Effects of Oral Chelation Drug Deferasirox in Iron Overload Conditions in Children

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Abstract:
Objective: To know the efficacy and adverse events of oral chelation drug deferasirox in multitransfused patients with iron overload i.e beta thalassemia & dyserythropoietic anemia’s who are attending Rajiv Gandhi institute of medical sciences Srikakulam for transfusions and management

Material & methods: Prospective study conducted in dept. of pediatrics at RIMS Srikakulam from August 2014 to December 2016, 25 children are iron overload with multiple transfusions i.e. either beta-thalassemia major or dyserythropoietic anemia’s were taken for this study. All these were started oral iron chelation therapy i.e., Deferasirox.

Results: In this study out of 25 children of iron overload 20 cases are thalassemia. In these children 18 are on follow up, out of them 1 male & 6 females children are below the age of 9 years. Remaining other are above 10 yrs. 5 children presented with dyserythropoietic anemia. The adverse clinical effects are not that much for stoppage of the drug and resolved spontaneously with symptomatic support.

Conclusion: The single daily dose oral chelation therapy deferasirox is effective in beta-thalassemia and dyserythropoietic anemia with minimal adverse effects. Deferasirox appears as an effective oral iron chelator for long term use.

Keywords: adverse effects, deferasirox, iron overload, children.

I. Introduction
Iron overload is a serious potentially fatal condition that results from multiple blood transfusions required lifelong in haemolytic anaemia such as beta thalassemia & dyserythropoietic anemia’s. Normal body iron stores in humans is 3-4 g, however an excess of iron 20g or more can lead to organ damage. They require life long chelation therapy to prevent complications associated with chronic iron overload including liver and cardiac disease retardation of growth and sexual development during adolescence.

Oral chelation drug deferasirox have high iron binding capacity and selectively it is recommended as once daily dose in children more than 2 years of age. It decreases the serum ferritin levels in dose dependent manner and is relatively safe drug but treatment requires individualization with full dose adjustment and proper monitoring. The recommended starting daily dose is 20 mg/kg dose adjustments should be made in increments of 5 or 10mg/kg. If the serum ferritin consistently falls below 500mcg/l temporary interruption of therapy should be considered. Deferasirox should be taken once daily on an empty stomach at least 30 mins prior to food preferably at the same time each day. Deferasirox was generally well tolerated with clinically manageable safety profile with regular patient monitoring and the most common adverse events were usually mild and or transient in nature and resolved spontaneously. Iron overload is an undeliverable and unavoidable effect of ongoing transfusion therapy regardless of the underlying cause of anemia. Iron chelation therapy is recommended for patients requiring frequent blood transfusion, including those with beta thalassemia & dyserythropoietic anemia or myelodysplastic syndrome.

Deferasirox maintains constant 24 hr levels with in the plasma, thus it exerts a sustained reduction in toxic plasma labile iron. Deferasirox is capable of chelating myocardial iron as demonstrated by in vivo studies and preliminary trial reports. Long term studies have reported deferasirox to have a clinically manageable tolerability profile with regular patient monitoring.

II. Material & methods
Prospective study conducted in dept. of pediatrics at RIMS Srikakulam from August 2014 to December 2016, 25 children of iron overload with multiple transfusions i.e. either thalassemia or dyserythropoietic anemia’s were taken for this study. All these were started oral iron chelation therapy i.e., Deferasirox.
Information regarding clinical and lab parameters including growth parameters, pain abdomen, rashes, jaundice, serum ferritin, creatinine and serum transaminase levels were recorded on proforma (for a period of 2 years).
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III. Results

In this study out of 25 children of iron overload 20 cases are thalassemia. In these children 18 are in follow up, out of them 1 male & 6 females children are below the age of 9 years. Remaining other are above 10 yrs. 5 children presented dyserythropoietic anemia. The frequency of clinical adverse effects are abdominal pain and nausea was in 70% rashes in 2 children jaundice in 6 children.

Who are receiving blood transfusion with iron overload are included in the study to know the efficacy in other than thalassemia their outcome was normal without any adverse effects clinically and shows decline in serum ferritin levels. In thalassemia children those who are taking the single dose daily regimen regularly shows the drastic decrease in the serum ferritin levels. Those children with irregular in take of medication, The results were not satisfactory. We evaluated the serum ferritin before starting the chelation and again assess the serum ferritin after 1 year. The adverse clinical effects are not that much for stoppage of the drug and resolved spontaneously with symptomatic support. Serum ferritin reduced with once oral dose of deferasirox on empty stomach @20mg/kg. After 1 year there significant reduction in the serum ferritin levels.

IV. Discussion

Deferasirox is an effective oral chelator for reducing iron overload in multiple transferred beta thalassemia patient and other hemolytic anaemias such as dyserythropoietic anemia. (1,2) Iron overload is associated with high morbidity and mortality due to tissue hemosiderosis. (3,4) These patients require continuous iron chelation with compliance and safety. In present study we started deferasirox as oral monotherapy due to its long half life and effective in reducing the tissue iron of heart and liver.

In the present study oral dose of deferasirox with low dose significantly reduced serum ferritin levels. In earlier studies it was shown that prolong treatment for more than twelve to thirty six months with high doses upto 40mg/kg decreases serum ferritin level significantly (5,6) In present study 80% had ferritin levels 1500 ng/ml to 2500ng/ml and 20% had above 5000ng/ml. After 12 months of optimal therapy the ferritin comedown to below 1000ng/ml in 80% group whereas in 20% group the serum ferritin levels comedown to around 2500ng/ml, probably due to higher serum ferritin levels at the beginning of chelation or inadequate compliance of the drug. It is also reported that changes in iron burden due to high transfusion requirement and variable gastrointestinal absorption of drug may contribute to variable patient response and require dose adjustments (7). Various studies have documented improved clearance with doses between 30-40 mg/kg/day without any adverse effects. In our study deferasirox was given in maximum dose of 20 mg/kg/day even with high serum ferritin levels. Deferasirox is although well tolerated with high safety profile but most common adverse effects reported are gastrointestinal disturbances, increase liver enzymes, maculopapular skin rash and elevation of serum creatinine levels. In the present study most frequently observed side effects of deferasirox were gastrointestinal symptoms including abdominal pain and nausea 70%, rash 6%, jaundice was found in 24% respectively. Other recent studies has also shown comparable results (8,9).

V. Conclusion

The single daily dose oral chelation therapy Deferasirox is effective in beta-thalassemia and dyserythropoietic anemia with minimal adverse effects. Deferasirox appears as an effective oral iron chelator for longterm use.

References