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Abstract
Background: "Thalassemia" refers to anemias caused by hereditary defects in haemoglobin synthesis. These hereditary illnesses are common in the Mediterranean region, the Indian subcontinent, Southeast Asia, and West Africa. A mutated globin gene causes excessive red blood cell destruction.

Materials and Methods: A prospective analysis of comparisons. Shadhan Institute of Medical Sciences, Hyderabad, Telangana, 50 children with thalassemia who had received multiple transfusions and were being treated daily with iron chelation participated in the current study. Children who have received multiple blood transfusions and are getting daily iron chelation therapy for thalassemia participated in the study, which was conducted from June 2021 to June 2022. Result: 50 thalassemia multitransfused children were included in the current study. They were given daily iron chelation therapy for a period of 12 months with either deferriprone alone (75 mg/kg/day in 3 divided doses), deferasirox alone (30 mg/kg/day single dose), or their daily combination (30 mg/kg/day single dose). Participants underwent the following daily treatments: Deferriprone alone (75 mg/kg/day in 3 split doses; n = 18), Deferasirox alone (30 mg/kg/day single dosage; n = 16), and Deferriprone and Deferasirox combined (n = 16) were the treatment groups. Conclusion: Deferiprone and deferasirox together were found to be more effective at reducing iron overload than either drug alone. Serum ferritin, hepatic and cardiac MRI*T2 scans, and urine iron excretion were evaluated in 50 thalassemia-afflicted children who had received multiple transfusions. However, in children with thalassemia who had received multiple transfusions, deferriprone and deferasirox were also efficient and secure when given alone.

INTRODUCTION

The term "thalassemia," which comes from the Greek words "thalassa," which means "sea," and "emia," which means "blood,"[1] refers to a group of anemias caused by inherited flaws in the production of haemoglobin. These conditions are among the most prevalent genetic diseases in the world, with higher rates in the Mediterranean region,[2] the Indian subcontinent, Southeast Asia, and West Africa.[3] It is a severe genetic blood condition in which red blood cells are excessively destroyed due to a globin gene mutation.[4] The anaemia is caused by both excessive red blood cell hemolysis and inefficient bone marrow erythropoiesis. Mature erythrocytes have roughly equimolecular levels of each chain because reticulocytes produce equimolecular quantities of alpha and beta chains.[5] Because their cells are unable to synthesise either the alpha or beta polypeptide chains of human haemoglobin, patients with thalassemia do not make enough haemoglobin (Hb) A (22).[6] Disorders associated with beta thalassemia are caused by a relative excess of alpha globin chains and a reduction in the formation of beta globin chains. The term "alpha thalassemia" refers to a category of diseases in which the alpha globin genes are inactivated, leading to a disproportionately high level of non-functional beta globin or gamma globin tetramers and associated cell damage.[7] Subcategories of the aforementioned categories are then created.[8] Children with beta-thalassemia major die before the age of three if they are not treated with a blood transfusion,[9] which can reduce mortality. Organ failure, however, can result from an excess of iron that builds up from transfused red blood cells.[10,11] Therefore, iron chelation therapy is regarded as a required adjuvant
therapy since it can lower iron stores in the body and increase the long-term survival rate of patients with thalassemia major.\(^{(12)}\)

Currently, desferrioxamine, deferiprone, and deferasirox are the three main iron chelators that are accessible for clinical usage. Despite the fact that desferrioxamine has been the “gold standard” for the past three decades, clinical research has shown that parenteral desferrioxamine therapy has low compliance rates and is ineffective at reducing myocardial iron burden.\(^{(13)}\) Deferiprone has good compliance, however there have also been reports of some serious adverse effects, including arthropathy, neutropenia, and agranulocytosis. Deferasirox is a once-daily oral iron chelator that has been shown in some studies to lower liver iron levels and increase patient compliance;\(^{(15,16)}\) despite having modest adverse effects. Despite the numerous uncomfortable injections and poor compliance, the combination of parenteral desferrioxamine with oral deferiprone or deferasirox has been effectively tested in several studies.\(^{(17,18)}\)

Deferiprone or deferasirox monotherapy may not always achieve ideal management, particularly in patients with high iron loads. Only a small number of studies have examined the combined use of oral iron chelation medications in children with thalassemia.\(^{(19,20,21,22)}\) The purpose of the current study was to examine the effectiveness and safety of oral iron chelators both individually and in combination in thalassemia-affected children.

**Aims and Objectives**

**Aim**
To compare the efficacy and safety of oral iron chelators (deferiprone and deferasirox) when used singly and in combination in multi-transfused children with thalassemia.

**Objectives**

1. Assess the efficacy and safety of oral iron chelator; deferiprone alone in multi-transfused children with thalassemia.
2. Assess the efficacy and safety of oral iron chelator; deferasirox alone in multi-transfused children with thalassemia.
3. Assess the efficacy and safety of oral iron chelators; (deferiprone and deferasirox) in combination in multi-transfused children with thalassemia.
4. Compare the efficacy and safety of oral iron chelators (deferiprone and deferasirox) when used singly and in combination in multi-transfused children with thalassemia.

**MATERIALS AND METHODS**

**Type of Study:** A Prospective comparative study

**Place of Study:** Shadhan Institute of Medical Sciences, Hyderabad, Telangana, India.

**Sample Size:** The present study was conducted among 50 multi-transfused children of thalassemia receiving daily iron chelation therapy.

**Period of Study**

The study was conducted from June 2021 to June 2022

**Study Population:** Multi-transfused children suffering from thalassemia and receiving daily iron chelation therapy.

**Ethics and Consent**

Approval was taken from the Institutional Ethics Committee before commencing the study. The participants were informed regarding the purpose, procedures, risks and benefits of the study. An informed written consent was taken from the parents/guardians of these patients.

**Inclusion Criteria**

Thalassemia major patients having serum ferritin levels >1500ng/ml.

**Exclusion Criteria**

Patients who had a history of anaphylaxis due to deferiprone and/or deferasirox.

Those with serum creatinine value above the upper limit of normal.

Those who are on combination therapy with parenteral and oral iron chelating drugs.

Children with any other chronic systemic illness.

**Methodology**

The Institutional Ethical Committee gave the study their seal of approval. Participants in the study included 50 children with multiple transfusions for thalassemia who were receiving daily iron chelation therapy with either deferiprone alone (75 mg/kg/day in three divided doses), deferasirox alone (30 mg/kg/day single dose), or their combination daily (same as dose monotherapy) for 12 months. They were split into 3 groups, each of which received the following daily treatment:

**Group 1:** Deferiprone alone (75mg/kg/day in 3 divided doses)

**Group 2:** Deferasirox alone (30mg/kg/day single dose)

**Group 3:** Combination of Deferiprone (75mg/kg/day in 3 divided doses) and Deferasirox (30mg/kg/day single dose)

To maintain pre-transfusion haemoglobin levels of 9–9.5 g/dL, packed red blood cell transfusions were given to all patients every three weeks. At the beginning of the study, at 6 months, and at 12 months following the corresponding chelation therapy, serum ferritin levels were assessed. In order to rule out any acute infection, which can artificially raise serum ferritin levels, C-reactive protein (CRP) was also assessed in conjunction with all serum ferritin measurements in each patient. All patients had their 24-hour urine iron excretion assessed at the start of the research and again 12 months later.
A lower iron loading for the liver and heart was indicated by a higher value. Iron overload in the heart was assessed as None if MRI T2* valves were >20 msec, Mild (12-20 msec), Moderate (8-12 msec), and Severe 8 msec, whereas iron overload in the liver was classified as None if MRI T2* values were >6.3 msec, Mild (6.3-2.7 msec), Moderate (2.7-1.4 msec), and Severe (1.4 msec) [7, 8]

RESULTS

50 thalassemia multitransfused children were included in the current study. They were given daily iron chelation therapy for a period of 12 months with either deferiprone alone (75 mg/kg/day in 3 divided doses), deferasirox alone (30 mg/kg/day single dose), or their daily combination (30 mg/kg/day single dose). The participants were split into 3 groups, each of which received the following daily treatment: Deferiprone alone (75 mg/kg/day in 3 separate doses) is in Group 1, Deferasirox alone (30 mg/kg/day single dosage) is in Group 2, and the combination of Deferiprone and Deferasirox (75 mg/kg/day in 3 divided doses) is in Group 3.

Gender:
Age: Female: Defective group (group1) [n=18] was seen to consist of 10 (55.56%) men and 8 (44.44%) females; [n=16] was observed to consist of 9 (56.25%) males and 7 (43.75%) females; and [n=16] was observed to consist of 10 (62.5%) males and 6 (45.45%) females in the combination of Deferiprone and Deferasirox group (group3).

Table 1: Demographic Characteristics among the Three Study Groups

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (Deferiprone) [n=18]</th>
<th>Group 2 (Deferasirox) [n=16]</th>
<th>Group 3 (Combination Therapy) [n=16]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age (+SD)</td>
<td>10.72 (+2.54)</td>
<td>10.69 (+2.82)</td>
<td>10.88 (+2.19)</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>(10/8)</td>
<td>(9/7)</td>
<td>(10/6)</td>
</tr>
</tbody>
</table>

Table 2: Serum Ferritin Values at Baseline, At 6 Months and at 12 Months in Study Participants

<table>
<thead>
<tr>
<th>Serum Ferritin (Mg-SD)</th>
<th>Group 1 (Deferiprone)</th>
<th>Group 2 (Deferasirox)</th>
<th>Group 3 (Combination Therapy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>3277.01 (+560.95)</td>
<td>2977.79 (+506.94)</td>
<td>3023.79 (+572.39)</td>
</tr>
<tr>
<td>At 6 months</td>
<td>3023.79 (+572.39)</td>
<td>2755.48 (+505.39)</td>
<td>3016.41 (+656.85)</td>
</tr>
<tr>
<td>At 12 months</td>
<td>2853.90 (+536.78)</td>
<td>2521.99 (+512.67)</td>
<td>2639.62 (+634.14)</td>
</tr>
<tr>
<td>P value</td>
<td>0.09</td>
<td>0.05</td>
<td>0.007</td>
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</table>

MRI T2*Liver

Baseline: The range of values in the Deferiprone group (group1) [n=18] was 3.9–5.7 msec, with a mean (+standard deviation) value of 4.90 (+0.52). The range of values in the deferasirox group (group 2) [n=16] was 4.8–5.7, and the mean (+standard deviation) value was 5.07 (+0.19). The range of values in the Deferiprone and Deferasirox group (group3) [n=16] were 4.88 to 5.55, and the mean (+standard deviation) value was 5.17 (+0.19). Values ranging from (3.9-5.7) msec were indicative of mild hepatic iron excess in all three research groups.

Follow up: (6 months): The range of values in the Deferiprone group (group1) [n=18] was 4.01–5.81 msec, with a mean (+standard deviation) value of 5.04–0.51. The range of values in the Deferasirox group (group 2) [n=16] were 4.95 to 5.55, and the mean (+standard deviation) value was 5.24 (+0.18). The Deferiprone and Deferasirox group (group 3, n=16) had values ranging from 5.0 to 3.75, with a mean (+standard deviation)
value of 5.38 reported. As a result, the values in the follow-up MRI performed after 6 months of respective therapy were found to be greater in all three groups, which was suggestive of a decreased iron load on the liver. The readings were still found to fall under the category of mild hepatic iron overload despite the lower iron burden. It was determined that the difference between the mean baseline and follow-up values was statistically significant. (p<0.05).

| Table 3: Mean Values of MRI T2* Liver at Baseline and Follow-Up |
|---------------------------------|-----------------|-----------------|-----------------|
| MRI T2* Liver (msec) Mean (+/SD) | Group 1 (Deferiprone) | Group 2 (Deferasirox) | Group 3 (Combination Therapy) |
| Baseline                          | 4.90 (+0.52)     | 5.07 (+0.19)     | 5.17 (+0.19)     |
| Follow up                         | 5.04 (+0.51)     | 5.24 (+0.18)     | 5.38 (+0.20)     |
| P value                           | P>0.05           | P>0.05           | P<0.05           |

<table>
<thead>
<tr>
<th>MRI T2*Heart</th>
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<tbody>
<tr>
<td><strong>Baseline:</strong> Baseline values in the Deferiprone group (group 1) [n=18] ranged from 31.02 to 34.05 msec, with a mean (+standard deviation) value of 32.84 (+0.79). The range of values in the Deferasirox group (group 2) [n=16] was 30.36–34.06, and the mean (+standard deviation) value was found to be 31.93 (+0.75). The range of values for the Deferiprone and Deferasirox group (group 3 [n=16]) was 30.25–32.98, with a mean (+standard deviation) value of 29.76 (+0.63).</td>
</tr>
<tr>
<td><strong>Follow up: (6 months):</strong> The range of values in the Deferiprone group (group 1) [n=18] at follow-up was 30.02–32.65 msec, with a mean (+standard deviation) value of 32.28 (+0.96). The values in the Deferasirox group (group 2) [n=16] ranged from 28.8 to 31.1, with a mean (+standard deviation) value of 31.63 (+0.74). The range of values for the Deferiprone and Deferasirox group (group 3; n=16) were 28.99–31.19, and the mean (+standard deviation) value was found to be 30.38 (+0.66). The statistical difference between the heart’s MRI T2* mean values at baseline and follow-up was determined to be statistically significant. (p&gt;0.05) The blood ferritin levels and the MRI T2* values of the heart or liver could not be correlated.</td>
</tr>
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</table>

| Table 4: Mean Values of MRI T2* Heart at Baseline and Follow-Up: |
|---------------------------------|-----------------|-----------------|-----------------|
| MRI T2* Heart (msec) Mean (+/SD) | Group 1 (Deferiprone) | Group 2 (Deferasirox) | Group 3 (Combination Therapy) |
| Baseline                         | 32.84           | 31.93           | 29.76           |
| Follow up                        | 32.28           | 31.63           | 30.38           |
| P value                          | P>0.05          | P>0.05          | P<0.05          |

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<thead>
<tr>
<th>24-Hour Urinary Iron Excretion</th>
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<tr>
<td>After a baseline mean of 193.49 (+25.99) mol/day, it was found that the 24-hour urinary iron excretion increased to 381.34 (+29.81) mol/day in group 1, 45.09 (+9.51) mol/day to 48.26 (+9.54) mol/day in group 2, and 81.04 (+12.85) mol/day to 365.76 (+25.00) mol/day in the combination group. The 24-hour urine iron excretion increased from baseline to follow-up in groups 1 and 3 statistically significantly (p 0.05), but not in group 2 (p &gt; 0.05).</td>
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<thead>
<tr>
<th>Clinical Evaluation</th>
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<tr>
<td>Following a clinical review of all patients, it was discovered that two patients in group 3, which received a combination of deferiprone and deferasirox, developed arthropathy of the major joints five weeks after starting treatment. When deferiprone was stopped, patients' arthropathy was seen to improve. One of the patients on deferasirox experienced slight abdominal pain, which was seen to go away after 10 days of taking oral proton pump inhibitors. Throughout the course of the trial, none of the side effects of the medications under investigation justified stopping chelation therapy. Additionally, no death was noted during the research period. Renal function tests and complete blood counts were both within normal ranges. No patient had any detectable proteinuria (as determined by uristix) during the investigation.</td>
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Although there were no clinical symptoms, liver enzyme levels were found to be high (less than twice the upper limit of normal).

**DISCUSSION**

The transfusion of packed red blood cells is the cornerstone of treating many refractory anemias, whether they are acquired or congenital, including transfusion-dependent thalassemia (pRBCs). In order to help patients with transfusional iron excess lower their iron load and avoid or delay long-term complications brought on by iron deposition in tissues, iron chelation therapy is often required. The burden of excessive transfusional iron is related to the frequency, volume, and duration of blood transfusion therapy. Untreated transfusional iron excess can have a number of negative side effects, including hepatic dysfunction and failure, endocrinopathies, and cardiac dysfunction. Theoretically, iron absorption and excretion, which are balanced at around 1 mg per day, are sufficient to meet biological needs for iron, necessitating iron chelation. Iron is used by erythrocytes to make heme, while other bodily cells need it for metabolic processes. The additional iron is stored in the hepatocytes and macrophages as part of a dynamic cycle of iron use and recycling. Macrophages
perform a critical role in iron recycling by digesting senescent erythrocytes and releasing heme-derived iron into the plasma. However, the body lacks a system to get rid of additional transfusional iron, which, for example, can reach 0.3-0.6 mg/kg/day in transfusion-dependent thalassemia, assuming a transfusion rate of 2-4 units per month with 200-250 mg of iron each unit.

Beta-thalassemias have been classified into three primary categories: thalassemia major, thalassemia intermedia, and thalassemia minor. Regular transfusion therapy results in endocrine problems as well as iron overload-related side effects such as dilated cardiomyopathy, liver fibrosis, and cirrhosis (growth retardation, failure of sexual maturation, diabetes mellitus, and insufficiency of the parathyroid, thyroid, pituitary, and less frequently, adrenal glands). Thalassemia major is treated with regular RBC transfusions, iron chelation, and care for any side effects of iron overload.

Age

In the current investigation, the mean age plus standard deviation for all patients was determined to be 10.78 (±2.56) years. The Deferiprone group (group 1) [n=18] had a mean age of 10.72 (±2.54) years; the Deferasirox group (group 2) [n=16] had a mean age of 10.69 (±2.82) years; and the Deferiprone and Deferasirox group (group 3) [n=16] had a mean age of 10.88 (±2.19) years [14,15,16,17].

In a comparable study by Gomber S et al. involving 49 children, the mean (SD) age of the patients was determined to be 11.6 (6.21) years. Many of the patients (51%) in a phase 3 study of deferasirox conducted by Cappellini MD et al. were under the age of 16, and the majority of them received one year of medication. The ESCALATOR experiment by Taher A et al. included 237 participants in total, with a mean age of 13.2 years and a range of 2-42 years. There were 162 paediatric patients with an average age of 9.5 years, ranging in age from 2 to 16 years, which is similar to what was observed in the current analysis. The efficiency of DFX was investigated in 407 individuals with transfusion-dependent thalassemia by Eshghi P et al.multicentric study's. Their mean age was 11.5 7.4 years, similar to the current study, with 108 patients (26.4%) in the 17-64 age group, 206 patients (50.6%) in the 6-14 age group, and 93 patients (23%) in the 2-5 age group. In their study, Totadri S et al. evaluated the safety and efficacy of combining deferoxamine and deferasirox medicine in 36 individuals with thalassemia major (TM); the patients' mean ages ranged from 136.9 to 4-29 years. Deferasirox's effectiveness as an iron chelator was assessed in a research by Merchant R et al. on 30 patients who had received several blood transfusions. The patients were 15.7 years old on average (range 6.5 to 29 years). In the EPIC study by Cappellini MD et al. which included 1115 thalassemia patients, the mean age ranged from 2-72 years. Within the first two years of life, people with thalassemia major often experience severe anaemia and require regular red blood cell (RBC) transfusions. If a regular transfusion programme is established and maintained, with a Hb concentration of 9.5 to 10.5 g/dL as a minimum, growth and development frequently continue to be typical up to the age of 10 to 12 years. The discrepancies and similarities in the mean age group between the current study and past studies show differences in research design between the various studies. Indian study often reported a younger age group when compared to other Asian and Western studies, according to the comparison (mean age 12 years).

Gender

In the current study, it was discovered that there were 10 (55.56%) males and 8 (44.44%) females in the Deferiprone group (n=16), 9 (56.25%) males and 7 (43.75%) females in the Deferasirox group (n=16), and 10 (62.5%) males and 6 (45.4%) females in the combination group of the Deferiprone and Deferasirox (group 3). There were 27 (40.3%) men and 40 (59.7%) women participants in the Cassinerio E et al. study. In the Gomber S et al. investigation, of the 49 patients, 30 (61.22%) were men and 19 (38.78%) were women. In the phase 3 research by Cappellini MD et al. 51.9% of the patients were female.

Serum Ferritin

In this investigation, the baseline mean (+standard deviation) serum ferritin values were 3277.01 (+560.95) ng/ml in the Deferiprone group (n=18), 2977.79 (+506.94) ng/mL in the Deferasirox group (n=16), and 3405.94 (+660.54) ng/mL in the Deferiprone plus Deferasirox group (n=16). The baseline serum ferritin levels in the three groups of the current study were comparable. Other studies have produced a variety of findings: The meta-analysis by Xia S et al. overall effect of two subgroups of four trials revealed no statistically significant difference between the two iron chelation regimens in SF level (SMD 0.01, 95%CI -0.31 to 0.34, P=0.93). The standard mean difference of subgroups at 12 months was -0.16 (95% CI -0.53 to 0.20, P=0.20), indicating a non-significant difference between the intervention and control groups. This meta-analysis showed that desferrioxamine, alone or in combination with deferasipone, did not substantially vary from desferrioxamine alone in its effect on blood ferritin levels. It suggests that desferrioxamine treatment is similarly effective on the SF level as deferasipone monotherapy and combination therapy (deferasipone + desferrioxamine).

In the study by Mourad FH et al. serum ferritin levels in the 14 patients receiving deferasirox dropped from 5506 635 ng/l (mean SEM) to 4856 699 Ng/l at 6 months (P 0.001) and to 3998 604 ng/l at 12 months (P 0.001). In the 11 patients receiving daily deferasirox and DFX, serum ferritin levels
dropped from 4153 517 ng/l to 3005 393 ng/l at 6 months (P 0.001) and to 2805 327 ng/l at 12 months (P 0.01). Group A (moderate iron overload) in the study by Lal A et al. had median blood ferritin values of 1,510 ng/mL as opposed to group B (4,750 ng/mL) (severe iron overload). (p=0.002) A 24% drop in median serum ferritin was observed. Even though the liver iron concentration increased, two patients in group B's serum ferritin level increased. Farmaki K et al. examined 16 patients over the course of two years. The serum ferritin estimate of the total body iron burden decreased statistically significantly, according to the efficacy measures study's findings. In the study by Gomber S et al. the mean serum ferritin values were evaluated at the start of the study, at 6 months, and at 12 months after the start of chelation therapy. The blood ferritin levels in each of the three groups (Deferiprone, Deferasirox, Deferiprone, and Deferasirox) were comparable at baseline. All three groups experienced a decline in serum ferritin levels after chelation therapy for 6 and 12 months. Serum ferritin fell much more quickly in the combination (Deferiprone and Deferasirox) group than in groups 1 and 2 (P=0.035 and P=0.04, respectively). Other research have observed similar results

In the study by Chang HH et al. the patients' mean serum ferritin levels dropped significantly throughout the course of the trial, from 4279 ng/mL at the start of deferasirox treatment (baseline) to 1713 ng/mL after 7 years of deferasirox treatment (P 0.001). Serum ferritin levels in the 14 patients using DFX fell in the Mourad FH et al. study from 5506 635 ng/l (mean SEM) to 4856 699 Ng/l at 6 months (P 0.001) and to 3998 604 ng/l at 12 months (P 0.001). Serum ferritin levels fell from 4153 517 ng/l to 3005 393 ng/l at 6 months (P 0.001) and to 2805 327 ng/l at 12 months in the 11 patients taking daily deferiprone and DFX (P 0.001). Farreirasirox) group than in groups 1 and 2 (P=0.035 and P=0.04, respectively).

MRI T2*Heart and Liver

MRI T2* has recently emerged as a prominent benchmark for assessing cardiac iron due to its non-invasive nature compared to biopsy, and left ventricular ejection fraction is another significant metric that is associated with cardiac iron. The current investigation's baseline MRI T2*Liver results revealed a little excess of hepatic iron in all three research groups. The levels were higher in all three groups in the follow-up MRI performed after six months of corresponding medication, which was suggestive of a decreased iron load on the liver. Despite the reduced iron burden, the findings were still regarded as mild hepatic iron overload.

The following sentences illustrate how the results of the current study agree with those of other studies: Desferrioxamine alone was shown to be less effective than deferiprone alone in the meta-analysis by Xia S et al. of seven randomised controlled trials for improving left ventricular ejection fraction and MRI T2*. It demonstrated that deferiprone mono- and combination therapy is more successful in improving cardiac function than desferrioxamine therapy. In the study by Cassinerio E et al. 67 patients on various chelation regimens received T2* cardiovascular magnetic resonance at baseline (t(0)), after 6–14 months (t1), and after 32–7 months (t2). The chelation therapy divided the patients into four groups: group A received deferasirox, group B received deferoxamine, group C received combination therapy, deferoxamine + deferiprone, and group D received deferiprone (deferiprone alone). Myocardial T2* at t (0) varied between 10 and 20 ms in 22 individuals and between 20 ms in 37 patients, with an average of 10 ms occurring in 8 cases. Progressive alterations in T2* were observed between t (1) and t. (2). Three patients from group B (3/15, 20%), ten from group A (10/36, 27.8%), and three from group C (3/12, 25%) all saw a change from abnormal to normal T2* levels.

After three years of deferasirox treatment, 41 patients in the Chang HH et al. study completed a cardiac T2* examination, and after seven years of deferasirox treatment, the mean cardiac T2* value dramatically increased from 30.6 16.6 to 45.9 22.6 ms (P 0.001). Patients showed liver MRI T2* values that indicated a modest hepatic iron overload, according to the findings of Gomber S et al. The data from the follow-up MRI still indicated minor hepatic iron excess after six months of the recommended treatment. At baseline and follow-up, heart MRI T2* individual and mean values were surprisingly similar. The mean 24-hour urinary iron excretion value in the combination group increased after 12 months compared to a mean baseline value. The slight difference between the liver and cardiac follow-up MRI values could be explained by the brief time interval between them. MRI T2* offers a rapid, non-invasive, and repeatable approach for detecting hepatic and cardiac iron overload, which blood ferritin is unable to do. Tannen MA et al. found improvements in myocardial T2* (5.7 +/- 0.98 ms to 7.9 +/- 2.47 ms; p = 0.010) and LV ejection fraction (51.2 +/- 10.9% to 65.6 +/- 6.7%; p 0.001). In the Tannen MA et al.
Dosage
Deferiprone was administered in the current experiment at a dose of 75 mg/kg/day divided into three doses, deferasirox at a dose of 30 mg/kg/day, and their daily combination was administered at the same dose as monotherapy. Similar dosages were employed in the study by Gomber et al. Desferrioxamine and deferasirox had respective beginning median daily dosages of 18 and 25 mg/kg and 21 and 23 mg/kg in groups A and B of the experiment by Lal A et al. At six months, the median dose of deferasirox was 21 mg/kg (18-22 mg/kg) in group A and 27 mg/kg (19-30 mg/kg) in group B. In contrast, the median dose of desferrioxamine was 18 mg/kg (14-19 mg/kg) in group A and 35 mg/kg (14-42 mg/kg) in group B. In the experiment by Tanner MA et al, desferrioxamine and deferiprone were prescribed at 38 +/- 10.2 mg/kg for 5.3 days each week and 73.9 +/- 4.0 mg/kg per day, respectively. All patients received deferiprone and deferoxamine for a full year.

In other comparable studies on patients with comparable iron loads, deferasirox (30 mg/Kg) and desferrioxamine (average daily dose 51 mg/Kg) both decreased liver iron concentration by 8.9 mg/g and 6.4 mg/g, respectively. Starting from the ESCALATOR study by Taher A et al., the mean doses of deferiprone and deferasirox were used at doses of 53.92 ±22.2 and 3.36 ±29.36 mg/kg/day, respectively. In combination therapy, various doses of deferiprone and deferasirox were given based on the patient's clinical state and laboratory findings. In the study by Totadri S et al, the mean doses of deferiprone and deferasirox were $8.4.52.5 (61-100 mg/kg/day) and $33.45.2 (20-40 mg/kg/day), respectively.

Adverse Effect
Five weeks after starting treatment with the combination of deferiprone and deferasirox, two patients in the current study developed arthropathy of the main joints. The arthropathy was shown to get better after quitting deferiprone. Minor stomach pain was reported by two (12.5%) of the deferasirox individuals; these symptoms were observed to disappear after using oral proton pump inhibitors for 10 days. No time during the investigation was chelation therapy stopped due to a side effect of the study medications (100 percent compliance). There were no recorded deaths during the study period. Complete blood counts and renal function tests were both within normal limits. None of the subjects displayed any detectable proteinuria during the course of the trial. Despite the absence of any clinical signs, higher liver enzyme levels were discovered (less than twice the upper limit of normal).

CONCLUSION
Deferiprone and deferasirox together were found to be more effective at reducing iron overload than either drug alone. Serum ferritin, hepatic and cardiac MRI*T2 scans, and urine iron excretion were evaluated in 50 thalassemia-afflicted children who had received multiple transfusions. However, in children with thalassemia who had received multiple transfusions, deferiprone and deferasirox were also efficient and secure when given alone. For the use of combination therapy as a routine method of treatment in multi-transfused children with beta thalassemia major, future studies with high sample sizes and long-term follow-up are required.

REFERENCES
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