An oral trace element supplementation has a potential beneficial effect on glucose homeostasis in transfused patients with β-thalassemia major complicated with diabetes mellitus

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INTRODUCTION

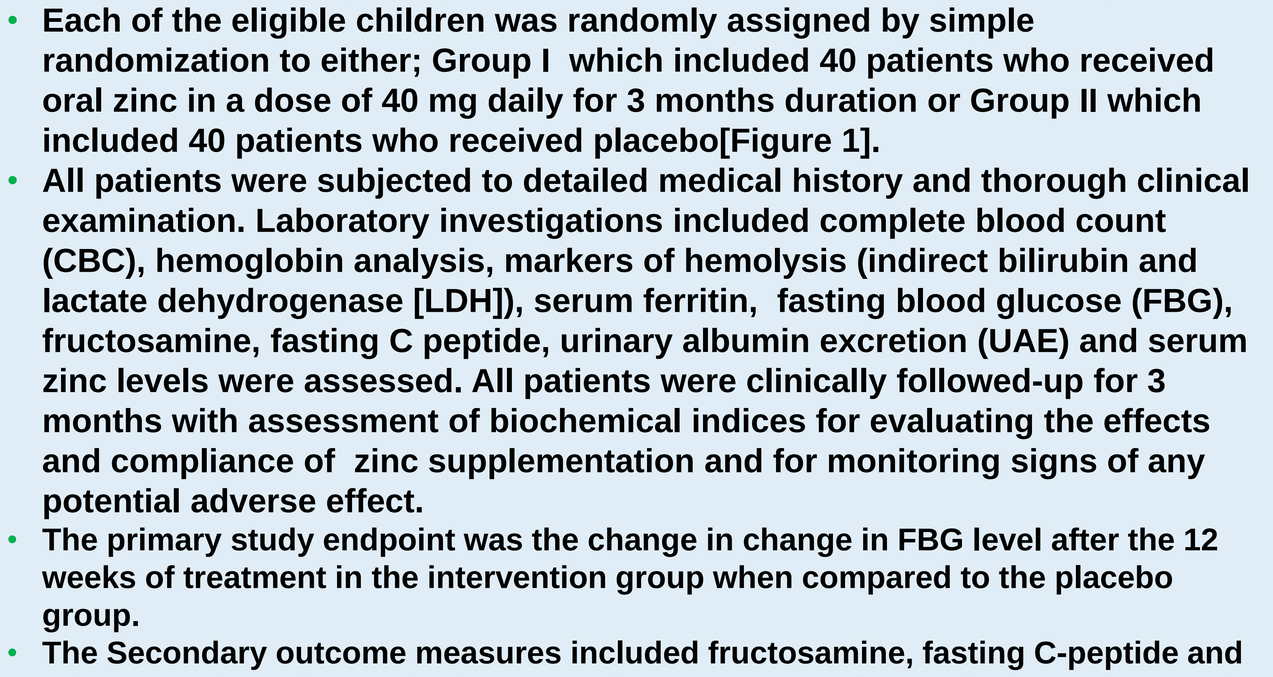
- β-thalassemia major (β-TM) is the most common genetically determined chronic hemolytic anemia. Studies reported that patients with β-thalassemia are zinc deficient due to ĺncreased utilization of zinc by oxidative stress, increased urinary zinc excretion and sequestration in the liver.
- The development of abnormal glucose tolerance in β-TM is associated with alteration in oxidant-antioxidant status. Zinc plays an essential element for insulin synthesis, storage and secretion.

AIM OF THE WORK

- The aim of this study is to investigate the effect of zinc supplementation on glucose homeostasis in pediatric patients with β-TM complicated with diabetes mellitus (DM) and its relation to clinical and laboratory parameters of these patients.

SUBJECTS AND METHODS

- ***Study design*** : Eighty patients with β-TM (aged ≥10 years old) were recruited from the regular attendants of the Pediatric Hematology Clinic.
- ***Inclusion criteria*** :Transfusion dependent β-TM patients with DM treated with insulin and aged 10-18 years old. Diagnosis of β-TM was confirmed by history, examination and investigations including complete blood count (CBC), reticulocyte count, markers of chronic hemolysis and hemoglobin analysis using (HPLC) . DM was defined using oral glucose tolerance test (OGTT) and diagnosed according to American diabetes association criteria.
- ***Exclusion criteria***: Other hemoglobinopathies as alpha thalassemia or sickle thalassemia patients, other disorders that may affect glucose homeostasis rather than β-TM, autoimmune disease, collagen diseases, hypo- or hyper-thyroidism, infections, tumors .Those who were taking any vitamins or food supplements one month before study and participating in a previous investigational drug study within three months preceding screening.
- Each of the eligible children was randomly assigned by simple randomization to either; Group I which included 40 patients who received oral zinc in a dose of 40 mg daily for 3 months duration or Group II which included 40 patients who received placebo[Figure 1].
- All patients were subjected to detailed medical history and thorough clinical examination. Laboratory investigations included complete blood count (CBC), hemoglobin analysis, markers of hemolysis (indirect bilirubin and lactate dehydrogenase [LDH]), serum ferritin, fasting blood glucose (FBG), fructosamine, fasting C peptide, urinary albumin excretion (UAE) and serum zinc levels were assessed. All patients were clinically followed-up for 3 months with assessment of biochemical indices for evaluating the effects and compliance of zinc supplementation and for monitoring signs of any potential adverse effect.
- The primary study endpoint was the change in change in FBG level after the 12 weeks of treatment in the intervention group when compared to the placebo group.
- The Secondary outcome measures included fructosamine, fasting C-peptide and HOMA-IR. The safety endpoints were the occurrence of any adverse events such as nausea, vomiting, abdominal pain, diarrhea, constipation and reduction of appetite during study period.



Figure[1]:Download CONSORT flow diagram for the enrolled patients with β-thalassemia major complicated with diabetes mellitus.

RESULTS

- Comparison between baseline clinical and biochemical data among β-TM patients in both groups showed no significant difference.
- In our study, all the enrolled thalassemia patients had significantly lower zinc levels compared with healthy controls (p<0.001).
- At 12 weeks, LDH, serum ferritin, FBG ,fructosamine and UAE were significantly lower while hemoglobin levels and fasting c peptide were significantly higher after zinc supplementation compared with baseline levels or with placebo group (p<0.05) [Figure 2].
- Baseline serum zinc was negatively correlated to FBG (r=-0.534, p<0.001) [Figure 3] and fructosamine (r=-0.555, p<0.001) while positively correlated to fasting C peptide (r=0.777, p=0.002).

Variables	β-TM patients with zinc supplementation		p value
	At baseline (n=40)	At 12 weeks (n=39)	
FBG (mg/dL)	148.8 ± 21.5	116.9 ± 4.6	<0.001*
RBG (mg/dL)	193.8 ± 25.9	162.5 ± 13.2	<0.001*
Fructosamine (mg/dL)	408.6 ± 84.0	282.1 ± 51.4	<0.001*
Fasting C peptide (ng/mL)	0.88 ± 0.2	1.5 ± 0.5	0.002*
HOMA-IR	2.5 ± 1.1	1.7 ± 0.4	0.029*
Insulin dose (IU/Kg/day)	0.94 ± 0.3	0.71 ± 0.2	0.076
Serum zinc (µg/dL)	60.4 ± 9.6	81.92 ± 13.6	<0.001*

Figure [2]:Comparison of glycemic profile and zinc level among β-TM patients with zinc supplementation at baseline and at 12 weeks.

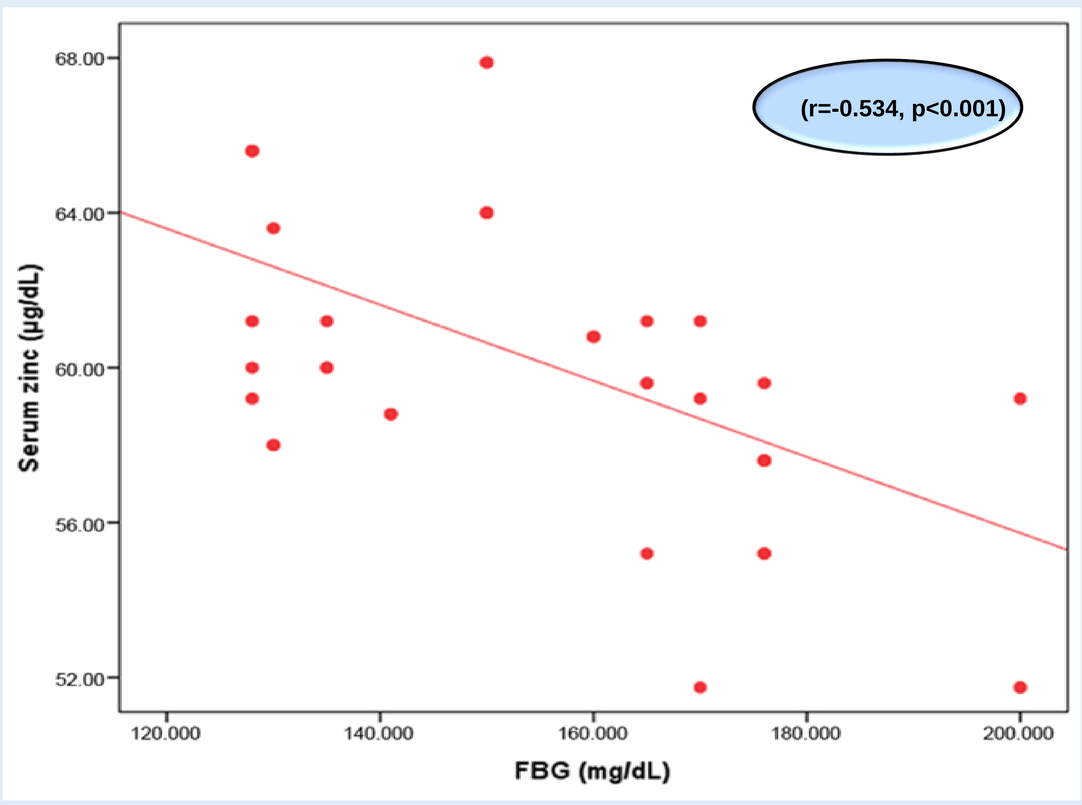


Figure [3]:Significant negative correlations between baseline serum zinc and fasting blood glucose.

CONCLUSION

- The present study concluded that supplementation with zinc was well tolerated with no side effects were reported throughout the study.
- Zinc intake for three months represents a potential therapeutic adjuvant agent decreasing hyperglycemia, improving insulin secretion, glycemic control and increasing the efficacy of iron chelation therapy in reducing hemolysis, iron burden and elevating hemoglobin levels among pediatric patients with β-TM.
- Further studies including larger number of patients and higher doses of zinc depending on the degree of its deficiency with longer duration of follow-up are needed for better results profiling.