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Serum Ferritin Levels in Patients of Beta-Thalassaemia Major, Receiving Repeated Blood Transfusion

KEYWORDS: β-Thalassaemia, Serum Ferritin

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ABSTRACT *Beta thalassaemia is a genetically inherited blood disorder that is oftenmanaged with chronic blood transfusions, typically every 15 to 25days depending upon the severity of anaemia.Regular blood transfusions, ineffective erythropoiesis and increased gastrointestinal iron absorption lead to iron overload in the body. The management of the iron overload is very important in these patients, requires the administration of iron chelatorsfrequently and evaluation of serum ferritin levels at regular intervals for the management assessment. In the present study serum ferritin levels of the patients with betathalassaemia major were measured. Majority of the patients revealed very high ferritin levels, i,e1969.69 ng/ml (SD 1195.706) ng/mland controls was only 83.75 (SD 25.968) ng/ml.These levels reflects inadequate chelation and vulnerability to develop iron overload related complications. Role of serum ferritin levels in thalassaemia is essential, because improvement in transfusion therapy in Beta thalassemia major patients, transfusion haemosiderosis has now become the major cause late morbidity and mortality.*

Introduction :

Beta-thalassaemia syndromes are the most common inherited haemoglobinopathies caused by a genetic deficiency in the beta-globin chain synthesis in adult haemoglobin(HbA_1) molecule[1]. Worldwide, there are 240 million carriers of beta-thalassemia in which 1,00,000 children born with thalassemia major are reported. In India 10,000 children are born with beta-thalassemia major with mean prevalence of 3.3%[2].

Beta-thalassaemia is managed with chronic blood transfusions, typically every 15 to 25 days depending upon the severity of anaemia. The progressive iron overload in thlalssaemia major patients is the consequence of ineffective erythropoiesis, increased gastrointestinal absorption of iron, lack of physiologic mechanism for excreting excess iron, and above all multiple blood transfusions[3]. Iron overload is the life limiting complication commonly found in thalassaemics. A unit of red blood cells transfused contains approximately 250 mg of iron, while the body cannot excrete more than 1 mg of iron per day[4].

The iron which exceeds the iron binding capacity of transferrin appears in the plasma as non-transferrin bound iron, which is highly toxic to tissues. The accumulation of iron results in progressive dysfunction of the heart, liver and endocrine glands. Effective management of iron overload requires frequent evaluation of the body iron stores[5]. Therefore, a need for quantitative, non-invasive methods for measuring body iron that are safe, accurate and readily available. The concentration of the plasma/ serum ferritin is positively correlated with the size of the total body iron stores in the absence of inflammation. Normal ferritin concentrations vary by age and sex[6]. Serum ferritin estimation is have a great clinical importance for measurement of body iron storage. It is non-invasive although easy to perform frequently, has too great a variability. Still, at present, no other simple test is a better predictor[7]. Direct assessment of hepatic iron concentration by liver biopsy is the best predictor of the total body iron, but the procedure is invasive, risky and difficult to perform repeatedly.

Iron-storage compounds in the body include haemoglobin, haemosiderin, myoglobin and the cytochromes. In most tissues, ferrrtin is a major iron-storage protein. Human ferritin has a molecular weight of approximately 450,000 daltons, and consists of a protein shell around an iron core; each molecule of ferritin may contain as many as 4,000 iron atoms. Under physiological conditions, this may represent 25% of the total iron found in the body. In addition, ferritin can be found in several isomers[8].

As a result of this improved survival due to transfusion therapy, the problems of transfusional hemosiderosis became conspicuous. Transfusional hemosiderosis is the major cause of late morbidity and mortality in patients with thalassemia major[9]. Thus iron chelation therapy has a very important role in the management of a thasassemia major child. Since the late 1960's deferoxamine mesylate has been the "gold standard" iron chelator, improving the quality of life and prolonging the life of transfusion dependent thalassemics[10]. Deferasirox is a new tridentate oral iron chelator approved by FDA for children above 2 years and is now available in India since April 2008. The benefit to risk profile of deferasirox is favourable. The cost effectiveness was favorable in costing models[11]. This promising new oral drug will decrease the burden of subcutaneous or intravenous infusion, which might improve compliance and hence the life expectation .

Materials and Methods

This was a prospective study carried out in the depart-

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ment of Biochemistry and the Department of Paediatrics, JSS Medical College and Hospital, Mysore. from September 2012 to April 2014. Known cases of Beta thalassaemia major that had been transfused at least ten units of blood, irrespective of their age and sex were included in this study. Patients who had been transfused less than 10 units of blood as part of their management were excluded. Blood samples collected from beta-thalasssemia major patients just before blood transfusion . Most patients were admitted either due to severe anaemia or they were receiving regular transfusion. The age group of the study were 2 to 14 years and the sample size was 32, and equal number of healthy controls of same age and sex were selected.

Clinical Account: The clinical details of patients were recorded with consent form according to the ethical comity guidelines. Performa taking into details of awareness about estimation of serum ferritin levels and ill effects of iron overload, age, sex, consanguinity, diagnosed age, number of blood transfusions received, last transfusion received, The record of Iron chelation therapy , i.e., days of week in which patients received chelation, route of administration type of drug etc.

Serum Ferritin Estimation: About 3 ml of patient's blood sample was collected in plain sample tube by a clean venepuncture. The blood was allowed to clot. Serum was separated and stored at –20 ^{0}C. Serum Ferritin levels were estimated by Chemiluminescence Immunoassay (CLIA) method using fully automated Advia Centur SIEMENS Hormonal analyzer. Samples were processed with healthy controls.

Results :

In the present work, a total 32 beta-thalassaemia cases were studied, in that 18 (56.25%) are male and remaining 14 (43.75%) cases are female. The results revealed in the patients, mean serum ferritin level was found 1969.69 ng/ml (SD 1195.706) ng/ml. Only eight patients (25%) had serum ferritin level less than 1000 ng/ml. Fourteen patients (43.8%) had serum ferritin level between 1000 to 2500ng/ml, while ten patients (31.2%) had values more than 2500 ng/ml. The mean serum ferritin level in selected controls mean was found to be 83.75 (SD 25.968) ng/ml.

Discussion :

Beta thalassaemia major is managed only by blood transfusion. But chronic blood transfusions increases frequency of complications due to iron overload. The ultimate cure of the disease is stem cell transplantation, but it is a very risky procedure and the availability of the fully matched donor is not always possible.

Iron overload is an unavoidable complication suffered by thalassemia major patients as a consequence of excessive number of blood transfusions. It is so common that it has been referred to a "second disease" during treatment of first[12]. Serum Ferritin is an easy and in-expensive indirect measurement of iron burden, however, a single measure may not provide reliable indication of iron levels. The new non-invasive method of measuring iron storage in the body such as MRI has greater sensitivity, but they have limited use in developing countries such as India because of cost and complexity. As excessive iron can lead to organ complications, chelation therapy is employed to lower its levels. Borgna-Pignatti et al reported that a lower Ferritin concentration predicted longer survival, and reduced risk of various complications[13]. Many studies concluded that cirrhosis of liver is associated with increase in serum Ferritin level[14].

When not provided with desferrioxamine therapy the patients suffer grave consequences of iron over load, the spectrum of which lies from generalized weakness, weight loss, joint pain, abdominal pain to critical illness such as cirrhosis, hepatoma, diabetes, cardiomyopathy, arthritis, arthropathy, hypopituitarism with hypogonadism and death[15]. Chronic iron over load in liver increases chances of cirrhosis and hepatic carcinoma, hepatoma. The death occurs mostly due to liver disease, hepatocellular carcinoma, diabetes or cardiomyopathy[16].

The serum ferritin level in our study was 1969.69 ng/ml (SD 1195.706) ng/ml in 31.2 % of the cases, which is markedly higher (>2500 ng/ml) when compared to normal serum ferritin levels in children in which the mean serum Ferritin level is considered to be in range of 12-122 ng/ml[17]. The values in our study are lower compared with similar regional and international studies.

Conclusion :

Looking after a thalassemics patient according to standard management is tedious and very expensive. All efforts should be concentrated on prevention of disease. It can be done by Public awareness, Population screening for carriers, Genetic counselling and prenatal diagnosis. More research is necessary on gene therapy and bone marrow transplantation for permanent solution to the thalasemic burden. It is concluded that, there is a dire need to rationalize the chelation therapy, as at present no chelation, inadequate chelation, improper methods of chelators administration, non availability of infusion pumps. Inappropriate evaluation of iron overload and high levels of serum ferritin gives an overall bleak view.

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