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Role of HPT Markers in β Thalassemia Major Patients

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ABSTRACT

Patients of beta thalassemia major undergo frequent blood transfusion along with chelating therapy as a part of their treatment regimen which considerably prolonged survival of patients. However, hyper-perfusion results in iron deposition in multiple endocrine glands which leads to endocrine dysfunction. Hypoparathyrodism is a well known syndrome which is associated with beta thalassemia and seems to be cause of hypocalcemia and hyperphosphatemia. The cause of hypoparathyrodism is assumed to be due to iron deposition in parathyroid glands. This study is conducted to determine the serum calcium and phosphorous in 30 patients of beta thalassemia major. We recommend parathyroid hormone profile should be checked regularly in all patients with transfusion dependent beta thalassemia major and suggest that these tools may be applicable to other cases of suspected HPT.

Keywords: Beta thalassemia, Hypoparathyrodism, Calcium, Phosphorous

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INTRODUCTION

Beta thalassemia is one of the most common genetic disorders in India. These haemoglobinopathies can cause life threatening situation & chronic ill health. Hence the population needs to be screened for hemoglobin disorders, so that appropriate measures for treatment & prevention can be taken in these patients.

Patients with beta thalassemia major need repeated blood transfusions for survival due to severe anemia [1]. Regular blood transfusions and chelation therapy have significant increase in the lifespan of these patients, but many endocrine abnormalities such as hypogonadism, diabetes mellitus, hypothyroidism and hypoparathyroidism (HPT) develop due to an iron overload.[2]

Hypoparathyroidism is thought to be a rarer complication ,usually, but not always, accompanied by hypocalcemia[3-7]. However, hypoparathyroidism may cause various neurological manifestations, including tetany, seizures, carpopedal spasms, and paraesthesia[8,9], and little is known about these associated complications in thalassemic patients [6]. Recently, abnormal cerebral computed tomography (CT) findings have been reported in high percentage of patients with thalassemia and hypoparathyroidism [5].

Repeated blood transfusions results in citrate toxicity and leads to iron deposition in the parathyroid gland, which in turn may cause decrease parathyroid level which in turn decreases calcium level. So scarcity of data and lack of studies promotes us to plan this work where serum calcium and phosphorus level will be measure in patients with β-thalassemia major, who have been given repeated blood transfusion and chelation therapy.

Aims and Objectives

The overall aim of this research work is to evaluate HPT markers in the patients of beta thalassemia major.

The specific objectives are:

1. To evaluate iron indices factors like iron, TIBC.
2. To evaluate HPT markers in terms of calcium and phosphorus.

Null hypothesis:

There is no association between increased iron level after multiple transfusions and HPT markers in beta thalassemia major patients.

Alternative hypothesis:

There is an association between increased iron level after multiple transfusions and HPT markers in beta thalassemia major patients.

MATERIALS AND METHOD

This case control study included clinically diagnosed 30 patients from tribal & non-tribal populations of MP regularly visited to Peoples medical college & RC Bhopal & compared with healthy controls on the basis of age, sex, dietary conditions & life styles, during the period of two month after acceptance of this project. All patients are transfusion dependent also all of them are treated with deferral.

All patients and normal healthy individuals (Control group) will told to fast (overnight) 12-14 hours and then the venous blood collected with all aseptic precautions from the anterior cubital vein in plain bulb for biochemical estimations. Blood allowed to clot at room temperature for about 30 minutes and then centrifuge at 3000 rpm for 10 minutes. Then separated serum used for biochemical analysis by fully automated analyzer(Biosystem A25)

Following investigations performed in each case.

1. The concentrations of iron and TIBC in serum will measure by Ferrozine method, using CREST BIOSYSTEMS kit.
2. Serum calcium will measure by using (Autozyme) Accurex Biomedical kit.
3. Serum phosphorus will measure by Ammonium Molybdate Method using ERBA Diagnostics kit.

This research protocol was approved by the ethics committee of Peoples Medical College and Hospital Bhopal.

Statistical Analysis

The data obtained in this study will analyze for its statistical significance using 'z' test. P value less than 0.05 is consider as the level of significance.

RESULTS AND DISCUSSION

Age (year)	Patients (30)	Controls (30)	P value
	9.26±3.16	9.42±3.95	0.86(ns)
Gender (Male/female)	15/15	15/15	--
Serum iron (µg/dl)	173.4±30.73	116.3±16.02	<0.0001
TIBC(µg/dl)	227±18.71	302.6±48.62	<0.0001
Sr. Calcium (mg/dl)	6.14±1.70	9.2±1.03	<0.0001
Sr. Phos. (mg/dl)	6.25±0.95	3.65±8.09	<0.0001

Results are mean ±SD or as indicated in table.*** Highly significant, p<0.0001

The mean age of patients was 9.26±3.16 and controlswas9.42±3.95yrs.This is not significant. There was a significantly higher serum iron levels in patients as compared to the controls (173.4±30.739 vs116.3±16.02µg/dl, p<0.0001) and

Serum total iron binding capacity (TIBC) level was significantly lower in patients as compared to controls (227±18.711µg/dl vs302.6±48.626µg/dl, p<0.0001).

The mean serum calcium level of patients and controls were 6.14±1.70 mg/dl and 9.2±1.03 mg/dl respectively. Patients show significantly lower mean serum calcium level than controls (p<0.0001). The mean serum phosphorus level of patients was 6.25±0.955 mg/dl and a control was 3.65±8.09 mg/dl. The value of mean serum phosphorus in patients was significantly higher than controls (p<0.0001).

DISCUSSION

Patients with beta thalassemia major need repeated blood transfusions for survival due to severe anaemia.[1] Regular blood transfusions and chelation therapy have significant increase in the lifespan of these patients, but many endocrine abnormalities such as hypogonadism, diabetes mellitus, hypothyroidism and hypoparathyroidism (HPT) develop due to an iron overload.[2]

Repeated blood transfusion results in citrate toxicity and leads to iron deposition in the parathyroid gland, which causes decrease parathyroid level which in turn decreases calcium level. The levels of extracellular calcium (Ca2+) and phosphorus (P+) are tightly regulated by complex mechanisms that have evolved from a phylogenetic perspective, in order to maintain their extracellular concentrations within relatively narrow limits. Among key participants in the regulation of Ca2+, parathyroid hormone (PTH), calcitonin and 1-25 dihydroxyvitamin D are major hormones involved in mineral ion homeostasis, through their effects on parathyroid glands, bone, kidney and intestine.

In this study, thalassaemic patients showed significantly low level of serum calcium and significantly high level of serum phosphorus as compared to normal control group. These results were agreed with the findings of previous studies[10,11] but disagrees with those obtained by Kontesis et al.[12]

Hypocalcemia and hyperphosphatemia in these patients seem to be related to hypoparathyroidism (HPT). Parathyroid gland harmone especially parathyroid and calcitonin regulate normal levels of calcium and phosphorus in blood and this gland becomes insufficient to produce these hormones because precipitation of iron in tissues of this gland.[13] It was documented that the function of osteoblast is reduced, which is thought to be the major cause of osteopenia and osteoporosis inbeta thalassemia major.[14] Osteoporosis is the most prevalent bone complication in beta thalassemia patients despite regular transfusion and iron chelation therapy.

The 25-hydroxy vitamin D3 and bone mineral density were significantly decreased among patients with beta thalassemia.[15]

Mahmoodi et al (2011) done a case study on 14 year old girl with beta thalassemia major diagnosed since the age of 9 months came to their center with generalized tonic clonic seizure. The investigations revealed diffuse intracranial calcifications in deep white matter, posterior fossa, basal ganglia and both thalami. The laboratory and neuroimaging also indicate hypoparathyroidism. Ghonaim et al (2010) was documented that the function of osteoblast is reduced, which is thought to be the major cause of osteopenia and osteoporosis in beta thalassemia major.

Modi et al (2012) found out that 84% patients with thalassemia major in spite of chelation therapy have hypocalcemia and phosphate level is also high in comparison with the control group hypocalcemia is due to hypoparathyroidism and phosphorous levels are due to effect of PTH suppression.[3]

CONCLUSION

Hypocalcemia and hyperphosphatemia in these patients seem to be related to hypoparathyroidism (HPT) due to iron deposition in parathyroid gland.

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