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Levels of Calcium, Corrected Calcium, Alkaline Phosphatase and Inorganic Phosphorus in Patients' Serum with β-Thalassemia Major on Subcutaneous Deferoxamine

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Abstract

Introduction: Combination of transfusion and chelation therapy has dramatically extended the life expectancy of patients with β-thalassemia major. Aim of this study was to determine of serum calcium, albumin corrected calcium, alkaline phosphatase and inorganic phosphorus in patients with β-thalassemia major on deferoxamine therapy.

Method: Sixty five patients with β-thalassemia major receiving blood transfusion with subcutaneous iron chelation therapy and 45 controls i.e. healthy individuals of the same age were enrolled in this study. Serum calcium, albumin corrected serum calcium, alkaline phosphatase and inorganic phosphorus levels were determined in all individuals.

Result: In patients with β-thalassemia major serum calcium and albumin corrected serum calcium levels were low as compared with controls ($p<0.01$ and <0.04 respectively). All patients had high alkaline phosphatase level than in controls ($p<0.001$). Levels of inorganic phosphorus were also high in patients than controls ($p<0.01$). Serum albumin did not show any statistically significant difference between patients and normal subjects ($p<0.11$).

Conclusion: It is concluded that bone health is greatly compromised in patients with β-thalassemia major and bone related biochemical abnormalities i.e. hypocalcaemia, hyperphosphatemia and hyperphosphatasia are common in thalassemia major patients.

Keywords: β-Thalassemia major; Calcium; Albumin; Corrected calcium; Alkaline phosphatase; Inorganic phosphorus

Introduction

Prevalence of β-thalassemia is high amongst the genetic disorders of hemoglobin synthesis. Frequency of β-thalassemia trait is about 5-6% in Pakistan. β-thalassemia major is characterized by severe hemolytic anemia that requires regular blood transfusion. Life expectancy of these patients is strikingly prolonged with repeated blood transfusion and iron chelation therapy but consequences associated with secondary hemochromatosis are still a challenge [1,2]. A series of complications including osteopenia, osteoporosis, scoliosis, spinal deformities, nerve compression and spontaneous fractures are frequently seen in transfusion dependent thalassemics [3].

Deferoxamine is a trihydroxamic acid produced by *Streptomyces pilosus* [4]. It is being used as iron chelator for over three decades [5]. Regular blood transfusion along with deferoxamine infusions has improved the management of patients with β-thalassemia major [6]. However, iron chelation has its own adverse effects on thalassemics [7].

Calcium, inorganic phosphorous and alkaline phosphatase are the essential bio materials of human bones and teeth [8]. Hydroxyapatite is the mineral form of calcium and phosphorous that provides rigidity to osseous skeleton. Alkaline phosphatase assists in the deposition of the hydroxyapatite crystals between the collagen fibrils of bone [9]. Calcium is the 5th most plentiful element in human body playing a major role in skeletal mineralization [10]. Serum calcium is found in free as well as in bound form with proteins especially albumin. Adjustment of serum total calcium concentration (corrected calcium) for albumin is essential for the diagnosis of hypo and hypocalcaemia [11]. Phosphorous has paramount effect in conjunction with calcium on development of bones [12]. Osseous tissue contains 85% of total body phosphorous. Alkaline phosphatase is responsible for promoting bone mineralization by increasing the local concentration of inorganic phosphorus [8].

Bone turnover is evaluated with various specific and sensitive serological markers. Serum calcium, phosphorous and alkaline phosphatase are characteristically altered with bone impairment in patients with thalassemia [3]. This study was conducted to evaluate the levels of calcium, albumin corrected calcium, alkaline phosphatase and inorganic phosphorus in patients with β-thalassemia major on deferoxamine infusion. In Pakistan no study has been conducted for the evaluation of these biochemical markers in patients with transfusion dependent β-thalassemia who are on deferoxamine therapy.

Method

The study was approved by ethical committee of Baqai medical university Karachi, Pakistan. Written informed consent was obtained from the parents of the patients and controls enrolled in this study. Sixty-five patients with β-thalassemia major and 45 healthy individuals (controls) aged between 15 to 25 years were recruited in this study. Venous blood samples were collected in un-anticoagulated tubes and allowed to clot. Serum was separated and analyzed within 6 hours. Serum calcium was determined by colorimetric method using methylmol blue indicator while serum phosphorus level was determined by ammonium molybdate end point method. Alkaline phosphatase was also measured by colorimetric method using p-nitrophenylphosphate. Serum albumin was determined by colorimetric method using bromocresol green method in semi auto analyzer.

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Parameters	Controls	Thalassemics	p value
Calcium (mg/dl)	9.5 ± 0.6	8.9 ± 0.47	0.01
Corrected calcium (mg/dl)	9.26 ± 0.54	8.83 ± 0.58	0.04
Alkaline phosphatase (IU/l)	124 ± 51.81	368 ± 176.36	0.001
Inorganic phosphorus (mg/dl)	3.42 ± 0.65	3.75 ± 0.26	0.01
Albumin (g/dl)	4.35 ± 0.46	4.08 ± 0.46	0.11

Data are shown as mean ± SD

Table 1: Levels of serum calcium, corrected calcium, alkaline phosphatase and inorganic phosphorus in patients with β-thalassemia major and controls.

Statistical Analysis

Independent t-test was used for the analysis of data; p value of <0.05 was considered statistically significant.

Results

Results of serum calcium, corrected calcium, alkaline phosphatase, inorganic phosphorus and albumin are shown in Table 1. Data analysis showed that serum calcium and corrected calcium were decreased in patients with thalassemia major as compared with controls ($p<0.01$ and <0.04 respectively). Alkaline phosphatase and inorganic phosphorus were significantly higher in thalassemic group than controls ($p<0.001$ and <0.01 respectively). Statistically no significant difference was observed for level of albumin among the patients and controls as shown in Table 1.

Discussion

β-thalassemia major is an inherited, autosomal recessive hemoglobinopathy that results in a large number of hematological, biochemical and systemic abnormalities. Results of this study showed decreased level of serum calcium and corrected serum calcium and high levels of inorganic phosphorus in patients with β-thalassemia major as compared with controls ($p<0.01$, <0.04 and <0.01 respectively) as shown in Table 1. Findings of this study are consistent with that of Modi [13] and Mirhosseini [14]. A study of Salama however showed no alteration in calcium level in β-thalassemia major patients as compared with controls [3]. Hypocalcaemia and hyperphosphatemia seems to be related to hypoparathyroidism, a well-known clinical condition associated with thalassemia major. Parathyroid hormone is responsible for the regulation of calcium homeostasis in body. Repeated blood transfusion results in iron deposition in the parathyroid gland which affects its normal functioning [15]. Several researchers have reported decreased levels of parathyroid hormone in patients with β-thalassemia major [15-17]. However parathyroid hormone was not evaluated in this study.

In this study it was observed that patients with β-thalassemia major have increased levels of serum alkaline phosphatase as compared with controls ($p<0.001$). Levels of alkaline phosphatase in this study were considerably higher than in other studies. Goyal findings are at variance with our findings that did not show statistically significant alterations in the levels of alkaline phosphatase in transfusion dependent thalassemia major patients [15]. High level of alkaline phosphatase may have an association with osteomalacia and liver impairments in thalassemia major patients [3].

Bone changes are frequently seen in patients with β-thalassemia major. These complications increase with regular blood transfusion, secondary hemosiderosis, iron chelation therapy, erythroid hyperplasia and nutritional deficit [15,18]. A paradigm of deferoxamine induced toxicity is failure of linear growth, associated with evidence of cartilaginous dysplasia of the long bones and spine. Frequency of fractures are high in these patients even with only mild anemia and normal serum ferritin levels.

Well balanced nutrition, patient education, diet counseling and supplementation therapy of calcium and vitamin-D for high risk group of β-thalassemics is strongly recommended. Regular monitoring of serum calcium, alkaline phosphatase and inorganic phosphorus is also recommended. Proper monitoring of parathyroid hormone may also improve skeletal status in these patients.

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