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ORIGINAL ARTICLE

Effect of Iron Chelator on Liver Function in Beta Thalassemia Major Patients

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ABSTRACT

Background: Due to Regular blood transfusions and Desferrioxamine therapy, beta-thalassemic patients can live for over 30 years. It is becoming increasingly common for liver diseases to cause mortality and morbidity in these patients. Chelation compliance has improved with the recent addition of the oral single-dose therapy Deferasirox (DFX). This study will investigate the impact of iron therapy on liver function tests in BMT patients.

Methodology: The patients enrolled in the study were HBV negative and treated with DFO and DFX after BTM. The LFTs include alanine transferase, Albumin, serum bilirubin and aspartate transferase. Sixty patients with Beta-thalassemia were followed every six months for serum ferritin concentrations.

Results: Therapy with Desferrioxamine significantly decrease serum ferritin levels inbeta-thalassemia patients and isconcerned with high reduction in serumalanine transaminase and serum aspartate transaminase. Albumin concentrations remain the same in DFX treatment. Association between serum ferritin levels ALT and AST levels were found. There is a negative correlation between serum ferritin concentration and ALT.

Conclusion: Patients with Hepatitis negative having thalassemia with iron overload may have some liver function impairment. As a result of DFX treatment, AST, ALP and ALT levels were significantly reduced.

INTRODUCTION

The most common inherited disease worldwide is Beta-thalassemia, with just one gene. Transfusion therapy promotes iron overload in the body, adversely affecting the heart, liver, and the endocrine system. despite the administration of effective chelation therapy via the subcuctaneous route, over half of the patients died before the age of 35, and poor compliance with the subcutaneous therapy in many studies, severe hepatic hemosiderosis (grades 3-4) has occurred.(1, 2).Patients with beta-thalassemia major may develop hepatic fibrosis. The reason BTM patients aren't satisfied with DFO treatment might be because the treatment is unsatisfactory. Transferrin and ferritin can only be synthesized in the liver, where iron is primarily stored. Ferrous iron is toxic and usually binds to proteins within the liver. Iron, when unbound, produces free radicals, which can induce hepatotoxicity and lipid peroxidation. Several studies suggest lipid peroxidation can contribute to hepatocellular injury caused by iron overload(3, 4).The amount of ferritin iron in the blood and liver iron is measured non-invasively by using a technique called SQUID differ significantly in people with BTM or hemochromatosis.(5, 6). Furthermore, patients with thalassemia are frequently infected with hepatitis B and C. People with Hepatitis C infection had higher levels of enzymes than normal. Liver iron levels are elevated in patients with chronic hepatitis C virus infection(7). There is no clear reason why some HCV-infected patients have high serum iron levels. This is why *-thalassemia has become the most prevalent inherited single-gene disorder on the planet(8). Desferrioxamine (DFO) is an effective subcutaneous iron chelation therapy that remains highly effective despite a high prevalence of hepatic iron overload(5).As well as beta-thalassemia major patients being at risk for hepatic fibrosis. It is possible that low compliance rates observed in several patients might be because of this. A timely and accurate diagnosis, followed by prompt treatment, is the best way to prevent more disease progression (8).The liver stores iron, and ferritin and transferrin are synthesized(9, 10). Iron in ferrous form is generally bound to proteins in the liver and is toxic when unbound. When iron is unbound, free radicals are formed, causing liver damage and lipid peroxidation. Note that when hepatitis is absent, there is an improvement in the relationship between serum ferritin concentration and liver iron. In patients undergoing chronic transfusions, liver histology, serum ferritin, and liver iron content (LIC) are closely associated(10). Additionally, people with thalassemia are at increased risk for hepatitis B and C. the current study aimed to find effect of iron chelation on liver function in thalassemia major patients.

PATIENTS AND METHODS

The study design was an experimental one. HMC Peshawar enrolled selected subjects into its haematology and endocrinology clinics, and samples were analysed in the hospital's Biochemistry Laboratory. A detailed history of the patient, mother, or attendant was necessary, including information about the age at the time of diagnosis, clinical presentation, and transfusion and chelation data. Patients were given informed consent. In all patients, BMT was diagnosed by Hb-electrophoresis. Every patient met the

inclusion criteria. A complete data collection sheet was submitted, and all information was collected. Forty-five subjects were in total. Randomly selected BTM patients over five with a diagnosed diagnosis were studied. Five days a week, a subcutaneous pump infusion of DFO was administered to all subjects and regular blood transfusions and iron chelation. Patients with type I or type II thalassemia, history of hepatitis, splenectomy, and positive hepatitis C or B test were excluded from the study. Enrollment was restricted to patients who had received DFO or DFX treatment for at least five years and who tested negative for hepatitis ALP, bilirubin, ALT, AST, and bilirubin, serum ferritin, ALT, AST, and aspartate transferase (AST) were evaluated regularly in all patients. They were calculated as mean, median, and standard deviationonStudents' t-tests or analysis of variance were then used to the compare variables DFX treatment.

RESULTS

Over 18 years, sixty beta-thalassemia patients were evaluated longitudinally every six months. After the study ended, their mean age was 17.9 plus/minus 1.7 years, compared to 5.4 plus/minus 1.2 years in the beginning. Iron chelation therapy with DFO began at 4.2 +/- 0.9 years. We switched from intravenous to oral administration of DFX (200mg/kg/day) at 12.9 +/-1.5 years of age. Table 1 presents a longitudinal liver function study. DFX curedeclined serum ferritin levels in all BTM individuals (p0.000). In addition, ALT, AST, and ALP serum concentrations were all decreased (p 0.01). (Figure 1-3) The albumin concentration in the blood did was not alter altered by curing. Serum bilirubin levels increased by a moderate amount after the treatment. Significant correlations were found between serum ferritin concentrations and serum alkaline transferase and AST levels (r = 0.45 and 0.33, respectively, p = 0.04). Patients with positive hepatitis screening but who received DFO treatment at an early age did not experience high liver failure. On the other hand, DFX curing lowered ALT, AST, and ALP significantly. Even in the absence of hepatitis, iron overload adversely impacts the synthesis of IGF-1 in patients with impaired liver function.

Table 1 Changes in liver functions in thalassemic patients

Years	5	6	7	8	9	10	11	12	13	14	15	16	17	18
ALT	53	69	70	63	54	43	41	45	55	40	45	44	48	45
AST	51	63	57	51	52	71	39	42	45	41	44	45	47	42
ALP	187	199	1808	225	215	234	214	239	212	231	224	179	130	115
Albumin	45	45	44	45	45	44	46	45	46	45	45	46	45	45
Bilirubin	27	25	28	30	31	33	35	35	38	39	39	42	46	51
S.ferrttin	2400	2400	2300	2000	2100	2200	2000	2200	2500	2200	1500	1500	1400	1300

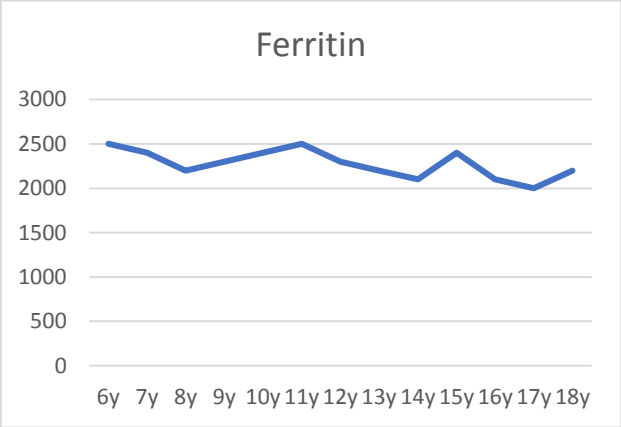

Figure1: Serum ferritin after and before the therapy

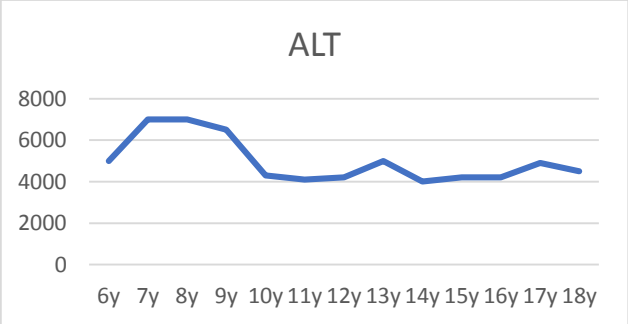

Figure 2: Serum Alanine transaminase concentrations after and before the therapy

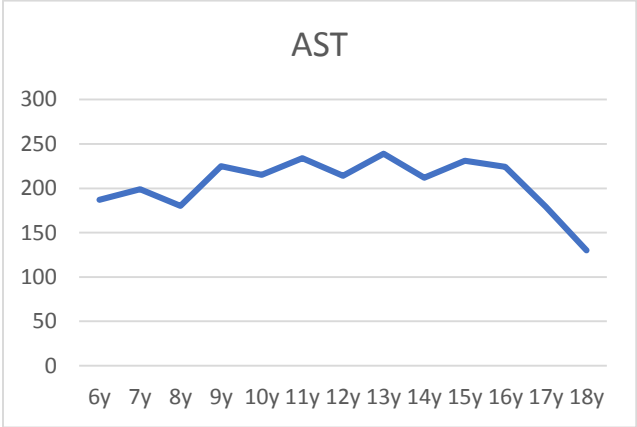

Figure 3: Serum Aspartate transaminase concentrations after and before the therapy

DISCUSSION

A thalassemia patient's liver appears to have abnormal function due to high ferritin levels and a high age at which transfusions have become necessary. Infection with viruses aggravates iron-induced liver damage. Hepatitis may be associated with increased serum ALT levels following multiple blood transfusions(6). The liver function tests and serum ferritin levels of BTM patients with a negative hepatitis B and C test were assessed longitudinally for more than ten years so that no possible influence of hepatitis could be seen on liver dysfunction. The children began iron chelation with DFO at 4.2 +/- 0.9 years. In this case, oral DFX (20 mg/kg/day) was prescribed at 12.9 +/-

1.5 years. Patients with BTM who were longitudinally followed concerning liver function showed significant reductions in serum ferritin levels following DFX(11). The outcomes suggest that DFX may improve liver function even more than DFO due to its greater compliance with treatment. ALT, AST, and ALP levels were markedly decreased when serum ferritin levels were reduced. Liver biopsy histological changes are significantly correlated with serum ferritin and ALT levels(12).

By determining the degree of severity of the disease, one can assess the progression of fibrosis. Liver enzymes and IGF-1 do not indicate the extent of liver fibrosis in patients with BMT, and these patients may suffer different outcomes as far as liver function is concerned. Using transient elastography to assess fibrosis allows the addition of liver damage data to the analysis at the end of treatment, compared with laboratory data to determine if treatment is effective(13-15).When individuals with persistent hepatic infectionhave high levels of IGF-1, their aspartate aminotransferase (AST) levels are negatively correlated(16). Therefore, IGF-I is produced by the liver and is present in the serum of individuals with adequate GH levels. Thalassemia significant patients had much lower levels of serum IGF-1 compared to people who suffered from GH deficiency. There was lower linear growth in children with GH deficiency treated with exogenous GH. These results indicate that thalassemic patients are relatively insensitive to growth hormones. Other factors can affect your liver's and blood's levels of IGF-1 besides GH. Chronic liver diseases are associated with increased insulin-like growth factor 1 (IGF-1), which stimulates hepatic stellate cells and speeds up liver regeneration(17). Low serum IGF-1 levels may be associated with chronic liver disease.Specifically, the hepatic growth factor is upregulated, while the transforming growth factor * 1.42 is downregulated(18, 19). Our results showed a substantial elevation in IGF-I after DFX therapy, indicates a better prognosis of hepatic regeneration.

CONCLUSIONS

Hepatic dysfunction was mild but significant in patients with BMT who were seronegative for hepatitis. In contrast, serum ALT, AST, and ALP levels were significantly decreased, and IGF-I concentrations wereaccording to the positive correlation between ALT and serum ferritin levels as well as the negative correlation between IGF-I levels and ferritin and ALT, hepatic iron overload impairs hepatic functions. It reduces IGF-I synthesis, even in the absence of hepatitis.

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