An Updated Study of Some Trace Elements in Patients with Thalassemia Major

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Abstract: Enhanced years of survival of thalassemia have led to unmasking related complications changes in some important trace elements including calcium, zinc and ferritin. This study aims at investigating serum zinc, calcium and ferritin levels in children with thalassemia major. 40 children with thalassemia major attending the Hematology Clinic of Cairo University Children's Hospital with age range 6-17 years were enrolled in this study. They were subjected to history taking, clinical examinations and laboratory investigations of serum calcium, zinc and ferritin. Zinc was normal in all patients; calcium was deficient in 16 patients (11 males and 5 females), 6 of them on desferal therapy and the other 10 on defriprone therapy. Concerning growth parameters like height and weight, they were higher in patient so ndesferal than those on defriprone with P value 0.001, 0.0006 respectively. There was positive correlation between serum calcium and height (P< 0.001), positive correlation between serum ferritin and age (P= 0.047) and negative correlation between serum calcium and age (P= 0.009). We can concluded that abnormalities in trace elements especially calcium with the advance of age should be frequently investigated for immediate replacement therapy.

Key words: Calcium • Zinc • Ferritin

INTRODUCTION

Thalassemia refers to a spectrum of inherited disorders of hemoglobin synthesis characterized by reduced or lack of production of one or more globin chains [1]. The affected children with thalassemia major suffer from anemia, poor growth and abdominal enlargement due to hepatosplenomegaly. Bony complications secondary to medullary hyperplasia results in widening of diploic spaces, thinning of cortex leading to frontal bossing, prominence of upper incisors and separation of orbit [2]. Over the course of the past three decades, hyper transfusion therapy in these patients is associated with significant systemic disturbances secondary to iron overload despite the presence of different chelation modalities [3]. Biochemical disturbances in trace elements as calcium and zinc is a subject that should be investigated as it may be a precipitating factor for many complications as stunted growth, hair changes, delayed puberty and psychological changes [4].

Hypocalcaemia may result from citrate toxicity secondary to parathyroid disturbance due iron deposition and vitamin D deficiency [5]. Zinc has an important role in growth and sexual development. Chronic zinc deficiency in thalassemia major may be multifactorial due to hyperzincuria, high ferritin levels, or secondary to chelation therapy [6]. Paucity of data and lack of studies including both serum calcium, zinc and serum ferritin together in the thalassemic patients attending the Outpatient Clinic of Cairo University prompted us to plan this work where serum calcium, zinc and ferritin have been estimated.

MATERIALS AND METHODS

The study was conducted on patients with thalassemia major attending the Pediatric Hematology Clinic of Cairo University Children's Hospital. The mean age was 13.0±3.2 (6-17 years) and there were 21 males and 19 females. All patients were subjected to full history taking including, onset of disease, frequency of transfusion and chelation therapy. The study protocol was approved by the Institutional Review Committee and conformed to the ethical guidelines of the 1975 Helsinki Declaration.
Clinical Examination: Anthropometric measurements including Weight, Height and BMI.

Laboratory Investigations:
Sampling: Each patient was subjected to withdrawal of 4 ml of venous blood collected on metal free propylene tube for determination of serum zinc and calcium.

Methodology: Serum calcium was assayed according the method of Gosling [7] using Hitachi 917 autoanalyzer. Serum zinc was measured according the method of Schwartz [8] by atomic absorption spectrophotometer (Model A analyst 800; Perkin Elmer). Ferritin (450 kD) is the main storage protein for iron, containing protein shell and a crystalline core iron oxide and phosphate. Low serum ferritin level is a useful diagnostic marker for iron-deficiency anemia. High ferritin levels may indicate iron overload in the case of hemochromatosis. Elevated serum ferritin levels may also be observed in acute and chronic liver disease. Ferritin was estimated using Ferritin [21] IRMA kit according to the method of Marcus and Zilberg [9].

Statistical Analysis: Data were statistically described in terms of range, mean± standard deviation (SD), frequencies (number of cases) and percentages when appropriate. Correlation between various variables was done using Pearson moment correlation equation with graphic representation using linear regression graphs. A probability value (P value) less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs Microsoft Excel 2003 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

RESULTS

The study has been conducted on 40 patients with thalassemia major attending the Cairo University Children's Hospital for follow up. They were 21 males and 19 females.

Table 1 shows the age of cases range 6-17 years with a mean of 13.0±3.2 and the anthropometric data including weight, with a range of 15-59 and mean of 39.3±12.6, the height range 93-167 with a mean of 136±19.7 and the BMI range 9.9-36.4 with a mean of 19.4±5.7.

Table 2 shows a comparison of the clinical data between patients on Desferal therapy (n=16) and those of Defriprone there was a significant difference between the two groups only in age as the age of patients on Desferal was significantly higher than those of Defriprone with a P value <0.001.

Table 3 shows a comparison of clinical data between male patients (n=21) and females (n=19). No significant difference regarding age, weight, height and BMI body mass index between both groups and they were eleven male patients suffering from hypocalcemia and only five females.

Table 4 shows that there were 16 patients suffering from hypocalcemia six of them were on Desferal therapy and ten on Defriprone.
Fig. 1: Correlation between height (cm) and serum calcium level (mg/dL) among the study cases (p< 0.001)

Fig. 2: Correlation between age (years) and serum ferritin level (ng/mL) among the study cases (P= 0.047)

Fig. 3: Correlation between age (years) and calcium level (mg/dL) among the study cases (P= 0.009)

**DISCUSSION**

Trace elements as calcium and zinc are essential for the normal growth and development in humans. With the increased survival of thalassemic patients after the improvement in their therapeutic plans including transfusion regimen and different chelation modalities, several investigators start to study different health aspects to decrease complication and improve their life style [10]. In this study, we found that there was hypocalcaemia in 16 patients with no significant difference between them either due to sex or different chelation modalities. These results are near to those reported by Goya [11] who studied parathormone (PTH) and calcium state in Indian thalassemics. These investigators found that there are reduced levels of serum PTH and 24 h. urinary calcium in thalassemics compared to controls. Aleem [12] found that out of 40 thalassemic patients 8 patients have parathyroid disturbance and hypocalcaemia with 2 symptomatic patients.
Hypocalcaemia in thalassemics may be multifactorial either due to hypoparathyroidism due to iron overload and iron deposition in the parathyroid or secondary to the chelation therapy [13]. In this study there were 16 patients with hypocalcaemia 6 on desferal and 10 on defriprone with no significant difference yet, this can be an indication that defriprone affects calcium absorption or bone metabolism more than desferral [14].

There was a significant correlation (P<0.009) between height and calcium in the cases of the study indicating that growth was better in patients on desferal than those on defriprone. Negative correlation between calcium and age indicate that patients on defriprone may need an adjuvant calcium therapy. So, elder patients need follow up of calcium and bone scanning for modification of therapeutic plans to achieve better growth patterns. In this study, although the difference in ferritin level between patients on desferal and those on defriprone was not significant yet, it was higher in patients on desferal and those on defriprone and this indicates that defriprone is a better chelator than desferal in these patients.

Concerning zinc there were no cases suffering from zinc deficiency in the current study, other studies reported zinc deficiency in thalassemics that this may be multifactorial either due to hyperzincuria, decreased zinc binding capacity and chronic hemolysis [15]. In Tehran University of medical sciences and health service, Bekheirnia [16] reported low serum zinc levels in 84% of the cases of their study compared to controls. They reported decreased bone mineral density (BMD) in 68.7% of these patients. In that study females reported lower BMD than males and serum zinc in females with low BMD was significantly lower than other females with normal BMD and this suggests that serum levels of zinc can be lowered in the thalassemic patients and partly affect the BMD.

Finally thalassemia is a genetic blood disease, molecular evaluation using various techniques as PCR helps studying the occurrence of common mutations in families whose ethnicity indicates origin from high risk communities. Genetic and racial variations explain differences in degree of severity of the disease, occurrence of complication and metabolic disturbances including hypocalcaemia and zinc deficiency [17].

It can be concluded that hypocalcaemia in thalassemics is multifactorial and follow up of serum calcium is mandatory for modifications in the therapeutic plans and to achieve better growth. Patients on defriprone should receive more adjuvant calcium therapy than those on desferral.

Conflict of Interest: The authors declare that there was no conflict of interest to this manuscript.

REFERENCES


