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Alteration of serum calcium and magnesium level in transfusion dependent thalassemic patients with combined iron chelator therapy

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Abstract

Background: Regular blood transfusion and iron chelation is the primary treatment of thalassemia patientsto maintain their life. Iron chelatormay alter serum total calcium and magnesium level in TDT patients. **Objective:** To evaluateany alteration of serum total calcium and magnesium level in transfusion dependent thalassemia patients treated with iron chelator. **Method:** The present cross sectional study was carried out in the department of Physiology, BSMMU, Dhaka between September 2017 to February 2019. Thirty cases of TDT, aged 5-40 year were included in the study group. Age and sex matched 30 healthy subjects were also studied as control. All the TDT patients were selected from the outpatient Department of Hematology and Transfusion Medicine, BSMMU, Dhaka. Serum total calcium, magnesium and ferritin levels were measured by colorimetric method. For statistical analysis independent sample t test and Chi-Square test and Pearson correlation coefficient test were used. **Result:** The mean serum total calcium and magnesium levels were significantly ($p<0.05$) lower and serum ferritin level was significantly ($p<0.001$) higher in study group compared to that of control. Again, in this study group 6.7 % TDT patients had hypocalcemia and 13.3% TDT patients had hypomagnecemia. **Conclusion:** This study may conclude that low serum total calcium and magnesium level may be associated with TDT patients treated by combined deferoxamine (DFO) & deferiprone (DFP) iron chelator.

Key words: TDT, total calcium, magnesium, iron chelators (DFP and DFO).

Introduction

Thalassemia is a group of autosomal recessive hereditary blood disorder in which there are defective synthesis of alpha or beta globin subunit of hemoglobin.[1-2] About 150 million people carry the thalassemia gene worldwide but it is most common in Mediterranean regions, Middle East, part of Africa, Central Asia, India sub-continent, Southern China and into the Pacific island.[2-4] According to World Health Organization about 3% population are carrier of beta thalassemia and about 4% population are carrier of Hb-E in Bangladesh.[5-6]

The principal treatment of thalassemia involve blood transfusion to correct anemia.[1] The repeated blood transfusion may lead to accumulation of excess iron in the body causing oxidative stress and organ damage. [3-5] The most common cause of death is heart failure due to transfusional iron overload.[1] So, several iron chelators have been used to remove the excess iron from the body.[3] Currently there are three approved commercially available iron chelators – deferoxamine (DFO), deferiprone (DFP), deferasirox (DFX).[7]

Ferritin binds with iron and stores excess iron within the cell and iron overload causes high concentration of serum ferritin. Therefore, estimation of serum ferritin is the most commonly used, easy and in-expensive test to evaluate iron overload in patients with thalassemia.[8-10]

Calcium is the main component of the body. More than 99% is stored in the bones and teeth. Less than 1% is found in extracellular fluid. Calcium is required for vascular contraction and vasodilation, muscle function, nerve transmission, intracellular signaling and hormonal secretion. Calcium deficiency causes fatigue, neuromuscular instability, numbness and tingling sensation of extremity, muscle cramp, chest pain, irritability.[11-15]

Magnesium play an essential role in the activity of many enzymes involved cellular metabolism. It act as a modulator in cell volume regulation, immune system, cardiovascular system and musculoskeletal system. Deficiency of magnesium causes fatigue, muscle cramp, irregular heart beat, neuromuscular instability, hypertension, diabetes.[11,13] Data on these minerals in TDT patients treated with iron chelator is vary few. Therefore, this study has been designed to evaluate calcium, magnesium and ferritin levels in TDT patients with iron chelator. Data on these minerals in TDT patients treated with iron chelator is very few. Therefore, this study has been designed to evaluate any alteration of serum total calcium and magnesium levels in TDT patients treated with iron chelator.

Methods

The present cross sectional study was carried out in the department of Physiology, BSMMU, Dhaka between September 2017 to February 2019 and protocol of this study was approved by Institutional Review Board, BSMMU, Shahbag, Dhaka. Serum total calcium, magnesium, ferritin and Hb levels on 30 TDT patients treated with combined iron chelator (DFP) and (DFO) and 30 healthy subjects (control), age ranged from 5-40 year were assessed. TDT patients were selected from outpatient Department of Hematology and Transfusion Medicine, BSMMU and control were selectedamong the relatives and attendants of patients, hospital staff and subjects available in the BSMMU campus and also personal contact. Subjects with history of renal disease, any acute and chronic disease, vitamin and minerals supplementation were excluded from

the study. After selection of the subjects, the purpose of the study was explained to each subjects and informed written consent was taken. Detailed family and medical history, Anthropometric measurement were recorded. For estimation of serum total calcium, magnesium, ferritin and Hb levels 5 ml of venous blood was collected from ante-cubital vein under aseptic precaution from each subject and serum was prepared for these biochemical tests.Serum total calcium, magnesium and ferritin was measured by colorimetric method. Data were expressed as Mean±SE. Data analysis was done with SPSS version 16. For statistical analysis independent sample t test and Chi-Square test and Pearson correlation coefficient testwere performed.

Results

In this study, all the groups were matched for age and sex but BMI ($p<0.05$) and Hb ($p<0.001$) were significantly lower in TDT compared to that of control (Table I). Mean serum total calcium and magnesium levels were significantly ($p<0.001$) lower and mean serum ferritin was significantly ($p<0.001$) higher in TDT patients compared to that of control (Table II).

Table I: Age, BMI and Hb inboth groups (N=60)

Parameter	Control (n=30)	TDT (n=30)
Age (years)	19.86±1.57	19.66±1.68
Male no(%)	15(50%)	15(50%)
Female no(%)	15(50%)	15(50%)
BMI (Kg/m^2)	21.87±0.89	18.54±0.56*
Hb (g/dl)	13.75±0.19	7.78±0.36***

Data are expressed as Mean±SE. Statistical analysis was done by independent sample t test and Chi-Square test. BMI-Body mass index; Hb-Hemoglobin; TDT-Transfusion dependent thalassemia; *p<0.05, ***p <0.001.

Table II: Serum total calcium, magnesium and ferritin levels in both groups (N=60)

Parameter	Control (n=30)	TDT (n=30)
Serum total calcium (mg/dl)	9.1±0.08	8.62±0.14***
Serum magnesium (mg/dl)	1.91±0.02	1.76±0.03***
Serum ferritin (µg/L)	40.39±7.68	6276.85±709.82***

Data are expressed as Mean±SE. Statistical analysis was done by independent sample t test. TDT-Transfusion dependent thalassemia; ***p <0.001.Cut point for total calcium-8.1mg/dl, cut point for magnesium-1.6 mg/dl

Again, in this study 6.7% TDT patients had hypocalcemia and 13.3% TDT patients had hypomagnecemia.No control had hypocalcemia or hypomagnecemia (Table III).

Table III: Frequency of subjects by hypozcalcemia, hypomagnecemia in different groups (N=60)

Parameter	Control (n=30)	TDT (n=30)
	no (%)	no (%)
Hypocalcemia	00 (0)	2 (6.7)
Hypomagnecemia	00 (0)	4 (13.3)

Data are expressed as %. TDT-Transfusion dependent thalassemia

In addition serum total calcium level was positively correlated and serum magnesium level was negatively correlated with serum ferritin level in study group (Figure 1,2). Moreover, serum serum total calcium and magnesium both were negatively correlated with duration of iron chelation therapy (Figure 3,4). All these correlations were statistically non-significant.

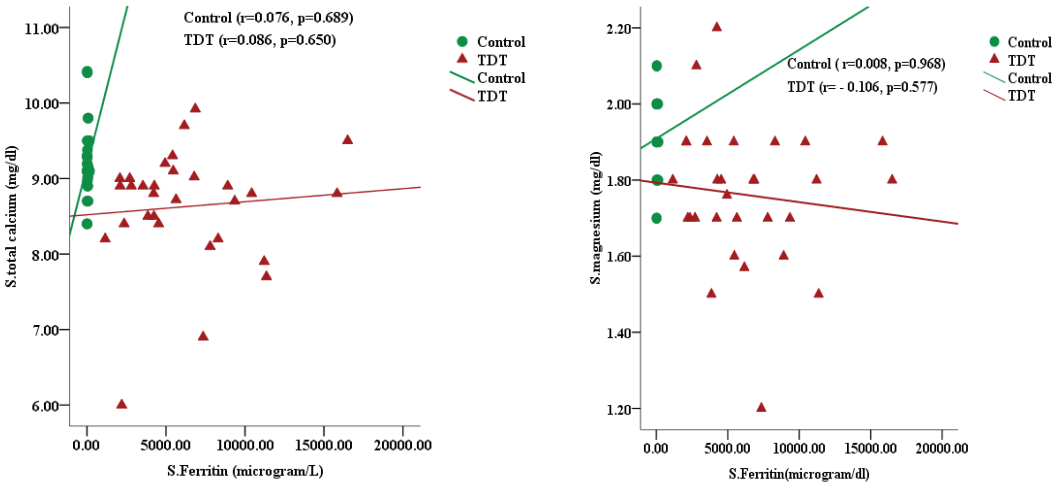

Figure 1: Correlation of serum total calcium and magnesium levels with serum ferritin level. Statistical analysis was done by Pearson's correlation coefficient test. TDT- Transfusion dependent thalassemia.

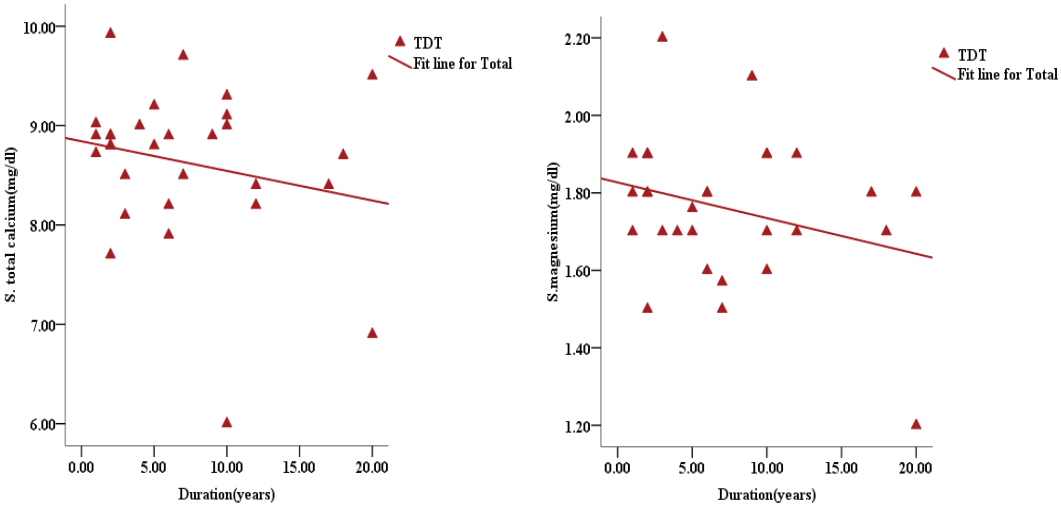

Figure 2: Correlation of serum total calcium and magnesium levels with duration of iron chelation. Statistical analysis was done by Pearson's correlation coefficient test. TDT- Transfusion dependent thalassemia.

Discussions

The present study observedany alteration of serum total calcium and magnesium levels in TDT patients treated with combined iron chelator.

The result of this study showed significantly lower serum total calciumand magnesium level in all TDT patientstreated with combined (DFP+DFO) iron chelatorthan control. On the other hand, Salva found significantly lower and Either et al. found non-significantly lower serum calcium level in TDT patient treated with DFP and DFO iron chelator separately.[16-17] Again, Genc et al. found significantly lower serum

magnesium level in TDT patient treated with only DFO iron chelator.[8] Moreover significant number of TDT patients in this study were suffering from calcium and magnesium deficiency.

In this study, non-significant positive correlation of serum calcium and negative correlation of serum magnesium with serum ferritin level was observed. Genc et al. also found negative correlation of serum magnesium with serum ferritin in TDT patient with DFP iron chelator[8].In addition, serum total calcium and magnesium levels were negatively correlated with duration of iron chelation therapy.

The presence of calcium and magnesium deficiency in the TDT patients under combined chelator therapy cannot be explained from this study. Various literaturesuggested that binding of iron chelator with metal depend on stability constant of metal ion, relative concentration of metal cation in blood and heterocyclic ring formation. In our body fluid calcium is readily available that is why calcium may first bind with chelator than other higher stability constant of metal such as iron and lead[18].Magnesium may form more number of heterocyclic ring with iron chelator. For this iron chelator may remove magnesium from the body along with iron[18-19].

Moreover, minerals alteration in TDT patients may be due to oxidative stress, excessive hemolysis, dietary deficiency, psychological problems (such as depression), metabolic and endocrine complications[20-21].

Conclusion

After analyzing the result of the study, it can be concluded that low serum calcium and magnesium level may occur in TDT patients treated with combined (DFP + DFO) iron chelator. So, estimation of serum total calcium and magnesium level may be helpful for proper management of TDT patients.

Conflict of interest None.

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