



Research Article

The Status of Some Trace Elements in Sickle Cell Homozygous and Heterozygous Subjects Attending Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nigeria

Manafa P.O¹, Okocha C.E², Nwogbo S.C¹, Chukwuma G.O^{1*}, Ihim A.C¹, Ebugosi R.S¹, Onyemelukwe A.O¹, Chukwuanukwu R.C¹, Iloghalu E.U¹, Ochiabuto O.M.T.B¹

¹Department of Medical Laboratory Science, Faculty of Health Sciences and Technology, College of Health Sciences, Nnamdi Azikiwe University Nnewi Campus.

²Department of Haematology, Nnamdi Azikiwe University Teaching Hospital, Nnewi

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Abstract

Finding a suitable cure for Sickle Cell Disease (SCD) remains a challenge many years after its discovery. In this study, 30 homozygous sickle cell patients in steady state, 30 heterozygous sickle cell disorder subjects and 30 normal control subjects were enrolled. Plasma levels of zinc (Zn), copper (Cu), selenium (Se), and magnesium (Mg) were measured by atomic absorption spectrophotometry. Results were analysed using SPSS. There was a significant increase in the mean serum Se and Zn levels of AA (control) subjects when compared with the heterozygous group (AS) ($p < 0.05$). No significant difference was observed in the mean values of Cu and Mg concentrations between the two groups studied ($P > 0.05$). Serum Se and Zn concentrations were significantly raised in AA subjects (control group) when compared with homozygous sickle cell subjects ($p < 0.05$). Homozygous sickle cell disease may exert greater demand for zinc and selenium utilization in patients thereby resulting in lower serum levels. We recommend dietary supplementation of essential trace elements in the treatment and management of subjects with sickle cell disease.

Keywords: Sickle cell, Blood, Trace elements, Homozygous, Heterozygous

Introduction

Sickle cell disease is an inherited disorder of haemoglobin formation of which the most common and severe type is sickle cell anaemia (SCA). People with sickle cell disease have red blood cells that contain only haemoglobin S, an abnormal type of haemoglobin. In certain situations, these red cells become sickled 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 three to six months since a large percentage of the erythrocyte haemoglobin is of the fetal type (Hb F). 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. 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. 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. Attempts have been made over a number of years, to treat the disease by modifying the hemoglobin S molecule so as to suppress the sickling process, but in recent years, trace element metabolism have been receiving increasing attention in sickle cell anemia research and attempts have been made to relate the concentration of the elements to the sickling process. This study is aimed at evaluating the effect of sickle cell disorder on the blood levels of some trace elements. Due to cost implication, this work is limited to four trace elements namely, Zn, Cu, Se and Mg.

*Address for Correspondence:

Email: georgechuma@yahoo.com; Tel: +234-8034101608

Materials and Methods

Study site: This study was carried out in the sickle cell center of Nnamdi Azikiwe University Teaching Hospital, Nnewi (NAUTH), Anambra state. This area was chosen because the participants were readily available.

Study population: A total of 90 subjects were randomly selected for this study. This includes 30 who were sickle cell homozygous patients (SS), 30 sickle cell heterozygous subjects (AS) and 30 normal subjects (AA) used as control.

Sample collection: Blood samples (8mls) were collected by veni puncture from each subject and 3mls transferred into an EDTA bottle for genotyping, while the remaining portion were centrifuged and the serum used for atomic absorption spectrophotometry.

Cellulose acetate paper electrophoresis: Cellulose acetate haemoglobin electrophoresis was performed using the procedure as described by Kohn and Smith (1960).

Concentration of Serum Trace Elements: The procedure was as described by L'vov (2005). The method was essentially Atomic absorption spectrophotometry.

Results

Table 1 shows the trace elements concentration in sickle cell heterozygous (AS) and control (AA) subjects. Here, a significantly low concentration of serum selenium and zinc were obtained from the comparison of sickle cell heterozygous subjects and normal control subjects ($P < 0.05$). There was no significant difference observed in the concentrations of copper and magnesium for the groups ($P > 0.05$).

Table 1:
Trace elements concentration in sickle cell heterozygous (AS) and control (AA) subjects.

Trace Element	Mean Value		p value
	AA	AS	
Se N=30	4.93 ± 1.25	0.31 ± 0.16	0.000
Cu N=30	0.13 ± 0.04	0.12 ± 0.05	0.355
Mg N=30	8.46 ± 1.96	8.71 ± 1.00	0.541

Table 2:
Trace elements concentration in sickle cell homozygous (SS) and control (AA) subjects.

Trace Elements	Mean Values		p value
	AA	SS	
Se (N=30)	4.93± 1.25	0.65± 0.35	0.000
Cu (N=30)	0.13 ± 0.04	0.13± 0.08	0.805
Mg (N=30)	8.46 ± 1.96	8.80 ± 1.16	0.420
Zn (N=30)	0.90± 0.12	0.40± 0.14	0.000

In table 2, a significantly low concentration of serum selenium and zinc were obtained from the comparison of sickle cell homozygous subjects and normal control subjects ($P < 0.05$) but, no significant difference was observed in the serum copper and magnesium concentrations in both groups ($P > 0.05$).

Discussion

A significantly low concentration of serum selenium and zinc were obtained from the comparison of sickle cell homozygous subjects and normal control subjects ($P < 0.05$). Selenium level was also low in the heterozygous subjects. On the contrary, there was no significant difference observed in the concentrations of copper and magnesium for the groups as shown in table 1. In a study conducted by Keen and Gershwin (1990), low concentration of red blood cell Zinc has been recorded in patients with sickle cell disease. This in turn is likely to contribute to recurrent infection resulting from poor immune system, growth retardation, hypogonadism in males, hyperammonemia, abnormal dark adaptation and a concomitant increase in other symptoms of sickle cell disease. Significantly low serum Zinc obtained in this study may also contribute to the low red cell Zinc level which is in agreement with the study of Keen and Gershwin (1990).

Zinc deficiency can also be the result of the adverse effect of hydroxyurea which increases Zinc excretion as reported by Sindel *et al.*, (1990). A statistically significant decrease in the concentration of Zn was found in the whole blood, erythrocytes and plasma of the sickle cell anemia subjects as compared with the controls (Prasad, *et al.*, 1976.; Prasad, *et al.*, 1975). Prasad, *et al.*, (1976) also found that the excretion of Zn in the urine of the sickle cell anemia subjects was higher than that of the controls suggesting that increased loss of Zn in hyperzincuria may be one of the mechanisms by which the sickle cell anemia subjects become Zn deficient. Ojo and Oluwole (2006) also observed that there was mild Zn deficiency, more seriously in males, in the study when they determined the trace elements in whole blood, erythrocytes, plasma, head, hair, and nail of sickle cell anemia patients and compared them with identical samples from normal control subjects. A significantly low concentration of serum selenium and zinc were also obtained from the comparison of sickle cell homozygous subjects and normal control subjects ($P < 0.05$), but no significant difference was observed in the serum copper and magnesium concentrations in both groups ($P > 0.05$).

Selenium plays an important role as a cofactor for the reduction of antioxidant enzyme such as glutathione peroxidase, an enzyme which reacts with potentially harmful oxidizing agent in substances like hemoglobin. High levels of glutathione function in the blood are associated with longevity. Deficiency of selenium can perhaps be attributed to the mortality in sickle cell disease. A decrease in selenium concentration was also observed in the study of the whole blood and plasma of the sickle cell anemia subjects but which was not statistically significant while there was no change in the plasma selenium concentration of the two groups as recorded by Natta *et al.* (1990). Natta *et al* (1990) also observed that there was a significant decrease in the Se concentration of whole blood and plasma of sickle cell anemia subjects as compared with the controls. It is however, important to study the Se status of the sickle cell anemia subjects as deficiency of the element can result in biochemical and functional abnormalities of the erythrocyte (Durosinmi *et al.*, 1993). No significant difference was observed in the

concentrations of Cu and Mg in all the groups under comparison, although their values are still below the accepted normal ranges. This finding is similar to the result obtained by Defrancheschi *et al.*, (1997), where 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). Low serum copper (hypocupremia) could be associated with microcytosis and relative neutropenia probably resulting from oral zinc therapy (JAMA, 1978). A significantly higher Cu level was also observed in the hair of Nigerian sicklers by Oluwole *et al.* (1990). Homozygous sickle cell disease may exert greater demand for zinc and selenium utilization in patients thereby resulting in lower serum levels. Therefore dietary supplementation of essential trace elements in the treatment and management of subjects with sickle cell disease is hereby recommended.

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