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Research Article

Chelation in Thalassemia: Improved Status Over a Decade

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A B S T R A C T

Optimal chelation of iron overload is a major determinant of both the lifespan and health-related quality of life in patients with transfusion-dependent thalassemia (TDT). With the introduction of Deferasirox (DFX) in India in 2008, it was hoped that once-daily oral dosing, superior efficacy, favorable safety profile, and the availability of generics would lead to improved compliance and better control of iron overload. This was favored in our earlier study of 36 months duration (2011–2013) published in 2013. In this brief communication, we present the trend of iron overload status in our cohort over a decade-long duration. An analysis of 85 TDT patients on deferasirox alone or on combination chelation was conducted. The mean age of the cohort was 15 years. The mean/ median serum ferritin values observed in 2011 and 2021 were 3042/ 2271 ng/mL and 1065/ 969 ng/mL, respectively showing a significant decline in iron overload. This was also reflected in T2* MRI values, which showed evidence of moderate to severe iron overload in the liver/ heart in 7%/ 2.3% of patients, respectively. No severe chelation-related toxicity was noted. Motivating patients for continued compliance as this cohort ages is the biggest challenge.

Keywords: Chelation, Deferasirox, Iron Overload, Thalassemia

Iron overload (IOL) is an inevitable consequence of regular blood transfusions in patients with transfusion-dependent thalassemia (TDT) and is a major determinant of both the life span and health-related quality of life (HRQOL) in these patients.[1] IOL affects the liver, heart and the endocrine system with cardiac and liver complications continuing to be the leading cause of morbidity and mortality in patients with TDT.[2,3] Iron chelation therapy (ICT) is, therefore, an essential component in the management of thalassemia patients and stringent control of IOL is associated with improved outcomes. Compliance with the ICT regimen is imperative for optimal management and the consequent improved patient survival.[4,5] Life-long compliance with chelation can, however, be challenging. In this regard, we find that the impact of deferasirox (DFX) has been transformative in the management and outcomes of patients with TDT.

Chelation was first introduced in the late 1960s. Deferoxamine (DFO), a parenteral agent, was first approved for clinical use in 1968, and it was the mainstay for iron chelation for over four decades. Deferiperone (DFP) was licensed in 1994 but received approval for medical use in the United States only in 2011. It has an unpredictable toxicity profile and is still not licensed in many countries. DFX, a tridentate chelator with excellent oral bioavailability was licensed in 2005 and became available in 2008 in India. Once daily dosing with excellent tolerability and safety profile has made it the first-line chelator in thalassemia.[6] The efficacy and safety of the more recently introduced film-coated tablet (FCT) has also been robustly established.[7]

We published the first three years of experience with DFX from our center in 2011.[8] The mean age of the cohort was 9.62 years. The mean and median values of serum ferritin at baseline and at 36 months were 4354, 3555, 3042, and 2271 ng/mL, respectively (Figure 1). Herein, we present a decade-on experience with DFX and the status of iron overload in our cohort.

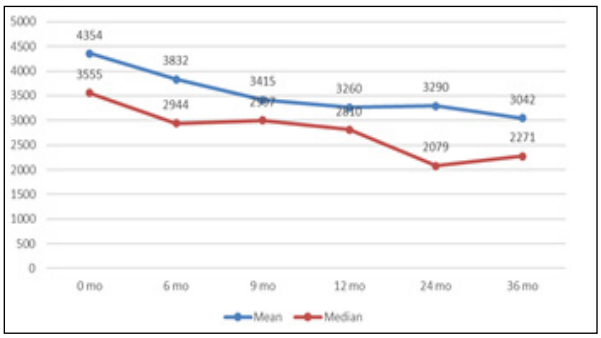

Figure 1.Trend of Serum Ferritin Mean and Median Values (in ng/mL) Seen in the Previous Study

All patients registered at our center are on regular follow-ups and are monitored as per the unit protocol with serial clinical and biochemical data documented in their records. Serum ferritin levels are measured at 3–6 month intervals, and for patients more than 10 years, T2* MRI scans are done annually wherever feasible. The patients are routinely monitored for growth, organ dysfunction, endocrinopathies, and adverse effects of ICT.

Complete data was available for a total of 85 patients with TDT. Of these, 75 were on DFX alone and 10 on combination chelation therapy (10/85). The mean/ median serum ferritin for each consecutive year was collated. Evidence of iron overload on T2* imaging and the presence of organ dysfunction was noted.

The mean age of the cohort was 15 years. The mean and median serum ferritin levels of this cohort at the time of analysis were 1065 and 969 ng/mL, respectively. Figure 2 depicts the trends over the last 10 years. T2* MRI scans were available for 42 of the 45 children older than 10 years.

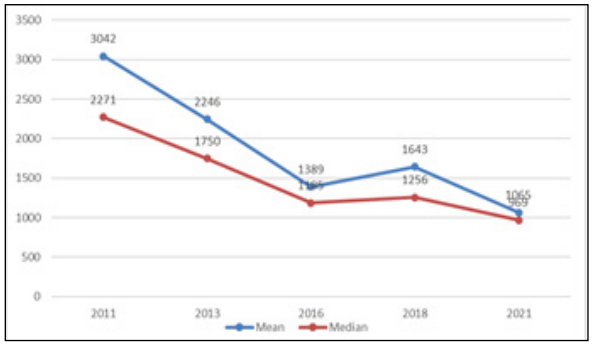

Figure 2.Trend of Serum Ferritin Mean and Median Values (in ng/mL) in the Current Study

Evidence of moderate to severe iron overload in the liver and heart were seen in 7.0% and 2.3% of patients, respectively. Evidence of endocrinopathy, defined as hypothyroidism, hypoparathyroidism, diabetes, and hypogonadism, was seen in 10 patients (22%). Endocrinopathy predated this decade in 7 of these patients. No severe chelation-related toxicity was noted in any patient.

Our data clearly documents the transformation in our cohort over the last decade. Although compliance was not objectively evaluated in the current study, the previous study[8] confirmed excellent compliance (> 95%) for DFX. Whilst other factors such as increased awareness and improved access may have contributed, the most significant impact is likely attributable to the introduction of deferasirox. It has superior efficacy due to its high affinity and specificity to iron,[9] as well as the ease of administration and lack of major toxicity, contributing to patient preference and compliance.

DFX in optimal doses has proven to be effective in lowering myocardial and liver iron load across various studies.[10–13] A retrospective study found a remarkable improvement in the prevalence of endocrinopathy, in addition to a significant improvement in bone mineral density in patients who were on DFX as compared to those on either DFO or DFP, or DFO + DFP.[14] The safety profile of DFX has been acceptable as evaluated in various studies.[15] The FCT formulation has shown further improved adherence with consequently reduced IOL.[7] Cumulatively, these factors may contribute to lowering the morbidity burden and improving the HRQOL in these patients.

To conclude, DFX appears to be transformational for this patient cohort as it is safe, effective, and acceptable to the patients. The biggest challenge for us as clinicians is to ensure ongoing compliance and maintain these results as the patient cohort ages.

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Conflict of Interest: None

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