International Journal of Contemporary Pediatrics
Chandra SP et al. Int J Contemp Pediatr. 2022 Aug;9(8):713-718
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20221852

Original Research Article

A study of growth pattern and serum ferritin levels in transfusion-dependent thalassemic children on oral iron chelating agents (deferasirox) in King George Hospital, Visakhapatnam

Satish Chandra P., Sneha C.*

Department of Pediatrics, Andhra Medical College, Visakhapatnam, Andhra Pradesh, India

Received: 23 May 2022
Revised: 13 July 2022
Accepted: 14 July 2022

***Correspondence:**
Dr. Sneha C.,
E-mail: snehaammu2K9@gmail.com

ABSTRACT

Background: In India majority of thalassemia children are under transfused and receive insufficient chelation therapy. Only few researches on growth parameters from this region are available making it difficult to comprehend the loopholes of the disease and its treatment.
Methods: It was a descriptive, prospective study of 50 cases of transfusion-dependent thalassemia children on oral iron chelator deferasirox observed during one year (November 2019-December 2021) at King George hospital, Visakhapatnam.
Results: Most commonly affected were more than 6 years of age. 98% of the children had mean pre-transfusion hemoglobin of less than 8 g/dl with the temporal association of growth retardation. Weight (64%) was more affected than height (36%). Only 46% showed effective iron chelation after using deferasirox.
Conclusions: 98% had low pre-transfusion hemoglobin and deferasirox alone was not an effective oral iron chelator resulting in growth retardation in the majority of children. Thalassemia that requires blood transfusions Children are at a high risk of developing morbidities such as growth retardation as a result of insufficient therapy. Many of them were the result of consanguineous marriage, suggesting the disease's genetic basis. 98 percent of children had low pretransfusion hemoglobin of 7 gm%, with a mean of 6.5 gm%, showing that blood transfusions were insufficient. There were no side effects associated with the use of deferasirox and it alone proved ineffective in lowering serum iron excess, highlighting the need to combine it with novel modalities to improve its effectiveness. Growth retardation is a common ailment and low hemoglobin levels increased with age, showing hypoxia as a cause.

Keywords: Thalassemia, An oral iron chelator, Dferasirox, Serum ferritin, Growth monitoring, Retardation

INTRODUCTION

The most common genetic disease on the planet is thalassemia.[2] A wide range of genetic disorders cause impaired hemoglobin chain synthesis in this syndrome. If the body is unable to manufacture sufficient amounts of these chains, an imbalance of hemoglobin chains will result in poor erythropoiesis and persistent hemolysis. This type of anemia develops in childhood and lasts the rest of a person's life. If the chain shortage affects the, chain of hemoglobin called thalassemia; however, reduced synthesis of haemhemoglobinin.[3] Homozygous-thalassemia major (TM) is a hereditary autosomal recessive disease that affects around 23000 newborns globally each year, with the majority of cases occurring in low- and middle-income countries.[4] Chelating therapy,

in addition to blood transfusions, has helped thalassemic patients live longer.[5]

Patients and governments are both willing to bear a significant financial burden. To provide appropriate therapies for these patients, these costs must be completely addressed.[6] Regular transfusions promote hyperabsorption and iron deposition because iron ligand proteins build in numerous tissues as ferritin or hemosiderin.[7] An excess of iron in the tissues is one of the primary reasons for death in thalassemic patients.[5] Iron excess can lead to hepatic dysfunction and endocrine problems. Growth impairment is one of the most common TM consequences. Chronic hypoxia causes anemia and growth hormone deficit (GHD) in thalassemia patients, resulting in growth retardation (GR), changes in appearance, bone deformities, and failure of the immune system (due to the liver's poor generation of somatomedin and the rapid destruction of RBC.[2,8]

Objective

Patients with thalassemia need regular blood transfusions to keep their hemoglobin levels around 10 g/dl, which causes iron excess that affects growth. The well-known parenteral desferrioxamine (DFX) therapy or the newly released deferiprone (L1), an oral iron chelator, are used to treat iron overload. Admission to DFX is excruciatingly unpleasant, time-consuming, and costly. The efficiency of deferiprone has received mixed reviews. In India, the majority of thalassemic children are under-transfused and receive insufficient chelation therapy.[1] With this in mind, the goal of this study was to measure ferritin concentration in transfusion-dependent thalassemic children receiving deferasirox at the King George Hospital in Visakhapatnam's thalassemia clinic. To determine the growth pattern. Compared with different et al available till now and assessed the next requirement.

METHODS

Children receiving frequently packed cell transfusions recorded in the Pediatric hematology OP at King George Hospital in Visakhapatnam were taken for hospital based prospective study. Approximately 50 transfusion-dependent thalassemic children on deferasirox who attended the thalassemia clinic at King George Hospital, Visakhapatnam, which was affiliated with Andhra Medical College, were enrolled in the current study between November 2019 and December 2021.

Inclusion criteria

The trial included children aged 1 to 18 years who had been diagnosed with thalassemia major based on hemoglobin electrophoresis, were getting regular transfusions and were prescribed deferasirox. Parents who were willing to grant consent to their children were included.

Exclusion criteria

Those children who did not receive blood transfusions on a regular basis; children who were suffering from a serious systemic ailment; children who stopped using deferasirox during the research period; and children under the age of one year and over the age of eighteen were excluded.

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. Chi square and fisher exact test has been used to find association of age and mean pre transfusion hemoglobin with weight for age and height for age as per ICMR standard. The odds ratio had been used to find relationship of age and mean pre transfusion of hemoglobin with ICMR of weight for age and height for age.

Statistical software

The software SPSS 11 and systat8 were used for analysis of data and Microsoft word and excel for graphs and tables.

Ethical approval

Ethical approval was obtained from ethical committee of the institution, Andhra medical college, Visakhapatnam. Written consent from parents of each child taken.

Data collection

Data was gathered using the following method: Transfusion-dependent thalassaemic children who had received more than 10 transfusions and had serum ferritin levels greater than 1500 ng/ml had their serum ferritin levels measured, and they were prescribed deferasirox oral chelation treatment. The reason for starting deferasirox was explained to parents, as well as how to report common adverse effects. Parents signed an informed written consent form before the initiation. Blood samples for serum ferritin measurement were taken before starting deferasirox by taking 2 ml of blood from the cubital vein, depositing it in sterile vacuum tubes, and storing it in the refrigerator until it was transferred to the laboratory. The serum ferritin levels were measured using a solid-phase enzyme-linked immunosorbent assay (ELISA), which is a quantitative technique. At each visit, pre-transfusion hemoglobin was assessed using a peripheral smear. During each appointment, the child was thoroughly examined to rule out any bad reactions.

Anthropometric measurements were performed at the start of the therapy and again one year later. In centimeters, height weight in kilogrammes. Anomalies such as pallor, edema, icterus, cyanosis and abnormal facial features. A thorough examination from head to toe was done. The investigations listed below were carried out. Perform a complete blood count.

RFT LFT

Electrolytes in the blood: calcium, sodium, magnesium, and potassium. Blood typing, grouping, and HB Coomb's test. RDW reticulocyte count. Levels of sr. ferritin, LDH, and TIBC. Thyroid profile and electrophoresis and peripheral smear.

RESULTS

Age distribution of the study

Among 50 transfusions dependent thalassemic children, 58% were more than 6 years of age. Mean age was 7 years.

Consanguinity

Out of 50 children, half of them (50%) were products of non-consanguineous marriage while 32% were born of third degree consanguineous.

Mean pretransfusion HB percentage

98% children in this study had hemoglobin less than 8 gm% during study period. Mean pretransfusion hemoglobin was 6.5g%. 82% had hemoglobin less than 7 gm% while majority of them (46%) had hemoglobin range of 6-7 gm%.

Mean pretransfusion hemoglobin and serum ferritin

The mean pre transfusion hemoglobin was 6.5 gm% with minimum being 5 gm% and maximum being 8.7 gm%. the mean serum ferritin before deferasirox was 2056 ng/ml and after treatment being 2806 ng/ml.

Table 1: Age distribution of the study.

Age (years)	Frequency	Percent
≤6	21	42.0
>6	29	58.0
Total	50	100.0

Table 2: Consanguinity.

Consanguinity	Frequency	Percent
2	9	18.0
3	16	32.0
Non-consanguinous	25	50.0
Total	50	100.0

Table 3: Mean pretransfusion HB percentage.

Mean	Frequency	Percent
5.0-6.0	18	36.0
6.1-7.0	23	46.0
7.1-8.0	8	16.0
8.1-9.0	1	2.0
Total	50	100.0

Table 4: Mean pretransfusion hemoglobin and serum ferritin.

Mean	MTH (G%)	No. of Tx	Serum ferritin (ng/ml) BD	Serum ferritin (ng/ml) AD
Mean	6.546	25.44	2056.72	2806.92
Minimum	5.0	7	1045	1248
Maximum	8.7	38	4980	5212

Table 5: Anthropometry study (NCHS and WHO standards).

Study	Weight (kg)	W/A	Height (cm)	H/A
Mean	17.94	5.82	109.96	8.74
Minimum	8	3	68	3
Maximum	29	25	134	25

Table 6: Serum ferritin before and after deferasirox.

Parameters	HB group (gm%)	N	Mean	SD
Weight	≤6	18	19.33	3.678
	>6	32	17.16	5.100
W/A	≤6	18	3.00	0.001

Continued.

Parameters	HB group (gm%)	N	Mean	SD
	>6	32	7.41	4.669
Height	≤6	18	115.11	9.609
	>6	32	107.06	14.465
H/A	≤6	18	3.22	0.647
	>6	32	11.84	9.347

Table 7: Association of mean pretransfusion HB with anthropometry.

Association (ng/dl)	Mean	N	SD
Serum ferritin BD	2056.72	50	858.066
Serum ferritin AD	2806.92	50	1026.818

Anthropometry study (NCHS and who standards)

The mean weight in our study was 17.94 kgs and mean height 109.96 cm.

Serum ferritin before and after deferasirox

An increase in serum ferritin levels from 2056 ng/ml to 2806 ng/ml was noticed which was statistically significant.

Association of mean pretransfusion HB with anthropometry

The present study indicated that growth parameters were affected when the pretransfusion hemoglobin was less than 7 gm% showing that recommended maintenance of hemoglobin 9-10 gm% was necessary for proper growth Weight was more affected than height with low pretransfusion hemoglobin in our study. In our study, low pretransfusion hemoglobin was associated with undernutrition in 64% and short stature in 36% of children. There was a positive correlation between hemoglobin level and growth in our study.

DISCUSSION

The present study was a prospective hospital study of growth patterns and serum ferritin levels in transfusion dependant thalassemic children on the oral chelating agent (deferasirox).

Age distribution

Among 50 transfusions dependent thalassemic children 58% were more than 6 years when compared to 67.3% in Bushra et al study.[9] the present study included children between 1 to12 years, with mean age being 7 years, comparable with other studies.

Consanguinity

History of consanguinity was present in 50% of our studies. among that 32% belonged to third-degree and 18% to second-degree consanguinity when compared with 70% in Reddy et al study which was done in 1975. This implies the awareness among people about the hazards of consanguineous marriage.[10]

Anthropometric observation in different age group (NCHS and WHO standard)

In our study, 58% of the children below 50th centile to 67.3% in Bushra study.[9] 58% of children less than 50th centile for height for age were above 6 years of age when compared with 60.6% in Bushra study for height age were above 6 years of age when compared.[9]

Mean serum ferritin levels (ng/ml) before treatment

The mean serum ferritin levels before the onset of treatment in our study was 2431 ng/ml which correlated with Shalitin s et al which had 2698 ng/ml as its mean indicating the iron overload in transfusion dependant thalassemic children. Chandra et al had 5909 ng/ml and Rathaur et al had 1560.9 ng/ml as their mean serum ferritin levels.[11]

High ferritin levels before treatment

24% of children in our study had high serum ferritin levels which are lower when compared to other studies. Bushra's study had 61.6% and Rathaur et al had 45.71% of the study population with high ferritin levels before the commencement of treatment.[9,11]

Serum ferritin levels after treatment

Our study had 46% of children with reduced serum ferritin levels which correlated well with other studies like Panigrahi et al with 45% and Cappellini et al.[13,14] With 45% indicating the effect of the drug on iron overload in transfusion-dependent thalassemic children

Mean pretransfusion hemoglobin

The mean pre-transfusion hemoglobin in our study was 6.5g% which is less than the recommended level of 9-10g% for adequate growth in thalassemic children.

George et al had 44.2% of children with less than 8 gm% whereas our study had 98% of children with low mean

transfusion hemoglobin treatment modalities such as blood transfusions and deferasirox was free of cost many had difficulties attending hospital regularly due to lack of transport from far off places, literacy financial instability.[17] In Gomber et al study there was no significant raise when a combination of deferiprone and deferasirox was given whereas Chandra et al showed that deferasirox was effective in reducing iron load in these children.[15,16] Hameed et al study showed that the efficacy of deferasirox can be improved when combined with antioxidants like selenium, vitamin E and zinc.

Association of mean pretransfusion hemoglobin with anthropometry

Low pretransfusion hemoglobin was associated undernutrition in 64% and short stature in 36% compared to 82% and 91% in Bushra et al.[9]

Limitations

The study was done in limited number of subjects who were selected by convenience sampling. Lack of motivation was prevalent in parents. cardiac MRI and liver biopsy could not be done due to financial constraints

CONCLUSION

Thalassemia that requires blood transfusions Children are at a high risk of developing morbidities such as growth retardation as a result of insufficient blood transfusion therapy. Many of them were the result of consanguineous marriage, suggesting the disease's genetic basis. 98 percent of children had a low pretransfusion haemoglobin of 7 gm%, with a mean of 6.5 gm%, showing that blood transfusions were insufficient. There were no side effects associated with the use of deferasirox. Deferasirox alone proved ineffective in lowering serum iron excess, highlighting the need to combine it with novel modalities to improve its effectiveness as Iron overload and insufficient blood transfusions are the leading causes of morbidity in transfusion-dependent thalassemic children. Major morbidities such as growth retardation and low haemoglobin levels increased with age, showing hypoxia as a cause of growth retardation. Importance of treatment options such as blood transfusions and oral chelating medications screening test, marriage counselling, and prenatal counseling is not deep rooted in the affected families.

Because the growth of transfusion-dependent thalassemic children in their first decade is contingent on maintaining an acceptable haemoglobin level, negligence about regular blood transfusions and adherence to chelation therapy Iron overload and anthropometry on a regular basis at a nearby health care facility is still lacking in India.

ACKNOWLEDGEMENTS

This work was supported by the department of pathology and the pediatric department, King George hospital, Visakhapatnam.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Verma IC, Choudhry VP, Jain PK. Prevention of thalassemia. A necessity in India. Indian J of Pediatrics. 1992;59:649-54.
2. Badfar G, Nasirkandy PM, Shohani M. Prevalence of short stature, underweight and delayed puberty in Iranian patients with thalassemia major: a systematic review and meta-analysis. Iranian J Pediatric Hematology Oncology. 2017;7(4):245-59.
3. Bajwa H, Basit H. Thalassemia; 2019.
4. De Sanctis V, Soliman AT, Canatan D. An ICET-A survey on Hypoparathyroidism in Patients with Thalassaemia Major and Intermedia: A preliminary report. Acta Bio Medica: Atenei Parmensis. 2017;88(4):435.
5. Shah S, Farooq N, Basharat A, Shah M, Mukhtiar S, Farhad S. Frequency of iron overload complications in beta thalassemia major patients. J Postgraduate Medical Institute (Peshawar-Pakistan). 2019;33(1).
6. Esmaeilzadeh F, Azarkeivan A, Emamgholipour S. Economic burden of thalassemia major in Iran, 2015. J Res Health Sci. 2016;16(3):111.
7. Safarinejad MR. Evaluation of semen quality, endocrine profile and hypothalamus-pituitary-testis axis in male patients with homozygousβ-thalassemia major. J Urology. 2008;179(6):2327-32.
8. GS C, MK S. Pattern of Growth Retardation and Sexual Maturation in Children having Beta Thalassaemia. J Nepal Paediatric Society. 2016;36(1).
9. Nasreen B. A prospective study on growth pattern and effect of serum ferritin, hemoglobin levels on physical growth in thalassemic children. Int J Paediatrics Geriatrics. 2020;3(2):01-06.
10. Reddi YR, Rao SV, Niranjan A, Laxman S. Thalassemias in Andhra Pradesh: a clinical haematologic study. Indian Pediatr. 1975;12(2):195-6.
11. Rathaur VK, Imran A, Pathania M. Growth pattern in thalassemic children and their correlation with serum ferritin. J Family Med Prim Care. 2020;9(2):1166-9.
12. Pemde HK, Chandra J, Gupta D, Singh V, Sharma R, Dutta AK. Physical growth in children with transfusion-dependent thalassaemia. Dove Press J Pediatr Health Med Therapeut. 2011:2;13-9.
13. Panigrahi M, Swain TR, Jena RK, Panigrahi A, Debta N. Effectiveness of Deferasirox in Pediatric

Thalassemia Patients: Experience from a Tertiary Care Hospital of Odisha. Indian J Pharmacol. 2020;52(3):172-8.
14. Cappellini MD, Bejaoui M, Agaoglu L, Canatan D, Capra M, Cohen A, et al. Iron chelation with deferasirox in adult and pediatric patients with thalassemia major: efficacy and safety during 5 years' follow-up. Blood. 2011;118(4):884-93.
15. Gomber S. Comparative efficacy of desferrioxamine, deferiprone and in combination on iron chelation in thalassemic children. J Indian Pediatrics. 2006;43:503-5.
16. Chandra J, Chaudhary H, Pemde H, Singh V, Dutta AK. Safety and efficacy of deferasirox in multitransfused Indian children with β-thalassaemiamajor. Annals Tropical Paediatrics. 2011;31(1):47-51.
17. Anice G, Bhaduri A, Sen S, Choudhry VP. Physicalgrowth parameters in thalassemic children. Indian J Pediatrics. 1997;64:861-71.

Cite this article as: Chandra SP, Sneha C. A study of growth pattern and serum ferritin levels in transfusion-dependent thalassemic children on oral iron chelating agents (deferasirox) in King George Hospital, Visakhapatnam. Int J Contemp Pediatr 2022;9:713-8.