Evaluation of Trace Elements in Adult Sickle Cell Anaemia Patients in Zaria, North Western Nigeria

Garba N1, Ifeanyichukwu OM2, Amilo GI1 and Audu I3

1Department of Haematology and Blood Transfusion, ABU Teaching Hospital, Zaria, Nigeria
2Department of Immunology, Faculty of Medicine, Nnamdi Azikiwe University, Nnewi, Nigeria
3Department of Haematology and Blood Transfusion, Federal Medical Centre Gusau, Nigeria

Corresponding author: Ifeanyichukwu Ositalimma Martin, Department of Immunology, Faculty of Medicine, College of Health Sciences, Nnamdi Azikiwe University, Nnewi Campus, P.M.B. 5001, Anambra State, Nigeria, Tel: +2348037200407, E-mail: moifeanyi@yahoo.co.uk

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Abstract

Sickle cell anemia is a genetic disorder that is caused due to the inheritance of a mutant gene that encodes haemoglobin S (HbS). The amino acid glutamic acid is replaced with valine in the sixth position of β-globin chain. Protection of red cell membrane from free radical mediated oxidative stress is crucial to the management of SCD. Trace elements such as Copper, Zinc and Magnesium are of great benefit towards relieving of oxidative stress associated with red blood cell membranes. This study was carried out to evaluate some trace elements in adult sickle cell anaemia patients attending sickle cell clinic, ABUTH-Zaria. Ethical clearance was obtained from ethics committee of Ahmadu Bello University Hospital Zaria, questionnaires were administered and informed consent was obtained from patients or their parents. One hundred and one (101) subjects aged 18 to 46 years participated in this study and these participants were divided into thirty five (35) confirmed sickle cell anaemia subjects in stable state (SS), thirty five (35) confirmed sickle cell anaemia subjects with history of vaso-occlusive crises in the last three months and (31) apparently healthy subjects (Hb AA) as control subjects (C). Haemoglobin electrophoresis was done using cellulose acetate method and serum copper, zinc and magnesium was analysed using Atomic Absorption Spectrophotometer (AAS) method. Serum copper, zinc and magnesium mean levels were significantly lower (P = 0.00) in SCA (SS and VOC) groups when compared with control group. No significance difference was observed in the mean levels of copper, zinc and magnesium in SS group when compared with VOC group (P = 0.36, P = 0.89 and P = 0.85) respectively. The mean levels of trace elements were significantly lower in SCA groups than the control group. Evaluation of trace elements is suggested in the management of sickle cell anaemia.

Keywords: Sickle cell anaemia; Stable state; Vaso-occlusive crises; Serum copper; Zinc; Magnesium

Introduction

Sickle cell anemia is a condition resulting from mutant autosomal gene responsible for the synthesis of haemoglobin S (HbS) [1,2]. The amino acid valine replaces glutamic acid in the sixth position of β-globin chain [3,4]. These chains are of 146 amino acids long, the fault occurs at the sixth amino in the chains. The homozygous inheritance of this abnormality produces, haemoglobin SS and individuals with this genotype suffer from sickle cell anemia [5]. Sickle cell anemia (SCA), a chronic debilitating disorder of genetic origin, is common in Africans and the Afro Caribbean. The disorder is characterized by varying clinical manifestations, referred to as crises among others [6]. Crises could be precipitated by a number of conditions like stress, extremes of temperature, infections - bacteria, viral, protozoa, particularly malaria, and a host of others [7-10].

Sickle cell anemia is a public health problem in Africa than any other continent in the world and it affects about 2% of Nigerian population [11].

Trace elements are important in red blood cell maintenance, body growth and development [12,13]. Trace elements are pharmacologically beneficial and toxic, thus the need for monitoring of the dosage [14]. People with sickle cell disease suffer from trace elements deficiency and higher rates of nutrients deficiency may be due to increased needs of many nutrients in sickle cell patients [15]. There is increased turnover of hemopoietic cells due to chronic hemolysis and cell death leading to tremendous red marrow expansion. These conditions lead to hyper-metabolic rate and increases in nutrient and energy demand [16].

The global use of trace elements in health care delivery system has taken central stage due to the realization of their importance in disease management. Protection of red cell membrane from free radical mediated oxidative stress is crucial to the management of SCD. Trace elements play an important role in maintaining red cell membrane integrity and function [13].

This study was carried out to evaluate trace elements in sickle cell anemia patients and compare findings with steady state and vaso-occlusive crises in sickle cell anaemia.

Methodology

This study was conducted amongst sickle cell anaemia patients attending haematology clinic of Ahmadu Bello University Teaching Hospital (ABUTH) Zaria between September to November 2014. Only confirmed HbSS adult patients attending sickle cell clinic, HbSS patients in steady or stable condition and those that had crises in the preceding three months and subjects that were not transfused in the last three months were included in the study. Patients with...
haemoglobinopathies other than sickle cell anaemia, patients who were transfusion dependent and those who receive transfusion in the last three months, patients on iron supplementation and unwillingness of the patients were excluded from the study. A total of 101 subjects (18-46 years) comprising of 70 subjects with sickle cell anaemia (SCA) and 31 apparently individuals with HbAA genotype were recruited into the study as control subjects (C). The SCA subjects comprised of 35 subjects in steady state (SS) and 35 subjects with vaso-occlusive crises (VOC). Twenty five (25) subjects had VOC in the last one month, eight (8) subjects had VOC in the last two months and two (2) subjects had VOC in the last three months. Control samples were obtained from interns and students on attachment. Questionnaires were administered to the participants and informed consent was obtained from all of them. All the patients were on routine tablets used in the sickle cell clinic; folic acid, paludrine and vitamin B complex tablets and none of them was on hydroxyurea because of the impact it could have on the result of the patient. Blood samples (4 ml) were collected from all the subjects in the study groups. Serum samples were separated and stored at -20°C until ready for analysis.

Laboratory Methods

The haemoglobin phenotypes were determined using the cellulose acetate electrophoresis method [17]. Serum copper, zinc and magnesium were determined with flame atomic absorption spectrophotometer (AAS) using a direct method as described by Kaneko [18].

Statistical Analysis

Data obtained was analysed using SPSS (version 17). Results were expressed as mean ± SD using ANOVA and Pearson's correlation and a P value of < 0.05 was considered significant.

Table 1 shows the age, sex and weight of the study groups. Table 2 shows the mean ± SD of copper, zinc and magnesium in the study groups using ANOVA and Post Hoc.

Table 2: Shows the mean ± SD of copper, zinc and magnesium in the study groups using ANOVA and Post Hoc.
Discussion

Trace elements are important in red blood cell maintenance, body growth and development and their deficiency have been observed in sickle cell disease [12,13]. There is increased turnover of hemopoietic cells due to chronic hemolysis and cell death leading to tremendous red marrow expansion. These conditions lead to hyper-metabolic rate and increase in nutrient and energy demand [16].

Copper is known to be essential in the proper functioning of different metal enzymes which include ceruloplasmin involved in iron metabolism [19]. Deficiency of copper is known to cause anemia [20]. Studies have suggested that the copper containing enzyme, ceruloplasmin may have specific role, probably related to its function in mobilization of stored iron in the liver which makes iron available for haemoglobin synthesis [21]. However, it has been observed that in copper deficiency induced anemia, in spite of elevated iron level in the liver, the rate of haemoglobin synthesis remain significantly reduced [22].

In this study, a significantly low serum copper level was observed from the comparison of sickle cell anemia group with control group and this is in agreement with the report of the study by Arinola et al. [22] in Ibadan, low level of copper have been noted in sickle cell anemia patients. However, it is contrary to work done by Bot et al. [23] and Nnodim et al. [24] which revealed a significantly elevated level of copper in sickle cell patients.

Zinc is known as an important nutrient for growth and development and plays an important role in iron metabolism [25]. The mechanism through which zinc exerts its effect in correcting anemia in SCD is not understood [26], but it is known that the proteins making up the cytoskeleton of cell membranes acquire some abnormal configurations and often get irreversibly damaged. Zinc prevents the formation of such irreversibly damaged sickle cells [25]. Furthermore, it has been proposed that the role of zinc in the management of sickle cell anemia centers on its calcium antagonism.

This work revealed a significantly low serum zinc level in sickle cell anemia compared with the control group [22] in Ibadan, low level of zinc have been noted in sickle cell anemia patients. However, it is contrary to work done by Bot et al. [23] and Nnodim et al. [24] which revealed a significantly elevated level of zinc in sickle cell patients.

Cellular dehydration occurs due to a loss of potassium and water, and is correlated with the polymerization process and increased presence of irreversibly sickled cells [31]. Low levels of total Magnesium in sickle cell erythrocytes have been associated with increased sickling due to propensity for red cell dehydration and hence, increased HbS polymerization [32,33]. It has been demonstrated that the dehydration is due to abnormally high red cell permeability and loss of potassium (K+) via at least three loosely connected pathways, in which the relative contribution of each is not yet known. One of these pathways, the K-Cl co-transport, is abnormally activated by low cell Mg2+ [32]. This causes rapid irreversible loss of K+ and Cl- ions, with water following osmotically.

This work revealed a significantly low level of serum magnesium in sickle cell anemia and this is in agreement with de Franceschi et al. [32] and Zehtabchi et al. [34].

In this study, there was no significant difference in the mean levels of copper, zinc and magnesium between SS and VOC groups. Lack of significant difference in the mean levels of copper, zinc and magnesium between SS and VOC groups might be attributed to increased dehydration and sickled red blood cell formation due to reduced levels of trace elements in sickle cell anemia patients. However, there was significant difference in the mean levels of copper, zinc and magnesium between SCA groups (SS and VOC) and control. This suggests that higher rates of nutrient deficiency may be due to increased needs of many nutrients in sickle cell patients.

Conclusion

The mean levels of copper, zinc and magnesium were significantly lower in SCA groups when compared with control. This suggests that higher rates of nutrient deficiency may be due to increased needs of many nutrients in sickle cell patients. Evaluation of trace elements is suggested in the management of sickle cell anemia to reduce complications (red cell dehydration, irreversible red cell damage and anemia) associated with sickle cell anemia.

Table 3: Shows the relationship of Copper (µg/dL), Zinc (µg/dL), and Mg (mmol/L) using Pearson’s correlation.

<table>
<thead>
<tr>
<th>Trace elements</th>
<th>Mean ± SD</th>
<th>r</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cu vs Zn (n = 101)</td>
<td>126.64 ± 17.79 vs 109.05 ± 21.21</td>
<td>0.64</td>
<td>0.00*</td>
</tr>
<tr>
<td>Cu vs Mg (n = 101)</td>
<td>126.64 ± 17.79 vs 0.64 ± 0.14</td>
<td>0.61</td>
<td>0.00*</td>
</tr>
<tr>
<td>Mg vs Zn (n = 101)</td>
<td>0.64 ± 0.14 vs 109.05 ± 21.21</td>
<td>0.44</td>
<td>0.00*</td>
</tr>
</tbody>
</table>

*significant at P < 0.005

References


