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Zinc Supplementation Effect on Linear Growth in Transfusion Dependent β Thalassemia

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Abstract

Objective: Thalassemic patients are at risk of zinc deficiency due to various causes including desferal injection, hyperzincuria, high ferritin levels, and hepatic iron overload. We evaluate the effect of zinc supplementation on linear growth of beta-thalassemia patients.

Methods: one-hundred beta-thalassemic major patients whose heights were within 3rd to l0th percentile were randomly divided into two groups, each group consist of 50 patients: Group I received oral zinc (60 mg per day) and Group II served as control group without zinc supplement. Patients were followed for 18 months and we control height. Data was analyzed by SPSS 11.5 software by nonparametric and T test.

Results: The mean age and height of the patients in Group I were 8.14±1.30 year and 120.83 ±6.41cm, and in Group II, 8.27±1.14 year and 121.85 ±6.18cm, respectively. Eighteen months later the mean height was 125.14±6.17 cm in Group I and 126.1±6.07 cm in Group II (P = 0.464).

No statistically significant difference in height was noted between the two groups after a period of eighteen months (P=0.464).

Conclusion: The results of the research revealed that whereas the role of zinc has been proved in the growth process. It is concluded that oral zinc sulfate has no significant effect on linear growth of beta-thalassemia patients.

Keywords: zinc, thalassemia, linear growth

Introduction

The thalassemias are characterized by an inherited defect in the synthesis of one or more of the peptide chains of hemoglobin (1-6). A serious problem in thalassemia major is growth impairment and clinicians have noticed growth retardation in patients with homozygous thalassemia. Biochemical changes, especially of the essential trace minerals such as zinc have been investigated in homozygous thalassemia (7). Zinc is an essential element in many metabolic activities in human such as DNA synthesis cellular growth and protein synthesis. Zinc absorbs in small intestine and over 80% of zinc binds to albumin in blood circulation. Zinc deficiency causes growth retardation, alopecia, diarrhea and weight loss in human. (7,8)

Urinary zinc excretion is increased with hemolysis, as seen in thalassemia. (1-6,8) Also, desferrioxamine use increases urinary zinc excretion.(4,5) Another explanation for growth retardation in beta- thalassemia may be somatomedin deficiency. (9) Other causes of growth delay in transfusion dependent thalassemia are included chronic anemia, genetic factors,

hypersplenism, cardiomyopathy, folate deficiency and endocrinopathy (9,10). Trace metal deficiency associated with thalassemia or aggressive chelation therapy is not commonly observed (11) .An occurrence of zinc deficiency in thalassemia has been reported but for detection of this status needs newer technique to analyze zinc concentration. It is well known that somatomedins mediate growth by contributing to the effect of growth hormone and they require zinc to be synthesized in the liver. Short stature, low body weight, anorexia, and hypogonadism found in the zinc deficient patients, (7-10) are also found in most of the patients with thalassemia.

In this study the effect of oral zinc supplementation on linear growth of homozygous beta-thalassemia patients were assessed in a case control manner.

Materials & Methods

Patients

This is a case-control prospective study on one hundred cases of beta-thalassemia major that were referred to the Thalassemia care and Research Center, Shahid Dastgheib Hospital. 49 cases were male and 51 cases were female. Patients were randomized in two groups with age range of 6 to 10 years and 3rd to l0th percentile height.

Group I: The case group was 50 beta-thalassemia major patients who received zinc supplement in addition to conventional blood transfusion and chelation (desferrioxamine) therapy. Zinc was given as zinc sulfate in the form of capsule or syrup, 60 mg once a day, for 18 months.

Group II: The control group included 50 sex and aged-matched beta-thalassemia major patients who treated by conventional transfusion and chelation (desferrioxamine) therapy without zinc supplementation.

The height of the patients of both groups was measured at the beginning of the study, 3, 6, 12 and 18 months later. The data were filling in form.

Statistical Analysis

The data were analyzed by SPSS 11.5 soft ware. We used nonparametric and t-test for independent samples of group. The result recorded as Mean±SD.

Results

The mean age and height of the patients in Group I were 8.14±1.30 year and 120.83 ±6.41cm, and in Group II, 8.27±1.14 year and 121.85 ±6.18cm, respectively. The mean weight of patients in Group I were 22.76±3.23 kg and in Group II 23.27±2.61 kg, respectively. The mean height of the patients three months after the beginning of the study in Group I was 121.67± 6.44cm, and in Group II 122.84± 6.47 cm (P= 0.316).

Six months later it was 122.84±6.42 cm in Group I, and 124.03 ± 6.27 cm in Group II (P = 0.298).

Twelve months later in Group I was 122.09±14.54 cm and in Group II 125.11±6.16 cm (P= 0.191).

Eighteen months later the mean height was 125.14±6.17 cm in Group I and 126.1±6.07 cm in Group II (P = 0.464). (Table 1)

Discussion

Growth disturbance is a major clinical feature of patients with beta-thalassemia major.(11) Failure of physical growth in beta-thalassemia major may be the result of chronic anemia, folate deficiency, hypersplenism, endocrine disorders (hypogonadism, hypothyroidism, growth hormone deficiency), chronic liver disease, iron overload, desferrioxamine (DFO) toxicity and zinc deficiency.

Table 1: *The mean height and standard deviation of 2 groups of children with Cooley's anemia at the beginning, 3,6,12 and 18 months after starting zinc therapy. Group I: group receiving zinc sulphate. Group II: control group*

	0 months		3 months		6 months		12 months		18 months	
	Mean Ht	SD	Mean Ht	SD	Mean Ht	SD	Mean Ht	SD	Mean Ht	SD
Group I	120.83	6.41	121.67	6.44	122.84	6.42	122.09	14.54	125.14	6.17
Group II	121.85	6.18	122.84	6.47	124.03	6.27	125.11	6.16	126.10	6.07
P value	NS	NS	0.316		0.298		0.191		0.464	

(12)

Factors such as derangement in function of the hypothalamic-pituitary-gonadal axis, abnormal hepatic conversion of steroids to their active metabolites and defective hepatic biosynthesis of somatomedin C have been postulated as factors contributing to these abnormalities (9,11).Another survey show a temporally cumulative damage to growth mediating mechanisms except those considered here is responsible in growth failure in thalassemia major(13). A gonadal function was found in 68% of thalassemic patient's (14).since the quality of life of these patients is an important aim, it is vital to monitor carefully the growth and pubertal development in order to defect abnormalities and to initiate appropriate and early treatment (15). Short stature and hypogonadism are extremely frequent in thalassemia, but correct blood transfusion and appropriate iron chelation therapy can prevent growth delay (16,17). Zinc deficiency in the presence of hyperzincuria in patients with beta-thalassemia has been postulated as a probable cause of delayed linear growth in these patients. (1, 2, 12). Also desferrioxamine use increases urinary excretion of zinc. (9). Moreover, it is well known that somatomedins mediate growth by contributing to the effect of growth hormone and they require zinc to be synthesized in the liver. In one study showed the mean serum zinc level significantly higher in thalassemia (17-20). No significant correlation between serum zinc level and short stature, serum ferritin level and Desferioxamine dose (18). Also in another study zinc deficiency was present in 10% of thalassemia and 52% of those had some degree of depression.(16.19)

Previous studies have shown that zinc deficiency is a growth-limiting factor in thalassemia major and linear growth in thalassemia patients who received zinc supplementation is equal to that of normal healthy children (1, 10,21). Moreover, experiments have shown that plasma somatomedin-C correlates with zinc status in animals and the activity of somatomedin-C decreases as a result of dietary zinc deficiency (13,22,23). On the other hand, growth retardation is a common feature of zinc deficiency in human and animals (7,20,24). Therefore, zinc deficiency observed in thalassemic patients due to chronic hemolysis, desferrioxmine therapy and increased urinary excretion might delay their growth through decreased somatomedin-C synthesis(21,25,26). In fact, zinc supplementation may increase hepatic synthesis of somatomedin-C. (19-22)

We could not study zinc status of our patients due to technical limitations but growth response to zinc supplementation has been considered as one of the most acceptable criteria of zinc deficiency. The results of our study revealed that although the role of zinc has been proved in the growth process, use of exogenous zinc in beta-thalassemia major patients couldn't improve their linear growth defect. One explanation may be that with modern transfusion regimens and desferrioxamine use with appropriate dose, the possibility of the deficiency is low and so the patients do not respond to zinc therapy because they are not zinc deficient. The results of the research revealed that whereas the role of zinc has been proved in the growth process.

In conclusion prophylactic oral zinc sulfate has no effect on linear growth of patients with beta-thalassemia major and should be used only in zinc deficient patients.

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