ORIGINAL ARTICLE

Altered Membrane Potential and Electrolyte in Sickle Cell Anemia

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Abstract:

Aim: This study has been to evaluate the level of membrane potential and electrolyte in sickle cell disease patients. *Material and methods:* 100 sickle cell patients in steady state ages 5 to 30 years attending General Hospital Owerri were used in the study while 100 normal subjects (HbAA) were used as control. Also 30 HbSS in crisis have been involved. *Results:* The results obtained showed that the level of membrane potential was significantly lower in sickle cell anemia as compared to the controls. Also, the level of the electrolyte was found significantly decreased in HbSS when compared with HbAA at $P<0.05$. *Conclusion:* The membrane potential translates to energy which means that there is less energy in sickle cell disease which is linked to electrolyte imbalance. Hence people with sickle disease should be monitored closely for their electrolytes to avoid crisis.

Keywords: Electrolyte, membrane potential, sickle cell anemia.

Introduction:

Sickle cell disease is an inherited disorder in which there is a point mutation arising from the substitution of glutamic acid by valine at the sixth position on the beta polypeptide chain [1]. It is a disease passed down through families in which red blood cells form an abnormal sickle or crescent shape. It is characterized by possession of abnormal type of haemoglobin [2]. Sickle cell disease is a public health problem and accounts for a lot of morbidity and mortality in the society. Sickle cell disease is much more prevalent in Africa and Mediterranean crescent. Patients with sickle cell disease have painful episodes which can last from hours to days. These crises can cause pain in the bones and chest. The painful sickle cell crises are precipitated by infection, dehydration and hypoxia. The infection of the respiratory tract, fever, abdominal, skeletal and bone pain crises are the main cause of morbidity [3, 4].

It is pertinent to note that in most marriages with children suffering from sickle cell are deprived of joy. In some situation, it leads to breakage of marriage particularly in Igbo land. The patients with sickle cell disease suffer some abnormalities. They may have pulmonary infarction that presents as acute chest crisis and dehydration. It is of interest to note one of the ways of managing sickle cell crises is by rehydration. The hydration is done using various concentrations of electrolytes such as 5% dextrose saline, normal saline and oral rehydration solution. Statius et al [5] has stated that sickling is accompanied by an intra erythrocytic loss of potassium and gain of sodium hence creating inequality in the ionic strength across the membrane. Also it has been demonstrated that haemolysis, intravenous potassium administration and blood transfusion increased potassium level. On the other hand, rehydration of patients with varying strength of electrolytes may precipitate shift in membrane potential. Membrane potential in other word is the difference in electrical potential between the interior and the exterior of a biological cell. All animal cells are surrounded by a plasma membrane composed of a lipid bilayer with a variety of types of proteins embedded in it. The membrane potential arises

primarily from the interaction between the membrane and the actions of two types of transmembrane proteins embedded in the plasma membrane. In sickle cell disease, there is a reduction of sodium ion and potassium ion concentration gradients. This could be due to increased permeability of these ions which is due to sickling. The failure of sodium potassium pump can be related to the membrane potential of sickle cell anaemia. The increased permeability of calcium ions is linked with the shift in the concentration gradients of potassium and sodium, leading to lowering of the calcium ion concentration gradients across the cell membrane [6]. It is pertinent to note that this is an indicator of the malfunction of the calcium pump which pumps calcium ions out of the cells hence maintaining the trans membrane concentration gradient high. The loss of potassium ion and increased intracellular calcium ions activate the Gardos channel [7]. Therefore, the decrease in the transmembrane concentration gradient of sodium, potassium and calcium ions can be individually or jointly used as a biomarker of the severity of sickle cell anemia by evaluating the change in the membrane potential. The membrane potential links with the Nerst equation in determining the energy. Therefore, this work is aimed at evaluating the membrane potential as well as electrolytes in sickle cell disease subjects in Owerri Imo State, Nigeria.

Material and Methods:

Subjects: 100 subjects of confirmed HbSS by haemoglobin electrophoresis were included in this study. 100 normal persons with HbAA were enrolled as controls. Also 30 persons with HbSS-crisis were included in this study. Equal number of females and males in each class were included to minimize bias due to known sex-related biochemical differences. All subjects from study and control group were above of the age of 5years. Their consent was taken and ethical approval from the ethics committee of the hospital was obtained. The extracellular cation concentrations were estimated from serum samples while intracellular calcium concentrations were determined from lysed erythrocytes.

Blood Collection: In all subjects 4ml of fasting venous blood was collected into plain and EDTA bottle. The serum was separated by centrifuging the whole blood in westerfuge (model 684) centrifuge at 5,000 RPM for 5 minutes.

Biochemical Assay: The serum sodium, potassium and calcium were estimated using Randox Kit. While membrane potential was determined by calculation using Nerst Equation.

Statistical Analysis:

The values were expressed as mean ± standard deviation. The student t-test was used to calculate the significant differences at $P<0.05$.

Results:

The levels of sodium, potassium and membrane potential were decreased in sickle cell disease (HbSS in steady state and HbSS-crisis) when compared with the control at $p<0.05$ (Table 1).

Table 1: Sex Distribution of Subjects of HbAA, HbSS, HbSS Crisis

Sr. No.	Study Groups	Male		Female	
		Numbers	%	Numbers	%
1	HbAA	50	50	50	50
2	HbSS	50	50	50	50
3	HbSS Crisis	15	50	15	50

Table 2: Mean ± SD of Serum Na, K, Ca RBC-Ca and Membrane Potential of HbAA, HbSS Steady state and HbSS-Crisis

Parameters	HbAA	HbSS Steady state	HbSS-Crisis
Serum Sodium (mmol/L)	141.44 ± 3.18	130.94 ± 5.67*	125.7 ± 3.57*
Serum Potassium (mmol/L)	4.08 ± 0.28	3.17 ± 0.18*	2.88 ± 0.13*
Red Cell Calcium (mmol/L)	0.58 ± 0.04	0.56 ± 0.11*	0.54 ± 0.09*
Serum Calcium (mmol/L)	2.51 ± 0.03	1.38 ± 0.10*	1.29 ± 0.07*
Membrane potential (J)	259.14 ± 38.8	148.52 ± 58.5*	143.06 ± 39.5*

*Significantly different from control at P<0.05

Commonest mode of presentation in sickle cell crisis was fever followed by dehydration & hypoxia, abdominal pain, skeletal & bone pains, respiratory tract infection & dehydration. Irrespective of presentation of sickle cell crisis, the level of sodium, potassium and membrane potential were further decreased (Table 2).

Discussion:

In sickle cell disease, the avoidance of dehydration is a good way to decrease the tendency of pain crisis [8]. In this study, it was observed that the serum levels of sodium and potassium were significantly less in sickle cell disease when compared with healthy controls. However, it is of interest to note that the level of sodium and potassium decreased more significantly in HbSS-crisis. This is in line with the work of Ibe et al [9]. The normal red cells have high level of intracellular potassium and low level of sodium ions within the extracellular environment. On the other hand, the level of potassium ions is low in the extracellular environment while that of sodium is high. The sodium potassium ATPase and sodium potassium ion pump maintains the concentration as well as inherent electrochemical gradients between the extracellular and intracellular environment. This pump takes out three sodium ions for every two potassium ions taken into the cell. Hence, this increased potassium concentration aids to draw water molecules into the cell [10, 11]. In the same way, it can constitute oxidative stress in sickle cell disease [12, 13]. This decrease in electrolytes could be associated with urinary losses coupled with skin losses. This in other words promotes sickling leading to more loss in sickle cell crisis. Similar findings have been recorded by Brugnara, [3] who has also reported appreciably depleted levels of serum electrolytes in sickle cell disease.

In the same way, the membrane potential was significantly decreased in sickle cell disease when compared with the controls. Also, the decrease in membrane potential has followed a systematic style in different HbAA, HbSS in steady state and HbSS-crisis state. This membrane potential translates the energy. This means that the energy in sickle cell disease is very low. This is linked to their fraity and weakness among sickle cell patients. Hence, there is a strong link between the depleted membrane potential and sickle cell intensity. This is consistent with the work of Osuagwu et al [7]

Therefore, decreasing level of electrolytes can lead to decreased membrane potential. It is quite necessary that dehydration in sickle cell patients be avoided to prevent decreased membrane potential, which in order words may encourage sickling.

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