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Evaluation of HPT Markers in β Thalassemia Major Patients

KEYWORDS: Beta thalassemia, Hypoparathyroidism, Calcium, Phosphorus

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ABSTRACT *Patients with beta-thalassaemia major are prone to metabolic complications, including endocrine dysfunction which can occur as single or multiple endocrine glands involvement. Treatment with transfusion programs and chelating therapy has considerably prolonged survival in thalassemic patients. However, as a result of hyper-transfusion therapy and increased longevity, iron tissue toxicity has become more common, and contributes significantly to morbidity in these patients. Hypocalcemia and hyperphosphatemia in these patients seem to be related to hypoparathyroidism (HPT) which is a well-known syndrome associated with thalassemia major. The cause of HPT is assumed to be due to iron deposition in parathyroid glands.*

This study was conducted to determine the serum calcium and phosphorus in 50 beta thalassemic patients. We recommend the periodic use of such measurements in all TM, and suggest that these tools may be applicable to other cases of suspected HPT.

1. INTRODUCTION

Beta thalassemia is one of the most common genetic disorder in India. The North Maharashtra region especially Dhule, Nandurbar and Jalgaon districts are tribal belts where sickle cell & β thalassemia are prevalent. These hemoglobinopathies 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].

Repeated blood transfusion 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. A few studies have reported that some of the thalassemic patients on regular PCV infusion develop hypoparathyroidism, especially after 10 years of age [3]. Several workers have found out low level of calcium and high level of phosphorus in β-thalassemia major [4-7], while in contrast few workers found out no change [8-12]. So scarcity of data and lack of studies in North Maharashtra population prompted us to plan this work where serum calcium and phosphorus level where measured in patients with β-Thalassemia major, who have been given repeated blood transfusion and chelation therapy.

2.MATERIAL AND METHODS

The study included clinically diagnosed 50 patients from tribal & non-tribal population in area around Dhule, Nadurbar & Jalgaon districts of Maharashtra & compared with healthy controls on the basis of age, sex, dietary conditions & life styles, during the period 2009 to 2013. All patients where transfusion dependent also all of them were treated with desferal.

The collection of blood was performed in the thalassemia center in Dhule. 5 ml blood was collected in plain tubes allowed to clot for 45 minutes after centrifugation serum was obtained and precaution were taken to avoid hemolysis. Biochemical analysis were done by:

1. Iron - Dipyridyl Method
2. Calcium - Cresolphthaiein complexone Method
3. Phosphorus - U V End point Method

The research protocol was approved by the ethics committee of ACPM Medical College and Hospital Dhule.

Statistical Analysis

The data obtained in this study was analyzed for it's statistical significance using 'z' test. P value less than 0.05 was considered the level of significance.

3.RESULTS

The demographic characteristics of patients with thalassaemia are shown in table:

	Control Group	BTM Group
n	50	50
Age(Year)	23.7 + 7.1	23.1 + 6.4
Sex (Male/Female)	25 / 25	27/23
Hb (g/ dL)	11.4 ± 0.2 *	9.5 ± 2.8
Serum Iron (µg/dl)	112.14 ± 15.28	165.55 ± 14.30*

Data are presented as means ± SD
*** Significant difference compared with controls (p < 0.05)**

There are no significant differences between Control Group and BTM Group regarding age or sex.

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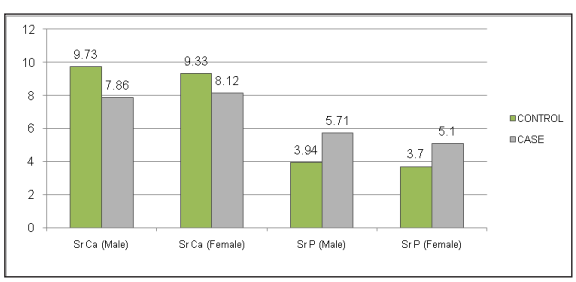
Serum calcium:
The values of mean and stander error of serum calcium for males and females of beta thalassemia major patients were: 7.86 ± 0.43; 8.12 ± 0.45 mg/dL, respectively and were significantly ($P < 0.05$) lower than control males and females 9.73 ± 0.34; 9.33 ± 0.46mg /dL, respectively.

Serum phosphorus:
Serum phosphorus for males and females of beta thalassemia major patients were: 5.71 ± 0.41; 5.1 ± 0.31mg/dL, respectively and were significantly ($P < 0.05$) higher than control males and females 3.94 ± 0.12; 3.70 ± 0.11 mg/dL, respectively.

4.DISCUSSION

The levels of extracellular calcium (Ca^{2+}) 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 $Ca^{2+,}$ parathyroid hormone (PTH), calcitonin and 1-25 dihydroxy vitamin D are major hormones involved in mineral ion homeostasis, through their effects on parathyroid glands, bone, kidney and intestine.

In this study, the thalassemic patients showed low level of serum calcium and high level of serum phosphorus as compared to normal control group. These results are agree with the findings of others studies [13, 14] but disagrees with those obtained by Kontesis et al [15].



Hypocalcemia and hyperphosphatemia in these patients seem to be related to hypoparathyroidism (HPT) which is a well known syndrome associated with thalassemia major [16, 17]. The cause of HPT is due to iron deposition in parathyroid glands [18].

Hormones of parathyroid gland especially parathyroid and calcitonin hormones 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 [19]. It 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 [20]. Osteoporosis is the most prevalent bone complication in beta thalassemia patients despite regular transfusion and iron chelation therapy. The 25-hydroxyvitamin D3 and bone mineral density were significantly decreased among patients with beta thalassemia [21].

A case control study done on the effects of intramuscular injection of a mega dose of cholecalciferol involving 40 beta thalassemia major patients and 40 non thalassemic controls [22]. They found that among thalassemia major patients, two had hypoparathyroidism and low 25-OH D, and two had hypocalcaemia with hypophosphatemia, high alkaline phosphatase (ALP), high PTH and serum 25-OH D below ng/ml. The remaining patients had low 25-OH D concentrations with normal serum $Ca^{2+}$and PO^{4} concentrations. Vitamin D deficiency is present in 100% of thalassemia major patients and treatment with mega dose injection of cholecalciferol is effective for hypovitaminosis D for 3months. A case study done 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 [23]. The investigations revealed diffuse intracranial calcifications in deep white matter, posterior fossa, basal ganglia and both thalami. The laboratory and neuroimaging also indicate hypoparathyroidism. They recommend periodic assessment and control of serum calcium in all patients with thalassemia major and prompt treatment with oral calcium and active form of vitamin D can prevent hypoparathyroidism and neurological complications in beta thalassemia major patients.

5.CONCLUSION

This study indicate that alteration in serum calcium and phosphorus play an important role in the pathogenesis of beta thalassemia major. Iron being the most important of all minerals was found to be significantly increased in beta thalassemia major patients. We recommend the periodic use of such measurements in all TM and suggest that these tools may be applicable to other cases of suspected HPT.

REFERENCE

1. Q. Shazia, Z. H.Mohammad et al. Correlation of Oxidative Stress with Serum Trace Element Levels and Antioxidant Enzyme Status in Beta Thalassemia Major Patients: A Review of the Literature. Anemia 2012; 02:1-7. | 2. Jensen CE, Tuck SM, Agnew JE, et al. High Prevalence of Low Bone Mass in Thalassaemia Major. Br Journal of Haematol 1998; 103(4):911-15. | 3. Goyal M, Arora P, Lal H. Parathyroid and calcium status in patients with thalassemia. IJCB 2010; 25,(4): 385-87. | 4. Sleem G A A M, Al-Zakwani I S, Almuslahi M. Hypoparathyroidism in adult patients with Beta-Thalassemia Major. Sultan Qaboos University Medical Journal2007; 7(3):215-18. | 5.Shamshirsaz AA, Bekheirnia MR, Kamgar M et al. Metabolic and endocrinologic complications in beta-thalassemia major: a multicenter study in Tehran. BMC Endocrine Disorders 2003; 3:4. | 6.Aleem A, Al-Momen A K, Al-Harakati M S, Hassan A, Al-Fawaz I.Hypocalcemia due to hypoparathyroidism in β-Thalassemia major patients. Annal of Saudi Medicine 2000; 20:5-6. | 7.Auwerx J and Bouillon R.Mineral and bone metabolism in thyroid disease: A Review. Quarterly Journal of Medicine 1986; 60(2):737-752. | 8.Angelopoulos N G, Goula A, Rombopoulos G et al. Hypoparathyroidism in transfusion-dependent patients with β-thalassemia.J Bone Miner Metab 2006; 24:138-45. | 9.Mahachoklertwattana P, Sirikulchayanonta V, Chuansumrit A et al. Bone histomorphometry in children and adolescents with β-thalassemia disease: Iron-associated focal osteomalacia. Journal of Clinical Endocrinology and Metabolism 2003; 88(8): 3966-72. | 10.P Dandona, R K Menon, S Houlder et al. Serum 1,25 dihydroxyvitamin D and osteocalcin concentration in thalassemia major. Archives of disease in childhood 1987;62:474-77. | 11.Goyal M, Arora P, Lal H.Parathyroid and calcium status in patients with thalassemia. IJCB 2010:25(4):385-87. | 12.Huisman THJ.The structure and function of normal and abnormal haemoglobins. Clin haematol 1993;6:1-30. | 13.Aleem A, Al-Momen A K, Al-Harakati M S, Hassan A, Al-Fawaz I. Hypocalcemia due to hypoparathyroidism in β-Thalassemia major patients. Annala of Saudi Medicine 2000; 20:5-6. | 14.Zafeiriou DI, Athanasiou M, Katzos G,Economou M, Kontopoulos E. Hypoparathyroidism and intracranial calcifications in beta-thalassemia major. J Padiatr 2001; 138:411. | 15.Kontessis P, Mayopoulou-Symvoulidis D, Symvoulidis A, Kontopoulou Griva I. Renal involvement in sickle cell beta thalassemia. Nephron 1992; 61:10-15. | 16.Pratico G, Di Gregorio F, Caltabiano L, Palano GM, Caruso-Nicoletti M. Calcium phosphate metabolism in thalassemia. Pediatr med Cbir 1998;20 :265-68. | 17.Al-Jumaili A,Khider S. Prevalance of hypercalcaemia among thalassemic patients and sicklers in thalassemic center in Ibn Al-balady hospital. Proceeding of the 1st Scientific Conference on thalassemia and hemoglobinopathies in Iraq. Mosul: University of Mosul Press 2000; 28-30. | 18.Marcus N,Garty BZ.Transient hypoparathyroidism due to amphotericin B- induced hypomagnesemia in a patient with beta thalassemia. Ann Pharmacother 2001;35:1042-44. | 19. Barton, J.C. Chelation therapy for iron overload. Curr.Gastroenterol.2007;9:74-82. | 20. Voskaridou E, Kyrtsonis MC, Terpos E and Skordili M. Bone resportion is increased in young adults with thalassemia major. Br. J. Haematol 2001; 112 :36-41. | 21. El-Edel RH, Ghonaim MM, Abo-Salem OM and El-Nemr FM. Bone mineral density and vitamin D receptor polymorphism in beta thalassemia major. Pak. J. Pharm. Sci.2010; 23(1):89-96. | 22. A. Soliman, A. Adel, M. Wagdy, M. Al, N. Mullah. Calcium homeostasis in 40 adolescents with beta thalassemia major: a case control study of the effects of intramuscular injection of a megadose of cholecalciferol. Pediatric endocrinology review 2008; 1:149-54. | 23. M.Mahmoodi, V. De Sanctis, M. Karimi. Diffuse intracerebral calcification in beta thalassemia major with hypothyroidism: acese report. Pediatric Endocrinology Review2011; 2:331-33. |