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Raihan Sajid
Aga Khan University

Farooq Ghani
Aga Khan University

Salman Adil
Aga Khan University

Mohammad Khurshid
Aga Khan University

Original Article

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Raihan Sajid, Farooq Ghani, Salman Adil, Mohammad Khurshid
Department of Pathology and Microbiology, The Aga Khan University, Stadium Road, Karachi, Pakistan.

Abstract

Objective: To determine the efficacy and adverse effects of deferiprone in patients with Thalassemia Major.

Methods: A prospective case series study was conducted at the Fatimid Foundation Blood Bank and Haematological Diseases center Lahore. A total of 87 patients entered into the study between September 2005 and November 2006. Deferiprone was given at subsidized rates at a dose of 75/mg/day for seven days. Physical examination and initial Laboratory investigations were done in all patients at the start of the study. Physical and laboratory data were filled on a questionnaire and analyzed using SPSS version10.0.

Results: Eighty seven patients with mean age of 10.0 ± 4.33 years (range 4-27 years) were included in the study. Mean follow up was 8 ± 3.94 months (range 2-12 months). The mean Ferritin at the start of study was 4656 ± 2052.5 ug/L (range 1200-14630 ug/L) and at the end of study period was 4139 ± 1710.4 ug /L (range 749-8961) ($p < 0.001$). Adverse events were joint pains in 10 % patients, gastrointestinal symptoms in 11% and no adverse events in 79 % patients. There was no evidence of agranulocytosis in any patient.

Conclusion: Deferiprone was well tolerated, had few adverse effects and was effective in lowering the patient's serum ferritin level (JPMA 59:388; 2009).

Introduction

Thalassemia syndromes are a heterogeneous group of disorders characterized by a lack or decreased synthesis of either alpha or beta chains of haemoglobin. Beta thalassemia is the most common haemoglobinopathy in Pakistan.[1]

The management of Thalassemia Major in most of the patients in our country is with blood transfusions and iron chelation therapy. However most of these patients develop progressive iron overload that is responsible for tissue damage and eventually death.[2]

Traditionally Desferrioxamine was administered to the patients for iron chelation as a subcutaneous infusion given over 8-12 hours, 5-7 days a week with a pump. This was a cumbersome mode of administration with pain at site and low compliance of the patients.

Deferiprone (Kelfer, Ferriprox) is an orally active hydroxypyridineone first used in humans in 1987.[3] It is a tridentate chelator i.e. three molecules surround one iron ion; carries no net charge and can easily penetrate membranes. Due to oral mode of administration the compliance is better.[4]

A study was therefore conducted to determine the efficacy, safety and adverse effects of oral iron chelator Deferiprone in patients with Thalassemia major.

Patients and Methods

This study was conducted at Fatimid foundation blood bank and haematological diseases center Lahore from September 2005 till November 2006.

A total of 87 patients were included in the study. From the diagnosed cases of Thalassemia major with more than twenty blood transfusions, only those were included who had serum Ferritin levels more than 1000 ng/ml. The baseline physical and clinical examination findings along with laboratory data were recorded on a questionnaire.

They were followed up for a minimum of two months. Deferiprone was given seven days a week at a dose of 75mg/kg/ day in two to three divided doses.

The patients were followed up for a period of one year. Complete blood count was performed every two weeks and on the day of the transfusion in all patients for the duration of the study period. Adverse events were recorded on the patient Performa and also recorded in the patients files. The primary outcome variable was serum Ferritin level at the start and at the end of study. A p-value of <0.05 was considered statistically significant.

Patients who had poor compliance and follow up were excluded from the study.

Serum Ferritin level was carried out by microparticle enzyme linked immunoassay on kits manufactured by Abbott Laboratories USA on Axsym automated analyzer.

ECG, Echocardiography and Magnetic Resonance Imaging could not be performed due to economic constraints.

All the data was entered and analyzed using SPSS (statistical package for social sciences) version 10.0. Descriptive statistics were expressed in the form of range, mean ± one standard deviation (SD). Student t test was applied to compare means of Ferritin at the start and end of study period.

Results

A total of 87 patients were included in the study. Mean age of the patients was 10.0 ± 4.33 years (range 4-24 years). Gender distribution showed that 58 (66.6 %) were male and 29 (33.3 %) were female. Mean follow up was 8 ±3.94 months (range 2-12 months).

The mean Ferritin at the start of study was 4656 ± 2052.5 ng/ml (range 1200-14630 ng/ml) and the mean Ferritin at the end of study period was 4139 ± 1710.4 ng/ml (range 749-8961 ng/ml) $p < 0.001$.

The most common adverse reactions observed during the study comprised of nausea, vomiting and abdominal pain. Nine (11%) of the patients reported these symptoms; however no interruption of therapy or decrease in dosage was necessitated because of these symptoms. None of the patients discontinued therapy because of gastrointestinal adverse effects. Agranulocytosis was not seen in any of the patients.

Bone pain and arthropathy was the most common complaint encountered in 8 (10%) patients, necessitating decrease in dosage or stoppage of therapy. The bone pain and swelling subsided in seven out of eight patients subsequent to stoppage of therapy with Deferiprone and these patients were then continued on Desferrixoamine. Patients not experiencing any adverse effect were 68 (79%). No patient died during the course of the study and no patient developed the clinical findings of congestive heart failure.

Discussion

To our knowledge, this is the largest study to date from Pakistan detailing Deferiprone administration and monitoring of adverse reactions in patients with Thalassemia major.

The results are indicative of good efficacy of Deferiprone in lowering patients' serum Ferritin level and low frequency of adverse reactions.

Ayyub et al[2] demonstrated good efficacy of the oral iron chelator over a 3.8 year study period with significant reduction in Ferritin, good compliance and acceptable safety profile. Gastrointestinal disturbances and Arthropathy were significant adverse effects with oral iron chelator and are comparable to our study.

Another study from India reported an increase in ferritin levels in the oral Deferiprone group but a decrease in Ferritin levels in the combination of Deferiprone and Deferrioxamine in patients with Thalassemia major.[4] Arthropathy was a significant side effect with Deferiprone in this study too.

In a meta-analytic review published in 1999,[5] the authors had confirmed the efficacy of Deferiprone which is comparable to the results of the presented study.

The adverse reactions profile was also similar to other studies.[2,3,6] The two most important observations were non-occurance of agranulocytosis in any of the patients who were administered this drug. Bone pain and arthropathy was found to be the most side effect which led to dose reduction and/or stoppage of therapy in these patients.

Non-compliance was also found to be a major factor while administering the drug. Although most of the patients were receiving the drug at subsidized rates, still about 19 % were unable to take the drug on a regular basis because of economic reasons. These were excluded from the final analysis.

Gastrointestinal symptoms were reported to be the most common symptoms associated with Deferiprone therapy by Cohen et al.[7] They found joint problems in 15% of the patients over a period of four years.

A latest literature review suggests that Deferiprone is not an alternative to Desferrioxamine and should be used in conjunction with Desferrioxamine for more effective iron chelation therapy.[8]

Conclusion

In this study Deferiprone was well tolerated, had few adverse effects and was effective in lowering the serum Ferritin level in patients with Thallasaemia Major.

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