DESFERRIOXAMINE INDUCED URINARY IRON EXCRETION IN THALASSEMIA

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ABSTRACT

Twenty one children of beta thalassemia major aged between 2 and 14 years of age on regular blood transfusion were given subcutaneous desferrioxamine. Their serum ferritin, 24 hours baseline urinary iron excretion and subcutaneous desferrioxamine induced urinary iron excretion were measured. The result showed a close correlation between serum ferritin and amount of blood transfusions received by the patient. There was good correlation between serum ferritin and desferrioxamine induced urinary iron excretion. A negative iron balance could be achieved in 15 out of 21 children with one dose of desferrioxamine therapy.

Key words: *Desferrioxamine, Thalassemia.*

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Majority of children with beta thalassemia major without regular blood transfusions die from anemia in early childhood. With regular blood transfusions, however, survival is prolonged into adolescence or early adult life(1). The major problem in the management and the chief factor limiting the life in such patients, then becomes that of iron overload, the excess iron being derived mainly from transfused red blood cells. Due to iron overload they develop cardiac, hepatic and endocrinal damage(2-4). Heart failure and arryhythmias due to iron overload are the usual causes of deaths in second or third decades of life in these children.

Improved survival and reversal of some of the pathological changes of iron overload has been reported in patients with hemochromatosis who are treated with regular venesection. This approach is not feasible in iron loading anemias and therefore the use of iron chelating agents of various effectiveness has been explored(6). Out of these, desferrioxamine has been proved to be most effective and least toxic chelating agent. Slow subcutaneous infusions of desferrioxamine has been found quite satisfactory in these cases(7,8). This finding has fostered hopes that this therapy could cause substantial iron excretion, thus preventing death from iron overload and prolonging life.

Although there are large number of thalassemic patients in our country, till date no study has been carried out to assess the amount of iron excretion after subcutaneous desferrioxamine therapy. The pre-sent study was, therefore, undertaken after subcutaneous desferrioxamine in such children.

Material and Methods

Twenty one cooperative regularly transfused children with beta thalassemia major were included in the study. They were between two and fourteen years of age. None of these children had received iron chelation therapy previously or had splenectomy done. Seven patients were less than six years and rest fourteen were more than six years of age.

Serum ferritin levels were measured on venous samples by ELISA method. Subcutaneous desferrioxamine (in a dose of 50 mg/kg) infusion was given slowly over 12 hours using microinfusion pump M.P. 20. The rate of infusion was adjusted by manipulating the rotary microswitches. Urine was collected in iron free bags for the next 24 hours starting with the start of infusion. Urine iron was measured using the method described by Torrance and Bothwell(9).

For each patient daily iron loading from number of blood transfusions received over the previous 6 months was calculated (1 unit of blood contains 200 mg of iron)(10). Iron balance was evaluated by subtracting 24 hours urinary iron excretion from daily iron loading.

For the analysis of data student 't' test and correlation coefficient (r) were calculated.

Results

There were 14 patients more than 6 years and 7 patients less than 6 years of age. Serum ferritin levels in most of these patients were very high and fell within range seen in untreated hemochromatosis (400 ng/ml to 18000 ng/ml) with mean of 8140 ng/ml (*Table I*). Most of the patients (81%) had received over 50 transfusions, without any chelation therapy. A highly significant correlation ($p<0.01$) was found between serum ferritin levels and number of blood transfusions received by these patients (*Table II*).

TABLE I–*Serum Ferritin Levels in Thalassemic Patients*

Serum ferritin (ng/ml)	No.	%
400 - 5000	7	33.3
5000 - 10000	7	33.3
10000 - 15000	5	23.8
15000 - 20000	2	9.6

Mean ± SD 8140 ± 5165.

TABLE II–*Correlation Between Serum Ferritin and Number of Transfusions*

No. of transfusions (Units)	No.	%	Mean serum ferritin (ng/ml) ± SD
1 - 50	4	19.1	1387 ± 929
50 - 100	9	42.8	7477 ± 3133
> 100	8	38.1	12550 ± 3909

$p<0.01$.

Baseline urinary iron excretion ranged from 0.08 mg/day to 2.4 mg/day (*Table III*). A significant increase in urinary iron excretion in comparison to baseline levels was observed in all the patients with desferrioxamine therapy (in dose of 50 mg/kg) (*Table IV*).

A significant correlation ($p<0.05$) between desferrioxamine induced urinary iron excretion and serum ferritin levels was also observed (*Table V*).

Negative iron balance could be achieved in as much as 15 patients, all except one being above 6 years of age.

TABLE III—*Baseline 24 Hours Urinary Iron Excretion*

Urinary iron (mg/day)	No.	%
0.0 - 0.5	11	52.4
0.5 - 1.0	5	23.8
1.0 - 1.5	2	9.5
1.5 - 2.0	2	9.5
2.0 - 2.5	1	4.8

Mean ± S.D. 0.77 + 0.66; Range 0.08 - 2.4.

TABLE IV—*Urinary Iron Excretion with Desferrioxamine*

Urinary iron (mg/day)	No.	%
0 - 10	7	33.3
10 - 20	9	42.8
20 - 30	4	19.1
30 - 40	1	4.8

TABLE V—*Correlation between Desferrioxamine Induced Urinary Iron Excretion and Serum Ferritin*

Serum ferritin (ng/ml)	No.	%	Mean urinary iron (mg/day) ± SD
400 - 5000	7	33.3	11 ± 9
5000 - 10000	7	33.3	14 ± 4
10000 - 20000	7	33.3	22 ± 8

$p < 0.05$.

Discussion

The definitive method for measuring the body iron stores is by repeated venesection to the point of anemia that is by measurement of mobilizable storage iron(11). This is obviously not feasible in thalassemic patients. The other method for estimating iron status is quantitative estimation of iron in liver biopsy specimens but repeated liver biopsy is not practicable. Another reliable guide is serum ferritin estimation. In this study a significant correlation between serum ferritin and the amount of blood transfused was observed which is in concordance with the study of Letsky *et al.*(12). So, serum ferritin can be taken as a reliable guide to estimate the iron status of the body and it can be useful in monitoring a child on iron chelation therapy. There was a significant increase in urinary iron excretion with desferrioxamine over baseline urinary iron excretion in all the patients. However, the effect of desferrioxamine on iron excretion is also directly related to iron overload and therefore negative iron balance could be achieved in all cases except one above the age of 6 years. In under 5 children iron excretion is relatively lesser due to less amount of labile iron available for chelation. Still chelation therapy is generally advisable at an early age as it decreases the rate of iron overloading.

A major finding in this study is the significant correlation between desferrioxamine induced urinary iron excretion and serum ferritin. A similar correlation was observed by Fargion *et al.*(13). Thus, desferrioxamine challenge test can also be used to estimate the iron status though this needs proper standardization.

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