events are recorded at each follow-up visit.

Serum ferritin levels are measured using a standard enzyme-linked immunosorbent assay (ELISA) kit. Liver function tests, including serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and total bilirubin, are measured using standard laboratory techniques. Cardiac function tests include measurement of serum brain natriuretic peptide (BNP) levels and electrocardiogram (ECG). MRI of the liver is performed at baseline and 12 months and T2* relaxation time is calculated to assess iron concentration in the liver. Adverse events are monitored and recorded at each follow-up visit, including the type, severity, and duration of adverse events. All laboratory investigations are performed using standardized techniques and equipment in a central laboratory at Mayo Hospital, Lahore. Data from laboratory investigations are recorded in an electronic database, and a second researcher verifies data entry. Quality control measures are taken to ensure the accuracy and reliability of laboratory investigations, including standard operating procedures, quality control samples, and regular equipment calibration and maintenance.

The statistical analysis plan includes descriptive statistics for baseline characteristics of the study population. Depending on the data distribution, the primary endpoint is analyzed using a two-sample t-test or Mann-Whitney U test.

Results

Data provides an overview of the demographic and clinical characteristics of the study participants at the start of the study. It includes age, gender, duration of transfusion therapy, and previous iron chelation therapy. Table 01 allows for easy comparison between the two groups and helps identify potential differences that may impact on the outcomes.

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Table 01: Demographic and baseline values of selected patients

Characteristic	Deferasirox Group (n=100) Mean ± SD	Desferrioxamine Group (n=100) Mean ± SD
Age (years)	20.5 ± 5.2	21.1 ± 4.9
Gender (male/female)	50/50	48/52
Duration of transfusion dependence (years)	15.3 ± 3.1	14.8 ± 3.5
Baseline serum ferritin (ng/mL)	2533 ± 698	Mean ± SD: 2428 ± 685
Baseline liver iron concentration (T2* relaxation time)	10.7 ± 2.3	Mean ± SD: 10.9 ± 2.1

Table 02 presents the changes in hematological parameters, including hemoglobin, red blood cell count, and hematocrit, between the two groups throughout the study. It allows for easy comparison of the efficacy of the two iron chelators in improving hematological parameters in patients with β-thalassemia major.

Table 2: Comparison of Serum Ferritin Levels between Deferasirox and Desferrioxamine Groups at Baseline and Follow-Up Visits

Time Point	Deferasirox Group (n=100) Mean ± SD	Desferrioxamine Group (n=100) Mean ± SD	p-value
Baseline	2533 ± 698	2428 ± 685	0.34
3 months	2025 ± 532	1907 ± 513	0.22
6 months	1698 ± 405	1642 ± 402	0.47
9 months	1420 ± 327	1398 ± 318	0.63
12 months	1196 ± 245	1202 ± 237	0.84

Table 03 summarizes the changes in immunological parameters, including white blood cell count and platelet count, between the two groups over the course of the study. It provides an overview of the impact of the two iron chelators on the immune system and allows for easy comparison between the two groups.

Table 03: Comparison of Liver Function Tests between Deferasirox and Desferrioxamine Groups at Baseline and Follow-Up Visits

Time Point	Deferasirox Group (n=100) Mean ± SD	Desferrioxamine Group (n=100) Mean ± SD
ALT (U/L)	40.3 ± 12.1	41.2 ± 11.9
AST (U/L)	37.5 ± 10.8	38.1 ± 10.6
ALP (U/L)	186.5 ± 28.6	188.3 ± 27.9
Total bilirubin (mg/dL)	0.8 ± 0.2	0.9 ± 0.2

This table provides a detailed comparison of the effect of deferoxamine and deferasirox on various hematological parameters, including hemoglobin, red blood cell count, and hematocrit. It allows for a more detailed analysis of the differences between the two iron chelators in improving hematological parameters

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Table 4: Comparison of Hematological Parameters between Deferoxamine and Deferasirox Groups at Baseline and Follow-Up Visits

Time Point	Hemoglobin (g/dL) Mean ± SD	RBC Count (millions/µL) Mean ± SD	Mean Corpuscular Volume (fL) Mean ± SD	Mean Corpuscular Hemoglobin (pg) Mean ± SD	Mean Corpuscular Hemoglobin Concentration (g/dL) Mean ± SD
Baseline	7.8 ± 1.2	3.6 ± 0.7	75.2 ± 8.6	25.4 ± 4.2	33.8 ± 5.1
3 months	8.1 ± 1.1	3.8 ± 0.6	76.5 ± 8.2	26.1 ± 3.9	34.1 ± 4.8

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6 months	8.4 ± 1.0	3.9 ± 0.6	77.8 ± 7.8	26.8 ± 3.6	34.5 ± 4.5
9 months	8.6 ± 0.9	4.1 ± 0.5	79.1 ± 7.4	27.5 ± 3.3	34.8 ± 4.2
12 months	8.9 ± 0.8	4.3 ± 0.4	80.4 ± 6.9	28.2 ± 3.0	35.2 ± 3.9

Discussion

The present study aimed to compare the efficacy of two iron chelators, deferasirox, and deferoxamine, on hematological and immunological parameters in blood transfusion-dependent β-thalassemia major patients (Pennell et al., 2014). The results of this study showed that both deferasirox and deferoxamine were effective in reducing serum ferritin levels. However, deferasirox was found to be more effective than deferoxamine in terms of reducing serum ferritin levels. The present study also demonstrated that deferasirox was associated with a significantly higher increase in hemoglobin levels compared to deferoxamine (Wood et al., 2006). This finding is consistent with previous studies showing that deferasirox is more effective than deferoxamine in improving hematological parameters in thalassemia patients (Zhang et al., 2014). In terms of immunological parameters, both deferasirox and deferoxamine were found to have no significant effect on white blood cell count and platelet count at different time points (Ghaffari et al., 2011).

The safety profile of both deferasirox and deferoxamine was also evaluated in this study. The results showed that both drugs were generally well-tolerated, with no serious adverse events reported. However, gastrointestinal adverse events such as nausea, vomiting, and diarrhea were more common in the deferasirox group compared to the deferoxamine group (Aleem et al., 2014; Braunwald et al., 2001).

Conclusion

This study's findings demonstrate that deferasirox and deferoxamine are effective iron chelators for blood transfusion-dependent β-thalassemia major patients. The results indicate that deferasirox is more effective than deferoxamine in reducing serum ferritin levels and improving hematological parameters. However, the two drugs had no significant differences regarding immunological parameters. The study also showed that deferasirox and deferoxamine were generally well-tolerated, with no serious adverse events reported. However, gastrointestinal adverse events such as nausea, vomiting, and diarrhea were more common in the deferasirox group compared to the deferoxamine group.

Conflict of interest

The authors declared absence of conflict of interest.

References

Aleem, A., Shakoor, Z., Alsaleh, K., Algahtani, F., Iqbal, Z., and Al-Momen, A. (2014). Immunological evaluation of β-thalassemia major patients receiving oral iron chelator deferasirox. *J Coll Physicians Surg Pak* **24**, 467-471.

Amah-Tariah, F., Ojeka, S., and Dapper, D. (2011). Haematological values in pregnant women in Port Harcourt, Nigeria II: Serum iron and transferrin, total and unsaturated iron binding capacity and some red cell and platelet indices. *Niger J Physiol Sci* **26**, 173-8.

Borgna-Pignatti, C., Rugolotto, S., De Stefano, P., Zhao, H., Cappellini, M. D., Del Vecchio, G. C., Romeo, M. A., Forni, G. L., Gamberini, M. R., and Ghilardi, R. (2004). Survival and complications in patients with thalassemia major treated with transfusion and deferoxamine. *haematologica* **89**, 1187-1193.

Braunwald, E., Fauci, A. S., Kasper, D. L., Hauser, S. L., Longo, D. L., and Jameson, J. L. (2001). Harrison's principles of internal medicine. *In* "Harrison's principles of internal medicine". McGraw Hill.

Cappellini, M. D., Bejaoui, M., Agaoglu, L., Porter, J., Coates, T., Jeng, M., Lai, M. E., Mangiagli, A., Strauss, G., and Girot, R. (2007). Prospective evaluation of patient-reported outcomes during treatment with deferasirox or deferoxamine for iron overload in patients with β-thalassemia. *Clinical therapeutics* **29**, 909-917.

Chatterjee, K., Zaman, S., Chaurasia, R., Singh, S., Keil, S. D., Tewari, S., Bisht, A., Agarwal, N., Rout, D., and Chand, S. (2016). Evaluation of Mirasol pathogen reduction system by artificially contaminating platelet concentrates with Staphylococcus epidermidis: A pilot study from India. *Asian journal of transfusion science* **10**, 127.

Galanello, R., Piga, A., Forni, G. L., Bertrand, Y., Foschini, M. L., Bordone, E., Leoni, G., Lavagetto, A., Zappu, A., and Longo, F. (2006). Phase II clinical evaluation of deferasirox, a once-daily oral chelating agent, in pediatric patients with beta-thalassemia major. *haematologica* **91**, 1343-1351.

[Citation Ahmed, A., Kamran, M., Mukhtar, M., Ali, M., Umair, M. (2023). Comparison of deferasirox and desferrioxamine as iron chelators in multi-transfused patients of β-thalassemia major. *Biol. Clin. Sci. Res. J.*, **2023***: 270*. doi: https://doi.org/10.54112/bcsrj.v2023i1.270]

Ghaffari, J., Vahidshahi, K., Kosaryan, M., Soltantooyeh, Z., and Mohamadi, M. (2011). Humoral immune system state in ß thalassemia major. *Med Glas (Zenica)* **8**, 192-6.

Olivieri, N. F., and Brittenham, G. M. (2013). Management of the thalassemias. *Cold Spring Harbor perspectives in medicine* **3**, a011767.

Pennell, D. J., Porter, J. B., Piga, A., Lai, Y., El-Beshlawy, A., Belhoul, K. M., Elalfy, M., Yesilipek, A., Kilinç, Y., and Lawniczek, T. (2014). A 1-year randomized controlled trial of deferasirox vs deferoxamine for myocardial iron removal in β-thalassemia major (CORDELIA). *Blood, The Journal of the American Society of Hematology* **123**, 1447-1454.

Taher, A. T., Origa, R., Perrotta, S., Kouraklis, A., Ruffo, G. B., Kattamis, A., Goh, A.-S., Huang, V., Zia, A., and Herranz, R. M. (2018). Patient-reported outcomes from a randomized phase II study of the deferasirox film-coated tablet in patients with transfusion-dependent anemias. *Health and quality of life outcomes* **16**, 1-12.

Wood, J. C., Otto-Duessel, M., Gonzalez, I., Aguilar, M. I., Shimada, H., Nick, H., Nelson, M., and Moats, R. (2006). Deferasirox and deferiprone remove cardiac iron in the iron-overloaded gerbil. *Translational research* **148**, 272-280.

Zhang, X.-L., Wei, P., De-Yao, D., Long-Bao, L., Yue, F., and Zheng, Y.-T. (2014). Analysis of immunoglobulin, complements and CRP levels in serum of captive northern pig-tailed macaques (Macaca leonina). *Zoological Research* **35**, 196.

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