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Original Research Article

Assessment of serum ferritin levels in transfusion dependent thalassemic children on oral deferiprone in a tertiary care centre

Suman Chirla[1], Lalita Wadhwa[1]*, Puneet Wadhwa[2]

[1]Department of Pediatrics, NRI Institute of Medical Sciences, Visakhapatnam, Andhra Pradesh, India
[2]Department of Pediatrics and Neonatology, Prime Hospital, Airport Road, Dubai, UAE

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***Correspondence:**
Dr. Lalita Wadhwa,
E-mail: lalita.simh@gmail.com

ABSTRACT

Background: Thalassemic patients require regular blood transfusions to maintain haemoglobin level around between 10gm/dl-15gm/dl, which would result in transfusional iron overload. The treatment of iron overload is carried out by using parenteral desferrioxamine (DFX) therapy or recently introduced oral Deferiprone (DFP,L1,Ferriprox,KELFER,CP20) an oral iron chelator, Oral deferiprone, DFP (3-hydroxy-1,2-dimethylpyridin-4-one) is a synthetic analogue of mimosine, an iron chelator isolated from the legume Mimosa paduca. Our study was undertaken to asses ferritin concentration in transfusion dependent thalassemic children on Deferiprone, attending thalassemia clinic in Anil Neerukonda hospital, Sanghivalasa, Visakhapatnam.
Methods: The present study was a hospital based prospective study, 50 transfusion dependent thalassemic children on Deferiprone, attending thalassemia clinic in Anil Neerukonda hospital, Sanghivalasa, Visakhapatnam attached to NRI Medical College, Visakhapatnam were enrolled during the study period October 2017 and September 2018.
Results: In our study authors found an increase in Serum ferritin concentration from 3067.99±1520.13 to 4281.10 ±1760.42 ng/ml at the end of 12 months, which was quite significant.
Conclusion: Authors concluded that oral Deferiprone is not an effective iron chelation agent and is associated with complications like GI symptoms, joint pains in significant number of children. So, search for an alternative iron chelator or combined chelation therapies which are safe and cost effective should be continued.

Keywords: Oral Deferiprone, Serum ferritin levels, Thalassaemia

INTRODUCTION

The inherited haemoglobin disorders are the most common single gene defect in man. The prevalence of hemoglobinopathies is on the rise worldwide. This is of special importance in developing countries, where it increases the burden of health care delivery systems.[1]

The thalassemia syndromes are a heterogeneous group of Mendelian disorder characterized by lack or decreased synthesis of either α or β globin chains of haemoglobin. It results in ineffective erythropoises as well as lysis of mature red cells in spleen.[2]

The Thalassemias are the most common genetic disorder in a worldwide basis. 3% of world population carries genes of β thalassaemia.[3]

The β-thalassemias are widespread throughout the Mediterranean region, Africa, the Middle East, the Indian subcontinent and Burma, Southeast Asia including southern China, the Malay Peninsula, and Indonesia.

Estimates of gene frequencies range from 3 to 10 percent in some areas.[4]

In 1964 wolman was the first to suggest that chronic blood transfusion may prevent many of the problems of the disease. 1974, were able to initiate clinical trials with desferrioxamine, an iron chelator. In 1980 introduced the concept of neocyte transfusion.[4]

There is evidence that the high frequency of β-thalassemia throughout the tropics reflects an advantage of heterozygotes against Plasmodium falciparum malaria.[5]

In India over 20 million people have thalassemia gene. The prevalence of the gene varies between 3 to18% in north and 1 to 3% in south with certain communities like sindhis, kutchis, lohanas, bhanushalis, Punjabis, mahars, agris, gouds, etc. showing a high prevalence.[6]

In 1982 Dr. E Donald Thomas performed the first bone marrow transplantation on a thalassaemic patient. The first bone marrow transplantation in India was successfully done by Dr. M. Chandy at Christian Medical College, Vellore.[6]

It has been estimated that over 6000-8000 children, who are homozygotes of ß- thalassemia are born in India every year and unfortunately most of these children die either undiagnosed because of inadequate facilities, poor management and/or financial constraints.[7]

Majority' of people still consider thalassemia as a curse rather than an inherited disorder.[8]

M Mukherji reported the first case of ß -thalassaemia from India in 1938 from Calcutta. 1935, Sheldon described the severe pathologic sequelae associated with iron overload.[9]

Deferiprone an oral iron chelator was discovered in 1981.

METHODS

Source of data

Our study was a hospital based prospective study of 50 transfusion dependent thalassemic children on oral Deferiprone, attending thalassemia clinic in Anil Neerukonda hospital, Sanghivalasa, Visakhapatnam attached to NRI Medical College, Visakhapatnam were enrolled, during the study period October 2017 and September 2018.

Inclusion criteria

Children diagnosed to have Thalassemia major based on HB electrophoresis, receiving regular transfusion and who were advised to take oral Deferiprone are included in the study.

Exclusion criteria

- Children who discontinued oral Deferiprone during the study period.
- Children who were not taking regular blood transfusion.
- Children who were having severe systemic illness.

Method of collection of data

Serum ferritin level was estimated in transfusion dependent thalassaemic children who had received more than 15 transfusions and those who had serum ferritin levels of more than 1500ng/ml were advised oral chelation therapy with Deferiprone.

Parents were explained about the indication for starting Deferiprone and to report common adverse effects. Informed written consent from parents was obtained for starting the therapy and blood sampling.

Blood samples were collected before starting Deferiprone for estimation of serum ferritin, by drawing 2ml of blood from cubital vein, into a sterile vaccume tubes and stored in fridge till it was transported to the laboratory. Serum ferritin was analyzed using MAGIWEL KIT by solid phase enzyme-linked immunosorbant assay (ELISA) - A quantitative assay.

At each visit pre transfusion haemoglobin was analyzed by Sahlis method and complete blood count was analyzed using peripheral smear. At each visit child was thoroughly examined for adverse reactions.

Statistical methods

Student t test has been used to find the significance of mean difference of Serum Ferritin concentration between baseline and First year of observation.

Statistical software

The Statistical software namely SPSS 11.0 and Systat 8.0 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

RESULTS

Age and sex distribution

In Table 1, there was male preponderance. Majority of children i.e. 37(74%) were males. Among 50 transfusion dependent thalassemic children majority i.e. 21(42%) were less than 6 years. Mean age was 7±3.05.

Mean Pre transfusion Hemoglobin percentage

In Table 2, All children had mean pretransfusion haemoglobin less than 8 gm% during the study period. Average Pretransfusion haemoglobin during study period

ranged from 5.5 to 8 gm %. Majority of the children had Pre- transfusion haemoglobin in the range of 7-8 gm%.

Table 1: Age and sex distribution.

Age in years	Female (%)	Male (%)	Total (%)
<6	7 (14%)	14 (28%)	21(42%)
6.1-7.0	2 (4%)	11 (22%)	13 (26%)
>7.0	4 (8%)	12 (24%)	16 (32%)
Total	13 (26%)	37 (74%)	50 (100.0)

Table 2: Mean Pre transfusion hemoglobin percentage.

Mean Pre transfusion Hb%	Number	%
5-6	11	22%
6-7	15	30%
7-8	24	48%

Serum Ferritin Concentration (ng/ml) before and after Deferiprone

In Table 3, The mean serum ferritin levels before starting oral deferiprone and after one year of starting oral deferiprone were compared. An increase in Serum ferritin concentration from 3067.99±1520.13 to 4281.10±1760.42 at the end of first year was observed, which was statically significant.

Table 3: Serum Ferritin Concentration (ng/ml) before and after deferiprone.

Study period	Range	Mean±SD
Before Deferiprone	1044.95-6861.00	3067.99±1520.13
After Deferiprone	1296.00-9465.90	4281.10± 1760.42
Significance (Baseline-First year)	Student t=4.68, p<0.001	

Complications

In Table 4, The complications observed during the study were Joint pains and GI symptoms like diarrohoea and increased gastric motility.

Table 4: Complications.

Complication	Number patients (n=50)	Percentage
Joint pain	14	28%
GI symptoms	4	8%

Joint pain was affecting 14 (28%) children in which knee joint was the main joint involved in most of the children. GI symptoms, like, increased gastric motility and diarrhoea was seen in 4 (8%) children.

None of these symptoms required discontinuation of the therapy.

DISCUSSION

The present study is a hospital (tertiary care centre) based prospective study of serum ferritin levels in transfusion dependent thalassemic children on oral Deferiprone.

The aim of our study is to assess the efficacy of oral Deferiprone in reduction of iron overload in thalassemic children.

In the study conducted serum ferritin levels were compared at 6th month and 12th month respectively after starting oral Deferiprone. In the present study, serum ferritin levels were analyzed after 12months of starting oral Deferiprone.

Descriptive statistics variables studied in our study were comparable to other studies.[10-12]

The age group of patients in the present study were between 4 to 14 years, as compared to 4-12 years in study conducted and 0-18 years in the study conducted.

Table 5: Age distribution.

Studies	Age range(years)
V.P Choudhry et al[11]	4-12
Anice George. et al[12]	0-18
Our study	4-14

Table 6: Mean pre transfusion haemoglobin level.

Mean Pre transfusion Hb%	Number	%
5-6	11	22%
6-7	15	30%
7-8	24	48%

Mean Pre transfusion haemoglobin level in our study was 6.93gm%. This is well below the recommended level of 9.5-10 gm% for adequate growth of thalassemic children. All the children in our study had mean Pre transfusion haemoglobin of <8gm% compared to 44.2 percent of children in study conducted indicating inadequate transfusion.

Normal growth of β-thalassemia children during the first 10 years of life depends upon the maintenance of haemoglobin levels above 8.5 g/dl. During this period of the child's life hypoxia may be the main factor retarding growth, and the maintenance of haemoglobin levels between 10-15g/dl together with adequate iron chelation therapy makes the β-thalassemia patients indistinguishable from their non-thalassemic peers, indicating need to ensure regular blood transfusion.

Table 7: Effect of Deferiprone on Serum ferritin (ng/ml) levels.

Studies	Before Deferiprone (Mean±SD)	After Deferiprone (Mean±SD)
Sunil Gomber et al[10]	2672.90±886.44	3422.65±1581.01
V.P Choudhry[11]	7214±4426	3785±2876 (p= significant)
Our study	3067.99±1520.13	4281.10±1760.42

Effect of Deferiprone on Serum ferritin (ng/ml) levels

In Table 7, in our study serum ferritin levels increased to a mean of 4281.10±1760.42 from 3067.99±1520.13 which was significant (p<0.001) indicating oral Deferiprone alone is not effective in reduction of iron overload. This finding correlates with the study of who observed increase in serum ferritin levels after oral Deferiprone alone was given. In the same study, when oral Deferiprone was given in combination with Desferrioxamine, no increase in serum ferritin levels was observed (From 3347±1526.46 to 3376.57±1222.41) after therapy. The observation of our study do not support the finding, who observed significant reduction in serum ferritin values after oral Deferiprone.

These findings cast doubt over the ability of the oral Deferiprone alone to reduce the iron burden in children with thalassemia, at least in short period. In her study Concluded oral Deferiprone does not adequately control body iron burden in patients with thalassemia and may worsen hepatic fibrosis.

Table 8: Complications.

Studies	% of Joint pains	% of GI symptoms
V.P Choudhry[11]	41%	-
Agarwal et al[14]	38.5%	3.5%
Present study	28%	10%

Complications

In Table 8, 28% of children in the present study complained joint pain involving the knee joint, which correlated well where it was seen in 38.5% of children. It was less compared to 41% of children in the study of V.P Choudhry.[11] GI symptoms were seen in 10% of children in our study correlating to 3.5% of children in study of Agarwal et al and GI symptoms were not observed in study of V.P Choudhry.

Other complications mentioned in literature14 like Neutropenia, Tachycardia and Renal failure were not observed in our study.

CONCLUSION

Thalassaemia syndromes are important cause of morbidity and mortality in children. All children had mean Pre transfusion haemoglobin of less than 8gm%; mean being 6.93gm%, indicating inadequate blood transfusion. Oral Deferiprone alone was not found to be effective in reducing the iron overload. Joint pains and GI symptoms were observed in significant number of children when on oral Deferiprone.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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