



INFLUENCE OF HAEMATOLOGICAL PROFILE ON THE EXERCISE CAPACITY OF CHILDREN WITH SICKLE CELL DISEASE IN KANO

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ABSTRACT

The Exercise Capacity (ExC) of children with sickle cell disease (SCD) may be influenced negatively by both haematological and environmental factors. This study aimed to assess the influence of haematological profile on the ExC of children with SCD in Kano and to ascertain the safety of conducting 6 minute walk test (6MWT) on those children. In the cross-sectional survey, 162 children were recruited from Murtala Mohammed Specialist Hospital, Kano. Each of them walked to-and-fro for 6 minutes on a 10 meter marked level floor at their own walking pace in order to determine their actual 6 minute walk distance (6MWD). The actual 6MWD was compared with a predicted one in order to determine their ExC. Full blood count was used to evaluate haematological profiles. The data were analysed with Pearson product moment correlation and unpaired t test, at a level of significance of $p < 0.05$ using SPSS version 20. Results showed that seventy (70) males (43.2%) and ninety two (92) females (56.8%) with mean age of 10.7 ± 3.27 years took part in the study. The actual 6MWD was $366.20 \text{ m} \pm 59.88 \text{ m}$ (95%CI = $356.91 \text{ m} - 375.49 \text{ m}$) which was 59.17% of the predicted one. ExC correlated with each of White blood cell count (WBC) ($r = -0.22$; $p = 0.005$), Sex ($r = -0.27$; $p = 0.001$) and age ($r = 0.19$; $p = 0.013$). None of the participants experienced exercise-induced vaso-occlusive crisis during or immediately after the 6MWT. It was concluded that infection (signified by increased WBC count) and female gender have negative influence on ExC. 6MWT is safe to be performed by children with SCD.

Key words: Sickle Cell Disease, Haematological Profile, Exercise Capacity, Six Minute Walk Test

INTRODUCTION

Sickle Cell Disease (SCD) is an inherited hemoglobinopathy (Chirico *et al.*, 2016; Martin *et al.*, 2018) that affects millions of people worldwide (Tsaras *et al.*, 2009). The disorder is most commonly found among the people living in the sub-Saharan Africa (Tsaras *et al.*, 2009; Mitchell, 2018). It occurs when a hydrophobic valine replaces a hydrophilic glutamic acid (Mitchell, 2018) at the sixth position on the beta globin chain on chromosome 11 (Steinberg, 2006) giving rise to abnormal hemoglobin (HbS) which is less soluble when deoxygenated (Mitchell, 2018). The increasing need for more oxygen supply to active muscles during strenuous (anaerobic) exercise may initiate metabolic changes that

lead to HbS polymerization, sickling of red blood cell (RBC), vascular occlusion and endothelial damage (Tsaras *et al.*, 2009; Waltz *et al.*, 2012). In SCD, strenuous exercise decreases arterial oxygen concentration leading to acidosis, excess lactate formation and intravascular sickling (Connes *et al.*, 2011). It has however been revealed that RBC stiffness is only possible with the combined effects of deoxygenation and low pH (Xue *et al.*, 2016). Strenuous exercise also leads to dehydration, hyperthermia (Tsaras *et al.*, 2009, Mitchell, 2018), rhabdomyolysis, splenic infarction (Thompson, 2013), hemolysis (Platt, 1982) and sudden death (Tsaras *et al.*, 2009, Fajardo and Tchanda, 2015; Mitchell, 2018).

Sudden death can stem from conducting strenuous exercise in high altitude (Mitchell, 2018), rhabdomyolysis, heat stroke, acute renal failure, intravascular coagulation (Tsaras *et al.*, 2009, Mitchell, 2018), dehydration (Mitchell, 2018) and cardiac dysrhythmia (Tsaras *et al.*, 2009; Fajardo and Tchandja, 2015). Due to the aforementioned severe complications that are associated with strenuous exercise in SCD, clinicians have rarely prescribed exercise to individuals with SCD.

On a positive note, studies have however found that engaging in regular moderate intensity exercise is beneficial rather than harmful in patients with SCD (Chirico *et al.*, 2012; Waltz *et al.*, 2012; Messonnier *et al.*, 2012; Faes *et al.*, 2014; Hedreville *et al.*, 2014). Moderate intensity exercise was found to decrease oxidative stress (Chirico *et al.*, 2012; Faes *et al.*, 2014; Chirico *et al.*, 2016, Martin *et al.*, 2018) inflammation and endothelial damage (Faes *et al.*, 2014) and improved nitric oxide bioavailability (Martin *et al.*, 2018). Moderate intensity exercise did not alter autonomic nervous system activity negatively (Hedreville *et al.*, 2014), and it decreased microcirculatory flow abnormalities (Waltz *et al.*, 2012). Beneficial exercise to individuals with SCD has to be aerobic (Tsaras *et al.*, 2009; Connes *et al.*, 2011), symptom limited, with adequate hydration (Tsaras *et al.*, 2009; Tripette *et al.*, 2010; Connes *et al.*, 2011) and not to be conducted under adverse weather conditions (Jones *et al.*, 2005; Connes *et al.*, 2011). The aim of this study was to assess the influence of hematological variables on the Exercise Capacity (ExC.) of children with SCD and to determine the safety of conducting 6 minute walk test (6MWT) with the view to help physiotherapist prescribe exercises that are safe to the patients with SCD in a city that could experience extreme of weather conditions.

MATERIALS AND METHODS

The study was a cross-sectional descriptive survey in which 162 children and adolescents with SCD, seventy males (43.2%) and ninety two females (56.8%) took part in the study. They were recruited from the out-patient SCD clinic in Murtala Mohammed Specialist Hospital, Kano using purposive sampling technique. The study was approved by the Ethics Committee of Kano State Ministry of Health and the consent of participants, and that of their caregivers, as the case applied, was sought and obtained. The height and weight of participants were measured using standard procedures; oxygen saturation

was assessed with finger pulse oximeter. Blood samples were collected for FBC using auto-analyser (Sysmex XP-300, Germany) (Akinbami *et al.*, 2012). The safety of the 6MWT was determined based on the presence or absence of crises during or after the exercise test. Occurrence of crises was score '0' point and absence of crises was scored '1' point.

Procedure for conducting 6MWT

The test was performed in a well-ventilated gymnasium 14-meter long between 9am and 1pm daily. Each participant was instructed to stand and keep walking at his/her own pace to the 10 meters line and then return to the 0 meter repeatedly for 6 minutes. The total distance covered during the 6MWT by each of the patients was recorded as the actual six minute walk distance (6MWD).

All precautions to guard against development of crises have been adhered to very strictly. The patients have been on routine medical care (and also on hydroxy-urea) and free of frequent vaso-occlusive crises at least in the last 3 months. The exercise was totally aerobic and symptom limited (i.e. exercise being terminated when symptoms of muscle cramping, fatigue, and shortness of breath ensues) with adequate hydration before and after the exercise and the training was conducted in a well-ventilated and conducive environment.

Determination of ExC

Participants that covered longer distance during the 6MWT (or have higher value of 6MWD) were regarded as having better ExC. However, ExC could also be categorised as normal, moderately decreased or severely altered by comparing the actual 6MWD for each patient with a predicted 6MWD (Dedeken *et al.*, 2014). The predicted 6MWD was obtained using the standard regression equation below:

Males Predicted 6MWD = $196.72 + (39.81 \times \text{Age}) - (1.36 \times \text{Age}^2) + (132.28 \times \text{Height})$

Females Predicted 6MWD = $188.61 + (51.50 \times \text{Age}) - (1.86 \times \text{Age}^2) + (86.10 \times \text{Height})$ (Geiger *et al.*, 2007).

1. When the actual 6MWD was greater than 80% of the predicted 6MWD = Normal ExC
2. When the actual 6MWD was between 60% - 80% of the predicted 6MWD = Moderately decreased ExC
3. When the actual 6MWD was less than 60% of the predicted 6MWD = Severely Altered ExC (Dedeken *et al.*, 2014).

Data Analysis

The data were summarised with descriptive statistics and analysed with inferential statistics of Pearson product moment correlation and unpaired t test, at a level of significance of $p < 0.05$ using SPSS version 20. It was not possible to conduct inferential statistics on the safety of 6MWT because none of the participants had any crises during the exercise.

RESULTS

The mean age and body mass index of the participants were of 10.7 ± 3.27 years and 13.44 ± 1.79 kg/m² respectively. The mean 6MWD covered by the participants was 366.20 m \pm 59.88m. The average value of their predicted 6MWD was 618.93 m \pm 48.09m. This implies that the study participants were able to exercise at 59.17% of their predicted ExC. Only 2 (1.2%) had Normal Exc, 80 (49.4%) had moderately altered Exc and 80 (49.4%) severely altered Exc. With regards to the safety of conducting 6MWT, none of the participants experienced any exercise-

related clinical sign of vaso-occlusive crisis during and immediately after the exercise. Significant correlations were observed between ExC and each of Sex ($r = -0.27$; $P = 0.001$) and age ($r = 0.19$; $p = 0.013$) of participants. Further analysis of ExC based on sex using student t-test analysis revealed that female participants have significantly lower ($P < 0.05$) ExC (mean = 352.17 ± 54.87 m) than their male counterpart (mean = 384.63 ± 61.57 m).

Correlation between haematological profile and ExC of participants

Mean values of haematological variables were 95.01 ± 4.43 % for oxygen saturation (SPO₂) post exercise, $16.16 \pm 6.10 \times 10^3/\mu\text{L}$ for white blood cell (WBC) count and 84.73 ± 8.38 fL for mean cell volume (MCV) as presented in Table 1. Furthermore, there was significant negative correlation between ExC and WBC count ($P < 0.05$).

Table 1: Correlation between Exercise Capacity of study participants and Haematological Profiles (N= 162)

Haematological Profiles	Mean \pm SD	r	p- value
Resting Oxygen Saturation(%)	95.11 \pm 4.72	0.27	0.73
Oxygen Saturation post 6MWT(%)	95.01 \pm 4.43	-0.004	0.958
WBC($\times 10^3/\mu\text{L}$)	16.16 \pm 6.10	-0.222	0.005*
RBC($\times 10^6/\mu\text{L}$)	2.95 \pm 1.78	0.44	0.581
MCV (fL)	84.73 \pm 8.38fL	0.049	0.537
MCH(pg)	26.75 \pm 3.10	0.029	0.718
MCHC (g/dL)	31.48 \pm 1.30	0.146	0.63
PLT ($\times 10^3/\mu\text{L}$)	441.56 \pm 177.92	0.74	0.334
Haemoglobin Concentration (g/ dL)	7.46 \pm 1.69	0.12	0.879

Key: *significant; 6MWD=six- minute walk distance; WBC = white blood cell count, RBC= red blood cell, MCV=mean cell volume, MCH=mean cell haemoglobin, MCHC=mean corpuscularhaemoglobin concentration, PLT= platelet.

DISCUSSION

Despite the fact that Kano City is known for having adverse weather conditions at specific times of the year, the outcome of this study has revealed that low-moderate intensity aerobic exercise in the form of 6MWT is safe to be performed by individuals with SCD. This is because none of the participants in this study experienced any exercise induced clinical sign of vaso-occlusive crisis both during and immediately after the exercise. The implication of this finding is that the 6MWT can also be used as a form of endurance training for individuals with SCD provided that all the necessary precautions have been observed. A study has also observed that moderate exercise did not

adversely affect the functioning of the autonomic nervous system in patients with SCD (Hedreville *et al.*, 2014).

The ExC of the participants in this study is less than sixty percent of the predicted value, and this implies that most of them have severely reduced ExC levels. The finding on the deterioration of ExC in individuals with SCD is in line with the outcomes of other studies (Liem *et al.*, 2009; Minniti *et al.*, 2010; Hostyn *et al.*, 2013; Waltz *et al.*, 2013; Dedeken *et al.*, 2014; Ohara *et al.*, 2014). Previous studies have reported ExC values of 83.26% (Dedeken *et al.*, 2014) and 74.56 % (Waltz *et al.*, 2013) of the predicted value which are higher than what was obtained in this study.

This study found that there was significant negative relationship between infection which is represented by increased white blood cells (WBC) count and ExC. An increase in WBC count as observed in this study connotes presence of bacterial or fungal infection. This implies that increased infection episodes will lead to reduction in ExC among individuals with SCD. Individuals with SCD are prone to having functional asplenia and recurrent chest infection. This may lead to reduction in the exercise ability of the patient if not adequately treated. The outcome of this study on infection is in line with the finding of another study where significant relationship was found between increased WBC count (WBC) and ExC (Melo *et al.*, 2017). Although the other selected haematological variables in this study all have no significant relationship with the ExC of the study participants at least individually, the observed reduction in ExC could probably be associated with the combined influence of the reductions in the concentrations of several haematological variables such as severe reductions in haemoglobin, pack cell volume, RBC and platelet in majority of the participants. The insignificant relationship between arterial oxygen saturation and ExC may probably be due to the fact that the average value of the arterial oxygen saturation of the study participant is within normal range both at rest and post exercise.

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- Contrary to the findings in this study, low haemoglobin level had previously been linked with the ExC of individuals with SCD (Setty *et al.*, 2003). Furthermore, significant correlation was also found between RBC deformability and ExC where it was revealed that it is not the total number of RBC that actually counts but the total number of viable ones (un-deformed RBC cells) (Liem *et al.*, 2009). Also, previous studies have found significant correlation between pack cell volume and ExC (Liem *et al.*, 2009; Waltz *et al.*, 2013). In addition, a study found a significant relationship between oxygen saturation and ExC (Hostyn *et al.*, 2013).
- Finally, this study found significant relationship between age and ExC. The positive correlation implies that the older the child the better the ExC. Furthermore, this study found that male participants have significantly better ExC than females. It is also possible that based on the positive correlation between age and ExC, males with higher mean age may have better ExC.
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