

ALTERATION IN TRACE ELEMENTS (S.IRON, S.ZINC, S.COPPER) IN THALASSEMIA MAJOR PATIENTS AFTER CHELATION THERAPY

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ABSTRACT

Introduction: Alterations in various trace element serum iron, serum copper and serum zinc in patients suffering from beta thalassemia major patients who are undergoing blood transfusion and receiving chelation therapy.

Objective: Present study was conducted to evaluate the effect of iron chelation therapy on trace elements (Iron, Copper, Zinc) in patient of beta thalassemia. **Materials and Method:** In the present Cross Sectional study, samples of 50 cases and 50 controls (normal healthy persons) were selected from Civil Hospital Ahmedabad (CHA), Gujarat. Serum Iron, serum Zinc, and serum copper levels were measured on XL-640 fully-auto biochemical analyser.

Results: Results showed increase in serum Iron and Copper in patients with compared to normal subjects while serum Zinc decreased in patients as compared to healthy subject. **Conclusion:** This study clearly shows a positive association between increased serum Iron and Copper while decrease serum Zinc in beta thalassemia major patients who are undergoing blood transfusion and receiving chelation therapy.

Keywords: Beta Thalassemia, Iron, Zinc, Copper.

INTRODUCTION

The term thalassemia is derived from the Greek words, “Thalassa” means “sea” and “haimia” means “blood”. The thalassemias are the group hereditary anemias caused by mutations which affect the synthesis of the globin chains, the protein component of hemoglobin. Thalassemias are massive public health problems in many parts of the world. They are one of the most commonest genetic diseases of humans and have been encountered practically in every ethnicity and geographic location in the world, however, they are most common in the Mediterranean, the equatorial, and near equatorial regions of Africa and Asia. (1, 2)

Thalassemias are classified according to the defect produced particular globin chain(s), which may cause

imbalance in globin chains synthesis, which may lead to ineffective erythropoiesis, hemolysis, and ultimately anemia. The Different types of thalassemias are α , β , $\delta\beta$, δ , and $\gamma\delta$. The most common classes of thalassemias are α and β thalassemia, and the most important and widely spread type is β thalassemia, in the homozygous and compound heterozygous states causes severe anemia. Thalassemias are classified clinically according to the severity of thalassemia major which requires blood transfusion regularly throughout life. It is also known as “Cooley’s Anemia” and “Mediterranean Anemia”. Thalassemia intermedia there is anemia but does not require regular blood transfusion, and asymptomatic carrier state is called Thalassemia minor. (1, 2)

The severity of the clinical manifestations of, β -thalassemia depends on the type of mutation in the gene. Most types of β -thalassemias are caused by point mutations, and large deletion mutations are found in rare cases. (3)

These mutation in β globin chains causes RBC destruction. Patient develop anemia, to compensate anemi, RBC stem cell shows accelerated erythropoiesis which may be ineffective because excess α globin chains which interfere with RBC maturation. The RBC are destroyed in bone marrow and ineffective erythropoiesis results in significant erythroid marrow expansion, abnormal skeletal development, characteristic deformities of the skull and face, anemia and over absorbtion of iron from small intestine.4

Blood transfusions are necessary to maintain pre-transfusion hemoglobin levels between 9.5g/dl to 10.5g/dl and to prevent other malfunctions. However, humans excrete limited amount of iron, so regular blood transfusion cause iron overload. Extra iron get deposited in the liver, heart, pancreas, thyroid, parathyroid, adrenal, renal medulla, bone marrow, and spleen. This parenchymal iron deposition is the one of the cause of morbidity and mortality in the β -thalassemias. The management of severe forms of the β -thalassemia diseases includes: regular transfusion of blood, removal of overloaded iron from blood with chelating agents such as deferoxamine, deferiprone or deferasirox and splenectomy when rate of transfusion is increasing. (5,6)

MATERIALS AND METHOD

Study Area: In the present study, 50 known cases of Beta Thalassemia major receiving chelation therapy for more than 1 year and 50 healthy subjects as a control group were studied. They were first diagnosed by clinical examination and further by Biochemical investigations. All cases were admitted to the Pediatric ward. The control group were selected from pediatric OPD at Civil Hospital, Ahmedabad.

Inclusion criteria: Study includes confirmed cases of Beta-Thalassemia major of both sex within age of 15 years, receiving chelation therapy for atleast 1 year

Exclusion criteria: We excluded patients aged more than 15 years. Known case of Liver disease, Cardiac disease, Renal disease, Cardiac disease, Protein energy malnutrition, Trauma: Surgical, Burns, Fractures,

Malignancy: Lymphoma, Carcinoma, Sarcoma, Leukemia

Biochemical analysis: 5ml venous blood drawn with patients consent samples were collected under all aseptic measures. Following Laboratory Investigations were done in study group and control group. Serum Iron, Serum Zinc, Serum Copper and analysis were done on fully auto analyzer ERBA XL – 640 at Hi-Tech Biochemistry Laboratory Civil, Hospital, Ahmedabad.

Data analysis: The Master chart was prepared using Excel 2007 software. Data were expressed as mean \pm standard deviation. Student t-test of two independent samples was used to compare between means. P values \leq 0.05 was considered as statistically significant. The statistical package for social sciences (SPSS version 20) was used to perform statistics.

RESULTS

Serum iron, zinc and copper concentrations in both thalassemia major patients and control are shown in table 1. The results clearly shows that in present study there is significant increase ($p < 0.001$) of iron concentration ($149 \pm 15.59 \mu\text{g/L}$) in comparison to control healthy subjects ($103 \pm 15.27 \mu\text{g/L}$). Serum copper concentration was increased significantly ($p < 0.001$) in patients ($97 \pm 10.82 \mu\text{g/L}$) when compared to control group ($141 \pm 15.17 \mu\text{g/L}$). On the other hand, Zinc was decreased significantly ($p < 0.001$) in β -thalassemia major patients ($70 \pm 8.78 \mu\text{g/L}$) in comparison to healthy subjects ($100 \pm 13.15 \mu\text{g/L}$).

Table 1:

	Metal ion concentration in study group and control group				
	Study Group		Control Group		P value
	Mean	SD	Mean	SD	
Iron	148.94	15.59	103.62	15.27	<0.001
Zinc	69.82	8.78	100.14	13.15	<0.001
Copper	141	15.17	95.84	10.82	<0.001

DISCUSSION

In Present study, it is clear from the results that a significant increase ($p < 0.001$) of iron concentration ($148 \pm 15.59 \mu\text{g/dL}$) in patients of beta thalassemia who are receiving regular blood transfusion and are on

chelation therapy in comparison to control healthy subjects ($103.62 \pm 15.27 \mu\text{g/dL}$), which correlate with other studies. Patients of beta thalassemia major require frequent blood transfusions which lead to iron overload in the absence of effective chelation therapy.^{7,8,9}

In present study serum zinc levels were found significantly decreased $69.82 \pm 8.78 \mu\text{g/dL}$ in study group and $100.14 \pm 13.15 \mu\text{g/dL}$ in the control group. ($p < 0.001$). Other studies conducted support the finding of present study. **(7, 9)**

In recent studies, decreased antioxidant levels and increased oxidative stress biomarkers were found in thalassemia major. Chronic iron overload, hemolysis, and inflammation causes chronic oxidative stress due to which there is increased consumption of vitamins and trace minerals. Increased urinary Zn excretion is one of the side effects of Iron chelators. **(11, 12)**

The above table 1 illustrates that in present study there was a significant increase in the levels of serum copper in cases all ($141 \pm 15.17 \mu\text{g/dL}$) as compared with the control groups ($95.84 \pm 10.82 \mu\text{g/dL}$) of the same ages ($P < 0.001$). These findings are supported by other studies. **(7, 9, 10)**

These observations could be explained by the antagonistic effect of the other metal ion like zinc, as zinc deficiency in beta-thalassaemia major could greatly increase copper absorption via the gastrointestinal tract. This negative correlation can be attributed to that elements having similar orbital valency might compete for specific binding sites on proteins involved in their absorption and perhaps also during de novo synthesis of metal isoenzyme. **(6, 10)**

CONCLUSION

We conclude that the chelation therapy causes significant effect on concentration of trace elements that was reflected by their altered serum levels.

The levels of serum iron were found to be elevated in patients of β thalassemia ($p < 0.001$).

Serum zinc levels were found to be decreased in study group ($p < 0.001$)

The levels of serum copper were found to be elevated in patients of β thalassemia ($p < 0.01$).

Chelation therapy alter blood level of Iron as well as other trace elements like Zinc, Copper which plays an important role in many biological system because they

participate in various bio-chemical reaction in human body.

Thus, there is a need of close monitoring of serum zinc and copper along with serum iron levels in patients receiving chelation therapy. This may help in promoting normal growth and development. Their serum levels could be used as diagnostic marker to prevent complications.

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