Serum Trace Element Levels In Sickle Cell Disease Patients In An Urban City In Nigeria

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ABSTRACT: Assessment of serum trace element levels was carried out in a total of eighty (80) subjects comprising of forty (40) sickle cell disease patients attending the sickle cell centre, Benin City and forty (40) age and sex matched apparently healthy control subjects. Blood samples collected from participants were analyzed for trace elements using atomic absorption spectrophotometer. The mean serum level of magnesium, zinc, manganese, copper, selenium and chromium in sickle cell disease patients were 11.03±1.77mg/L, 120.85±10.29µg/dL, 68.30±3.63µg/dL, 68.54±10.49µg/L, 60.98±7.29µg/L and 62.90±5.97µg/L respectively. Serum magnesium, zinc and selenium levels were significantly lower ($p<0.05$) while serum manganese levels were significantly higher ($p<0.05$) in sickle cell disease patients when compared with apparently healthy control. Serum trace metal levels was not age or sex dependent, as similar pattern of serum trace metals was observed in both male and female sickle cell disease patients. Conclusively, assessment of trace element levels is vital in the management of sickle cell disease. Supplementation with deficient trace elements may reduce the severity of symptoms and complications associated with sickle cell disease, thereby improving the chances of survival in sickle cell disease.

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INTRODUCTION

Sickle cell disease is an inherited blood disorder that affects red blood cells. People with sickle cell disease have red blood cells that contain mostly hemoglobin S, an abnormal type of hemoglobin. In certain situation, these red cells become sickle and have difficulty in passing through blood vessels (Platt, 2000; Platt et al., 2004). Although sickle cell disease is present from birth, symptoms are rare before the age of 3 to 6months since a large percentage of the erythrocyte hemoglobin is of the fetal type (Hb F). As more Hb S replaces Hb F in the subject, the main symptoms; episode of anemia, pains and infections and associated crisis become manifested due to irreversible sickling of the erythrocytes when Hb S molecules polymerizes invariably leading to vaso-occlusion in the small capillaries (Durosinmi et al., 1993). Trace elements are essential inorganic molecules found in minute quantities of milligram or microgram per kilogram of body weight. Trace elements include zinc, copper, selenium, manganese, chromium, magnesium, fluorine, cobalt, iron and iodine. Some such as lead, cadmium, arsenic, aluminium and nickel are classified as pharmacologically beneficial and toxic hence monitoring of dosage is required (Burtis et al., 2008).

People with sickle cell disease suffer from many micronutrient deficiency but preliminary research on dietary habits show that food and nutrient intake by sickle cell patients meet or exceeds recommendation and is not significantly different from healthy controls. This suggests that higher rates of nutrient deficiency may be due to increased needs of many nutrients in sickle cell patients. (Tagney et al., 1989). The global use of micronutrients in health care delivery system has taken central stage due to the realization of their importance in disease management. Sickle cell disease is among the disease plaguing a sizeable population of the developing world and the cost implication of its management is very high. Sickle cell disease is characterized by anemia and immunological disturbances. Free radicals are generated in sickle cell disease; hence a balance between minerals and antioxidants is imperative in maintaining red cell membrane integrity and function (Okpuzor and Okochi, 2009). Protection of red cell membrane from free radical mediated oxidative stress is crucial to the management of sickle cell disease. Minerals such as copper, zinc, iron, chromium, magnesium, selenium, vanadium as well as vitamins like vitamin

A, C, E, folate and vitamin B complex have been found to relieve oxidative stress associated with red cell membranes (Reed et al., 1987).

MATRIALS AND METHODS

Study Design

This is a case control study with sequential recruitment of study participants with sickle cell disease and those without the disease (apparently healthy) with genotype AA or AS who served as control.

Study Subjects

A total of 40 sickle cell disease patients and 40 apparently healthy controls were recruited for this study from the sickle cell centre, Benin City after obtaining ethical clearance from an ethical review board and appropriate informed consent from the subjects as well as their parents/guardian. The recruited participants were appropriately age and sex matched.

Sample Collection/Analysis

Blood samples (5mls) were collected by venepuncture from each subject into a plain container. The labeled samples were spun in a bucket centrifuge at a speed of 2500rps to separate serum from red cells. The serum obtained was stored in a chest freezer at a temperature of -20^0C. Serum trace elements (copper, zinc, chromium, magnesium and selenium) levels were determined by atomic absorption spectrophotometer technique as described by Kaneko (1999).

Data Analysis

Data obtained was analyzed using SPSS version 17 statistical soft ware package. Results were expressed as mean ± SD and a P value of <0.05 was considered significant.

RESULTS

As shown in Table 1, there was a reduction in serum Mg, Zn, Se and Cr levels. This reduction was however, significant (P<0.05) for serum Mg (11.03±1.77mg/L), Zn (120.85±10.29 µg/dl) and Se (60.98±7.29µg/dl) levels when compared with control. This was also the case in male and female sickle cell disease patients. However, in male sickle cell disease patients the reduction in the serum zinc concentration was not significant (P>0.05) when compared with control (Table 3). The serum manganese concentration (68.3±3.63 µg/dl) was significantly elevated (P<0.05) in the sickle cell patients when compared with apparently healthy control (63.10±5.70µg/dl). This profile was also observed in male and female sickle cell disease patients (Table 2 and 3). However, among the different sickle cell age groups examined there was no statistically significant difference in serum trace metal levels when compared with apparently healthy control within the same age group.

Table 1: Serum Trace Element Levels in Sickle Cell Disease Patients

Trace Elements	Patients N = 40	Controls N = 40
Mg (mg/L)	11.03±1.77*	12.35±0.89
Zn (µg/dl)	120.85±10.29*	127.10±14.25
Mn (µg/dl)	68.3±3.63*	63.10±5.70
Cu (µg/dl)	68.54±10.49	67.45±3.37
Se (µg/dl)	60.98±7.29*	65.75±5.49
Cr (µg/dl)	62.90±5.97	64.43±6.15

Values are expressed as Mean ± SD, P<0.05 is considered significant compared with control

Table 2: Serum Trace Element Levels in Female Sickle Cell Disease Patients

Trace Elements	Patients N = 16	Controls N = 16
Mg (mg/L)	11.43±0.81*	12.54±1.00
Zn (µg/dl)	116.88±10.18*	129.69±13.64
Mn (µg/dl)	68.30±3.74*	62.38±4.50
Cu (µg/dl)	67.56±5.24	67.31±3.59
Se (µg/dl)	61.38±8.67	65.94±4.68
Cr (µg/dl)	61.88±7.18	63.25±7.33

Values are expressed as Mean ± SD, P<0.05 is considered significant compared with control

Table 3: Serum Trace Element Levels in Male Sickle Cell Disease Patients

Trace Elements	Patients N = 24	Controls N = 24
Mg (mg/L)	11.18±0.74*	12.22±0.80
Zn (µg/dl)	123.5±9.67	125.69±14.68
Mn (µg/dl)	68.25±3.63*	63.42±6.45
Cu (µg/dl)	69.04±3.28	67.54±3.30
Se (µg/dl)	60.75±6.40*	65.63±6.06
Cr (µg/dl)	63.58±5.05	65.21±5.24

Values are expressed as Mean ± SD, P<0.05 is considered significant compared with control

Table 4: Age Distribution of Serum Trace Element Levels in Sickle Cell Disease Patients

Trace Elements	Patients/Age Groups (years)			Control/Age Groups (years)		
	1-15, N=18	16-25, N= 12	≥ 26, N= 10	1-15, N= 20	16-25,N= 17	≥ 26, N =3
Mg (mg/L)	11.36±0.94	11.32±0.87	11.08±0.59	12.24±0.97	12.35±1.04	13.07±1.11
Zn (µg/dl)	120.11±5.41	123.33±3.47	119.2±2.17	127.65±3.24	126.06±6.78	126.33±9.71
Mn (µg/dl)	67.78±2.13	68.58±4.15	68.9±3.21	61.20±2.49	64.88±5.23	64.33±3.48
Cu (µg/dl)	68.89±5.25	67.08±2.47	69.3±5.78	66.95±6.27	67.82±4.57	68.67±4.47
Se (µg/dl)	60.11±3.17	61.67±2.65	61.70±3.21	64.70±4.15	66.59±3.23	68.00±4.67
Cr (µg/dl)	62.33±6.42	62.08±4.19	64.90±7.13	62.30±3.25	65.88±4.29	70.30±6.78

Values are expressed as Mean ± 2SD, P<0.05 is considered significant compared with control

DISCUSSION

The deficiencies of essential trace elements some of which are important in red blood cell maintenance, body growth and development have been observed in sickle cell disease (Durosinmi et al., 1993; Okpuzor and Okochi, 2009). A significantly low serum magnesium, zinc and selenium concentration was obtained from the general comparison of sickle cell disease patients with control subjects. In a study conducted by Defrancheschi et al., (1997), low concentration of red blood cell magnesium have been noted in patients with sickle cell disease, this in turn is thought to contribute to red blood cell dehydration and a concomitant increase in the symptoms of sickle cell disease. Significantly low serum magnesium obtained in this study may also contribute to the low red cell magnesium level which is in agreement with the study of Defrancheschi et al., (1997). The significantly low serum zinc level is in agreement with the report of Prasad and Cossack, (1993) and Prasad, (2002) who related zinc deficiency in sickle cell disease to manifestations such as growth retardation, hypogonadism in males, hyperammonemia, abnormal dark adaptation and cell mediated immune disorder. Zinc deficiency can also be the result of the adverse effect of hydroxyurea which increase zinc excretion as reported by Silliman et al., (1993). The significantly low serum selenium level is in agreement with the report of Durosinmi et al., (1993). Selenium plays an important role as a cofactor for the reduction of antioxidant enzyme such as glutathione peroxidase, an enzyme which helps react with potentially harmful oxidizing agents in substances like hemoglobin. High levels of glutathione function in the blood are associated with longevity. Deficiency of selenium can thus be attributed to the mortality in sickle cell disease. The reason for the significantly elevated serum manganese level in sickle cell disease patients is not yet known. Our findings demonstrate a similar trace element profile in both male and female sickle cell disease patients when compared with sex matched controls. This suggests that the serum pattern of trace element is not sex dependent.

CONCLUSION

Although, not much discoveries have been made on the relevance of trace elements in sickle cell disease, it can be concluded from our findings that deficiency of essential trace elements important in maintenance of erythrocyte stability and in proper growth and development, occur in sickle cell disease. Hence, dietary supplementation with essential trace elements may be used as adjuvant in sickle cell therapy.

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