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ORIGINAL ARTICLE

Parathyroid and Calcium Status in Patients with Thalassemia

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Abstract Thirty patients with thalassemia major receiving repeated blood transfusion were studied to see their serum parathyroid hormone (PTH) and calcium status. Serum PTH, serum and 24 h urinary calcium, and serum alkaline phosphatase, phosphorus, and albumin-corrected calcium levels were determined. Half of these patients, in addition to transfusion, were also supplemented with vitamin D (60,000 IU for 10d) and calcium (1500 mg/day for 3 months). Serum PTH, and serum and 24 h urinary calcium concentrations of the patients receiving transfusions were found to be significantly reduced while their serum alkaline phosphatase, phosphorus, and albumin-corrected calcium levels were not significantly altered when compared to the respective mean values for the control group. Vitamin D and calcium supplementation significantly increased their serum PTH and calcium levels. Supplementations also increased urinary excretion of calcium. The results thus suggest that patients with thalassemia have hypoparathyroidism and reduced serum calcium concentrations that in turn were improved with vitamin D and calcium supplementation.

Keywords Parathyroid hormone · Calcium · Thalassemia

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Introduction

Thalassemia is a heterogeneous family of inherited disorders of hemoglobin synthesis. It is characterized by the complete absence or reduced synthesis of one or more types of globin chains. The affected infants present with pallor, poor growth, and abdominal enlargement due to hepatosplenomegaly. In untreated children, characteristic bone changes appear, such as thinning of cortex of long bones, widening of medullary spaces, bossing of skull, widening of diploic spaces, and prominence of the upper incisors and separation of orbit [1, 2].

The main stay of treatment of severe β thalassemia is regular blood transfusion (PCV infusion) with an attempt to maintain hemoglobin levels greater than 10 g/dl [3]. Repeated blood transfusion results in citrate toxicity and lead to iron deposition in the parathyroid gland, which in turn may cause hypoparathyroidism. A few studies have reported that some of the thalassemic patients on regular PCV infusion develop hypoparathyroidism, especially after 10 years of age [4, 5]. As a result of hypoparathyroidism, low vitamin D and PTH levels have been reported in such patients. Limited studies have also shown that supplementation with vitamin D and calcium improves serum calcium status. Paucity of data and lack of studies in Indian population prompted us to plan this work where serum PTH, and serum and urinary calcium levels have been estimated with and without vitamin D and calcium supplementations in children with

Table 1 Serum PTH, serum and urinary calcium, and serum phosphorus, alkaline phosphatase, albumin and albumin-corrected calcium levels in control subjects, and in patients of thalassemia receiving packed cell transfusion with and without vitamin D and calcium supplementations

Parameters	Controls (group I)	Patients (group II)	Patients receiving supplementations (group III)	
			Before supplementation	3 Months after supplementation
PTH (pg/ml)	44.3 ± 5.63	32.2 ± 0.96*	31.9 ± 2.22*	33.4 ± 2.07*,**
Serum calcium (mg/dl)	9.98 ± 0.16	8.42 ± 0.32*	8.46 ± 0.33*	9.78 ± 0.13**
Urinary calcium (mg/24 h)	159 ± 17.0	120 ± 2.6*	119 ± 3.1*	129 ± 1.8*,**
Alkaline phosphatase (KA U/L)	7.66 ± 0.60	7.67 ± 0.85	7.64 ± 0.61	7.65 ± 0.03
Albumin (g/dl)	3.53 ± 0.02	3.54 ± 0.04	3.53 ± 0.11	3.55 ± 0.10
Albumin-corrected calcium (mg/dl)	4.48 ± 0.03	4.47 ± 0.01	4.47 ± 0.05	4.48 ± 0.02

Values are mean ± S.E.M. for 15 subjects in each group

* $P < 0.05$ when compared to group I

** $P < 0.05$ when compared to the mean value before supplementation (group III)

thalassemia major receiving packed cells transfusion therapy (Table 1).

Material and Methods

Thirty patients of thalassemia major (8–18 years old) receiving packed cells transfusion, to maintain hemoglobin concentration between 9.0 to 10.5 g/dl, were selected for the study. Results were compared with a group of fifteen normal healthy controls (group I). Patients were subdivided into two groups, whereas every alternate patient attending the Thalassemia Clinic and receiving packed cell transfusion therapy was included in group II, the remaining 15 patients were included in group III. The patients in group III, in addition to packed cell transfusion, were supplemented with calcium (1.5 g/day, for 3 months) and vitamin D_3 (60,000 IU/day, for 10 days). These patients were again re-evaluated after 3 months of the supplementation of the two micronutrients.

All the subjects were assessed for routine anthropometric and laboratory investigations that were found to be within normal limits. Mean age of the children in different groups was also comparable and was 11.87 ± 2.13 years for group I, 12.01 ± 2.82 years for group II, and 11.61 ± 2.89 years for group III, respectively. The three groups were also sex matched.

All the patients were on regular PCV infusion since the age of 1–2 years, after the diagnosis of thalassemia was confirmed. Inclusion criteria were—(a) age 8–18 years, (b) diagnosis of thalassemia major, and (c) those recieving regular PCV infusion and chelation therapy. Exclusion criteria were—(a) poor compliance, (b) very sick patients, (c) those that cannot be followed, (d) having some renal disease, (e) malabsorption syndrome, or (f) on long term anticonvulsant therapy. Informed consent of the parent was obtained. Approval of IRB and ethical committee were also taken.

Five ml venous blood was collected in a plain vial, asceptically. Serum was separated and analyzed immediately (except for PTH), using Konelab 30i Clinical Chemistry Analyzer. For PTH, serum was frozen and used within a week. Concentrations of serum and 24 h urinary calcium were estimated using O-cresolpthalein complexone [6], serum phosphorus according to Fiske and Subbarow [7], alkaline phosphatase according to King and Armstrong [8], and albumin by dye-binding method using bromocresol green [9]. Albumin-corrected calcium was calculated (to obtain a reasonable estimate of the free calcium) according to Pyane [10], who suggested that albumin-corrected calcium gives an estimate of the free calcium level when albumin levels are within the normal range. Serum intact PTH was estimated by two-site labeled antibody radioimmuno assay [11]. Results were statistically analyzed by Student's *t*-tests.

Results and Discussion

Results of the present study demonstrate significantly reduced levels of serum PTH, and serum and 24 h urinary calcium in patients with thalassemia as compared to the controls. Supplementation of vitamin D and calcium for 3 months resulted in an increase in these parameters. The mean value for serum calcium, in group III after supplementation became comparable to the mean value for the control group and that the two values were not found to be significantly different from each other. The improvements seen in serum PTH and 24 h urinary calcium levels were small (though potentially significant) as the mean values for these parameters were found to be increased they however, remained lowered than the controls.

Hypoparathyroidism due to iron overload is a common feature in patients of thalassemia [5]. Further, hypoparathyroidism in turn is also known to cause hypocalcemia. Several workers have reported reduced levels of PTH in patients with thalassemia [5, 12–14]. Autio et al [12] observed that 61% of their patients with β-thalassemia had hypocalcemia. They further observed that these patients were benefited with vitamin D and calcium supplementations. Aleem et al [13] also observed hypoparathyroidism in patients of Thalassemia. They suggested that hypoparathyroidism seen in these patients is due to chelation therapy. Some workers have also reported that patients with thalassemia major have 24 h urinary calcium below the normal range [14, 15]. They further suggested that an early and effective treatment should be taken in order to improve their bone health. However, there is no report from this part of the continent. Supplementation of vitamin D and calcium to the patients of the present study resulted in normocalcemia, however, they still had reduced levels of serum PTH. It could be due to the reason that supplementations received by these patients might not be sufficient and should have been continued for a longer duration. The limitation of the study is also the small number of cases. It is now proposed to continue this work in a larger group, also with calcium supplementation for a longer period (say 1 year) and vitamin D supplementation repeatedly after every 3 months to observe more significant results.

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