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STUDY OF RENAL PROFILE IN PATIENTS WITH THALASSEMIA MAJOR ON IRON CHELATION THERAPY

Paediatrics

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ABSTRACT

Aim- To study the renal function tests,i.e blood urea and serum creatinine in patients of beta thalassemia on oral iron chelators.

KEYWORDS

INTRODUCTION

The β thalassemias are a heterogeneneous group of inherited disorders of haemoglobin (Hb) synthesis characterized by a reduction(β+) or absence of (β0) synthesis of the β globin chains of Hb, resulting in an imbalanced chain synthesis.[1]

As per WHO estimates 4-5% of the world's population are carriers of hemoglobinopathies. World wide 15 million people have clinically apparent thalassemic disorders. There are about 240 million carriers of β thalassemia world wide and in India alone ,the number is approximately 30 million with a mean prevalence of 3.3. The carrier rate for β thalassemia major gene varies from 1 to 3 percentage in Southern India to 3to 15 percentage in Northern India.[2]

Anaemias results when rate of destruction exceeds the capacity of marrow to produce RBCs . During haemolysis RBC survival is shortened, RBC count falls, erythropoietin is increased and marrow activity results in increased RBC production reflected by increased percentage of reticulocytes in blood (Nelson 20th edition).

Management of thalassemia is by repeated blood transfusions and iron chelators as and when indicated.

Common clinical features are pallor, fatigue, poor appetite, lethargy due to anaemia. Children with severe disease who are not frequently transfused have "thalassaemic facies" which include frontal bossing, depressed nasal bridge, maxillary hyperplasia. The other features are growth failure, hepatosplenomegaly, and in some cases mild to moderate jaundice due to liver dysfunction.[4] There is requirement of regular blood transfusion and iron chelating agents to remove excess iron which results from repeated blood tansfusions . However definitive treatment is bone morrow transplantation . It has been seen that children who are well transfused have normal growth and development. The most dreaded complication of thalassemia is iron overload and results in high mortality and morbidity lack of physiological mechanism for excreting excess iron. Due to repeated blood transfusions, the patient have excess iron. Iron is very toxic to tissues, normally iron is bound to carrier protein transferrin . Due to repeated blood transfusions, the patients have excess iron that saturates transferrin and "free iron" level increases in blood and accumulates in different tissues mainly heart, exocrine gland, liver and leads to congestive heart failure, cardiac arrhythmias . Exocrine dysfunction like hypothyroidism, hypoparathyroidism, hypogonadotropic gonadism, growth deficiency , diabetes mellitus can occur.[5]

Iron chelators are used to decreased iron overload, these bind to "free iron" and prevents its accumulation in various tissues. [7]

Iron chelators should be started when :

a) 10 or more transfusions have been given.
b) The serum ferritin is >1000 microgram/L
c) Chelation should not be started before 2 years of age.
d) The child has received regular blood transfusions for more than 1 year.

The commonly used iron chelators are Deferoxamine, Deferiprone, Deferasirox.

Deferasirox (Exjade®, Novarti, Switzerland, ICL670) is an oral chelator with high iron-binding potency and selectivity (Nick *et al.*). It is chelated to the iron from the reticulo-endothelial (RE) cells as well as various parenchymal organs and the chelated iron is cleared by the liver and excreted through the bile (Hershko *et al.*). The most prevalent complications that arise from thalassemia and deferasirox are transient increase of serum creatinine (Eshghi *et al.*).[5]

Several investigations about renal involvement in adult patients with β-thalassemia major have been reported but there is a dearth of paediatric data (Aldudak *et al.* ; Koliakos *et al.*) and the main underlying cause of tubular dysfunction in these patients remains unknown (Sumboonnanonda *et al.*). However, renal damage can be attributed to chronic anaemia and iron overload (Aldudak *et al.*).

This prospective study is aimed to investigate renal involvement in paediatric patients with transfusion dependent β-thalassemia major and in those taking iron chelator (deferasirox), using conventional and early markers of glomerular dysfunctions.

Present work will determine the frequency and the prevalence of the thalassemia of the study group, the geographical distribution, clinical findings and renal function test parameters. The data will be introduced into electronic system and will be statistically analyzed.

MATERIALAND METHODS

A prospective observational study will be carried out at pediatrics Out Patient Department (O. P. D.) and in patent department, RIMS, Ranchi.

The study will include 110 cases of children between the age of 1-18 years with beta thalassemia .

All the cases and control registered in the study will be interrogated for detail history, clinically examined thoroughly and investigated. It covers following parameters.

Ethical consideration:

The synopsis of the study along with the informed consent form (in English & Hindi) was submitted to the Institutional Ethics Committee of Rajendra Institute of Medical Sciences (RIMS) ,Ranchi for approval. Study was done after approval was obtained in writing.

Consent :

Written informed consent was taken from each participant . illiterate patients gave their fingerprint (left thumb impression) instead of signature on consent form .

a) Anthropometric measures

I) Height
ii) Weight
iv) Upper segment:lower segment ratio

b) Detailed medical history

I) Family genetic studies
ii) Pedigree analysis

iii) Total amount of transfused blood and hemoglobin level at the time of transfusion

c) Investigations

i) Complete blood count (CBC)
ii) High performannce liquid chromatography (HPLC)
iii) Blood urea estimation
iv) Serum creatinine estimation

PLACE OF STUDY

DEPARTMENT OF PEDIATRICS
RIMS, RANCHI

INCLUSION CRITERIA

1) Children of age 1-18 years (both boys and girls) attending Pediatric O. P. D and admitted cases and diagnosed as beta thalassaemia major by H.P.L.C(high performance liquid chromatography)
2) Children who are transfusion dependent and are on oral chelator therapy.

EXCLUSION CRITERIA

1) Children with known case of chronic medical problem (renal disease, anemia (other than thalassemia), endocrine disorder).
2) Children taking drugs which cause renal dysfunction.
3) Unwilling for study

Duration of Study:

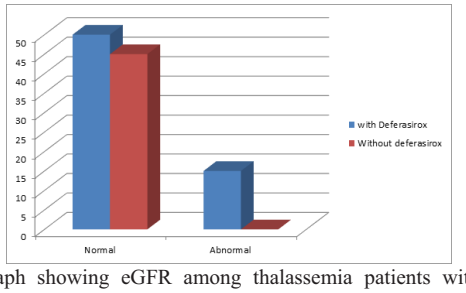
May, 2017 to June, 2018

RESULTS-

eGFR MEASUREMENT IN PATIENTS OF THALASSEMIA MAJOR WITH AND WITHOUT DEFERASIROX

Table no-10

eGFR	WITH DEFERASIROX	WITHOUT DEFERASIROX
Normal	40	45
Abnormal	15	0
Total	65	45



10 Graph showing eGFR among thalassemia patients with and without Deferasirox.

SUMMARY AND CONCLUSION

- Mean age of children in present study was 6 year.Majority of children were male (54.9%).Majority of children belonged to hindu family(75%). .

eGFR of thalassemic patients on iron chelator (65 children) was found abnormal in 15(23.07%).Iron chelating agent like deferasirox have significant role in reduction of serum ferritin levels and improved growth of thalassemic children on blood transfusion. our results showed that in patients with no pre-existing renal dysfunction or disease,iron chelator(deferasirox) appears to produce a mild effect on renal haemodynamics, which was reversible after drug interruption over the short and long term, with no progressive worsening of renal function.

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