

A COMPARISON OF SIX MINUTE WALK TEST IN SICKLE CELL PATIENTS VERSUS AGE & SEX MATCHED CONTROLS IN CENTRAL INDIA

STUDIU DE COMPARAȚIE PRIVIND TESTUL DE MERS DE 6 MINUTE LA PACIENȚII CU SICLEMIE, ÎN FUNCȚIE DE VÂRSTĂ & GEN, DIN INDIA CENTRALĂ

Y.Praveen Kumar¹, Pankhuri Multani², Y.Pallavi³

Keywords: sickle cell anemia, six minute walk test, six minute walk distance

Cuvinte: siclemie, test de 6 minute mers, test de mers pe distanță în 6 minute

Abstract

Background. Sickle cell anemia (SCA) is a genetic disease characterized by production of abnormal hemoglobin, & associated by chronic hemolytic anemia with acute and chronic tissue damage. SCA patients complain of significant exercise intolerance, which goes unnoticed. So the study is conducted to know the importance of exercise limitation in patients with SCA when compared to age & sex matched healthy counterparts.

Aim. To determine the cardiopulmonary responses on performance of 6 minute walk test (6MWT) in patients with SCA versus controls.

Materials and Methods. Experimental case control study was carried out at Sickle cell anemia and Physiotherapy outpatient department by age and sex matching in order to obtain 40 individuals in each group (n= 40 in SCA and Control group respectively) and initial parameters (weight, hemoglobin) were documented followed by performance of 6 MWT after which SCA and control were compared for 6 Minute Walk test parameters.

Results. The result indicated that in SCA mean hemoglobin levels & weight was less when compared to the controls. The results obtained also indicate that there is a change in the cardiopulmonary responses on performance of 6MWT. It is also to note that dysfunctional RBC's reduced 6 MWD in SCA when compared to healthy counterparts. SCA group had higher respiratory rates compared to controls.

Conclusions. There is a marked reduction in the 6MWD & 6MWT values when SCA were compared to control group. The reduced cardiovascular responses in SCA are compensated by increased respiratory rates.

Rezumat

Introducere. Siclemia (SCA) este o afecțiune genetică, caracterizată prin producerea de hemoglobină anormală, asociată cu anemie cronică hemolitică și distrugere tisulară acută și cronică. Pacienții cu SCA acuză o intoleranță semnificativă la practicarea exercițiilor, de care nu se ține seama. Deci, studiul urmărește stabilirea importanței gradului de limitare la practicarea exercițiilor, la pacienții cu siclemie, comparativ cu subiecți sănătoși, în funcție de vârstă și gen.

Scop. Determinarea performanței cardiopulmonare ca răspuns la efectuarea testului de 6 minute de mers (6 MWT) la pacienții cu siclemie versus grupul de control.

Material și metodă. Studiul experimental s-a realizat în Departamentul ambulator de fizioterapie pentru pacienți cu siclemie, pe două grupuri de 40 de subiecți, unul de control și unul format din pacienți cu siclemie, selectați în funcție de vârstă, gen și parametric inițiali (greutate, hemoglobină) și în funcție de performanțele obținute la testul de mers de 6 min.

Rezultate. Rezultatul a arătat că în siclemia medie, nivelele de hemoglobină și greutate au fost mai mici în comparație cu grupul de control. Rezultatele obținute au mai indicat faptul că există modificări în răspunsurile cardiopulmonare privind performanța la testul de mers de 6 min. Este semnificativ și faptul că la pacienții cu siclemie rezultatul testului de mers este mai slab și rata respiratorie mai mare comparativ cu grupul de control.

Concluzii. Există o reducere semnificativă a valorilor pacienților cu siclemie la testele de 6 min. mers și 6 min./distanță mers comparativ cu grupul de control. Răspunsurile cardiovasculare reduse ale pacienților cu siclemie sunt compensate de rata respiratorie crescută.

¹ associate professor, VSPM College of Physiotherapy

Correspondance author: Digdoh Hills, Hingna, Nagpur 440019, INDIA, email. praveenwhy@ yahoo.com

² clinical therapist ,criticare hospital ,Nagpur,INDIA pankhuri.multani@gmail.com

³ associate professor, VSPM College of Physiotherapy, Digdoh Hills, Hingna, Nagpur 440019,INDIA pallaviy86@ yahoo.com

Introduction

Sickle cell anemia, as defined by the World Health Organization, is a genetic condition due to a hemoglobin disorder-inheritance of mutant hemoglobin genes from both parents. [1] 11th pair of chromosomes contains a gene responsible for normal hemoglobin production. A mutation or error in this gene causes Sickle cell disease. [2]

SCD is a serious disorder in which the body produces sickle-shaped red blood cells. "Sickle-shaped" red blood cells are shaped like a crescent. Sickle cells contain abnormal hemoglobin called sickle hemoglobin or hemoglobin S. Sickle hemoglobin causes the cells to develop a sickle, or crescent, shape. Sickle cells are stiff and sticky so they tend to block blood flow in the blood vessels of the limbs and organs. Blocked blood flow can cause pain, serious infections, and organ damage.[3]

Sickle-cell anemia is globally widespread. About 5% of the world's population carries genes responsible for SCD.¹ Average incidence of sickle gene among Indians is approximately 4.3%. The presence of sickle cell trait has also been reported in South India, Orissa, and in Western India. In India, the frequency is much higher (up to 45%) in many tribal populations [4]. The presence of Sickle cell disease cannot be ruled out from central India. Therefore a regional center for sickle cell disease is present in central India.

Anemia has a negative impact on physical work capacity in different age groups as measured by changes in maximal oxygen uptake and other metabolic parameters[5,6,7]. Few studies have been done on exercise tolerance in normal and also in SCA children on treadmill, in western countries and occasional ones in India [8,9,10], where the subjects were subjected to walk on treadmill. But in the current study 6MWT has been carried out to know the cardiovascular responses in sickle cell anemia & compared with cardiovascular responses of 6MWT in age & sex matched controls.

Although therapies for the treatment of SCA have evolved, has increased median life expectancy. [11] Mortality has improved but morbidity remains significant, and patients with SCA complain of significant exercise intolerance. [12] Multiple factors contribute to exercise intolerance in patients with sickle cell anemia, but little information exists regarding the 6MWT or the mechanisms of exercise limitation in these patients. [11] The purpose of the present study was to examine these issues.

Aim

To determine the cardiopulmonary responses on performance of 6 minute walk test (6MWT) in patients with SCA. Versus age & sex matched controls.

Methodology

Experimental case control study was carried out to compare 6 MWT in SCA patients and also determine 6 MWD in both the groups (SCA and control). The study was conducted at outpatient regional center of sickle cell anemia and Physiotherapy outpatient department. Total 40 individuals in each group, amounting to 80 will undergo for a test protocol for a given period of time.

Subjects: The subjects who volunteered to participate for the study were included. SCA patients were selected first & normal healthy individuals were selected later who were age and sex matched provided they fulfilled the inclusion criteria and signed the written consent.

Inclusion criteria: Patients with SCA (any trait) males & females aged 12-25 with ability to complete 6 minute walk test.

Exclusion criteria: SCA

Avascular necrosis, Stroke, Pregnancy, Leg ulcers, Echo cardiographic significance of any heart disease (cardiac arrhythmia /ischemia), Sickle cell patients on blood transfusion (3 weeks prior from the commencement of research and also during the study period).

Inclusion criteria: Control

Normal healthy individuals, Age group 12-25 years of age, having the ability to walk, Individuals not using walking aids for locomotion.

Exclusion criteria: Control

Fever, Cough /Cold, Pregnancy, Any history of musculoskeletal/ cardiac/ neurological compromise, Patients unable to walk.

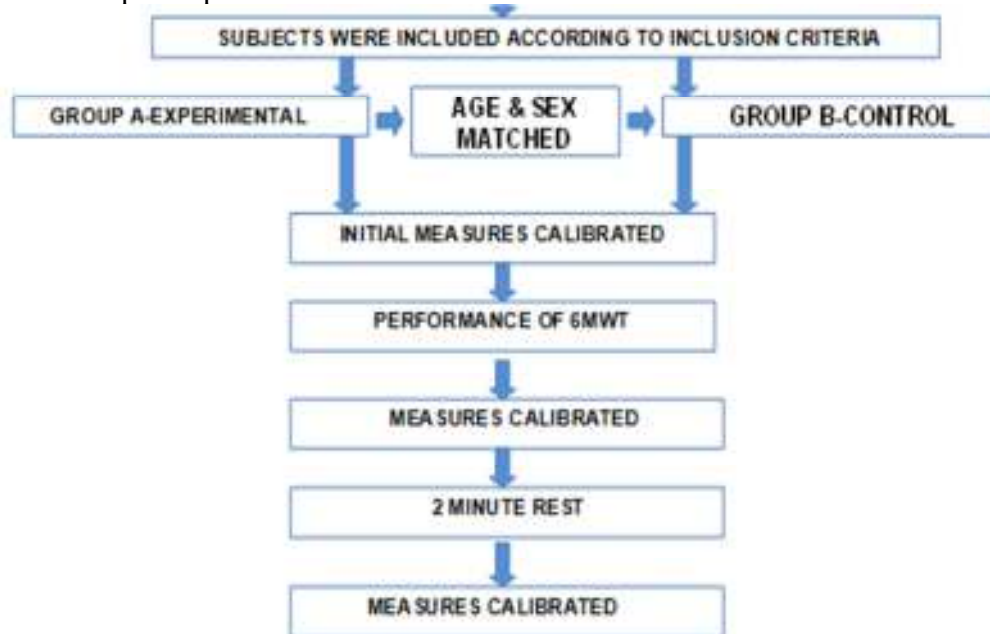
Equipment & material: weighing machine for documenting the weight, sphygmomanometer for measuring the systolic & diastolic blood pressure, stop watch for documenting the time for six minute walk test, Portable (finger) pulse oxymeter for documenting the saturation levels, measuring tape for constructing the walking track & also for measuring the distance on completion of 6MWT, traffic cones for marking the turnaround points of the track, Modified Borg Scale for monitoring levels of perceived exertion, oxygen cylinder in close vicinity for administering oxygen during emergency situations.

Six minute walk test: walking course was 30 m in length. The performance of Six Minute walk test was in accordance with the guidelines of American Thoracic Society [13].

Measures: Weight in kg, hemoglobin in gm%, blood pressure in mm of Hg (S.B.P & D.B.P), pulse rate in beats/min, respiratory rate in breaths/min, level of perceived exertion by Modified Borg scale was calibrated initially & in second & third measure except weight in kg, & hemoglobin in gm% all other measures were taken. The second reading was calibrated soon after completion of Six Minute walk test along with total distance covered in Six Minute walk test and number of pauses taken. The third measure was calibrated after 2 min rest after completion of Six Minute walk test.

General procedure

The study was approved by the ethical committee. The requisite permissions for carrying out the study were obtained. Study Protocol was followed after obtaining written informed consent from the participants as shown below



Flow chart of procedure

Statistical analysis

Raw data was spread in Microsoft excel sheet 2007 and analyzed by STATA version 10.0. Continuous variables (age, hemoglobin, weight, hemodynamic parameters) were presented as mean \pm SD. and were compared between SCA and control by paired t- test. Mean changes in various hemodynamic parameters were compared between SCA & Control group by Wilcoxon

Rank Sum test. P-value <0.05 was considered as statistical significance. Data was analyzed using statistical software STATA version 10.0.

Results

80 individuals were studied. The mean age of the subjects in SCA was 18.62 ± 4.60 and that of Control was 18.6 ± 4.56 . Subjects ranged between 12-25 years, and were age and sex matched.

The mean hemoglobin concentration value was 8.40 ± 0.76 gm % for the subjects in SCA and ranged between 7.2-10.3 and that for Control was 11.46 ± 1.51 gm % and ranged between 9.2-14.5. Mean weight was 40.62 ± 7.10 in SCA 54.82 ± 13.38 in Control group respectively.

Safety measures: Patients were subjected to assessment for cardiovascular and respiratory parameters before commencement of 6 MWT including the level of perceived exertion for which the value was 0.05 ± 0.15 and 0.01 ± 0.08 which was found to be non-significant.

SCA: The various cardiovascular parameters before the commencement of 6 MWT were considered as baseline values. The SBP, level of perceived exertion, SpO_2 , were found to be non-significant and DBP significant, HR and RR were found to be highly significant.

This was followed by administration of 6 MWT. The values obtained after 6 MWT were tabulated and compared with baseline values. In which all values were non-significant except level of perceived exertion which is highly significant

Control: The various cardiovascular parameters were assessed before the commencement of 6 MWT. This was followed by administration of 6 MWT. The values obtained after 6 MWT were tabulated and compared with baseline values. All values were highly significant except level of perceived exertion which was non-significant. The values obtained after 6 MWT were tabulated and compared with after 2 minute rest values. All values were found to be non-significant. The values obtained after 2 minute rest were tabulated and compared with baseline values. All values were found to be non significant except RR(respiratory rate) which was found to be significant. The values obtained after 6 MWT were tabulated and compared with after 2 minute rest values. The values were significant except for level of perceived exertion. The values obtained after 2 minute rest were tabulated and compared with baseline values. All values were found to be significant except DBP which was non-significant.

The total distance walked in 6 MWT in SCA group was 310.45 ± 17.44 which was quite less when compared to controls, the value being 427.53 ± 6.21 which was highly significant ($P < 0.05$)

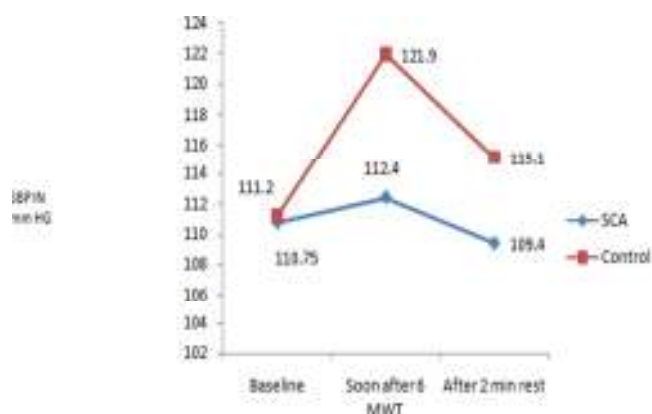


Fig: 1 SBP

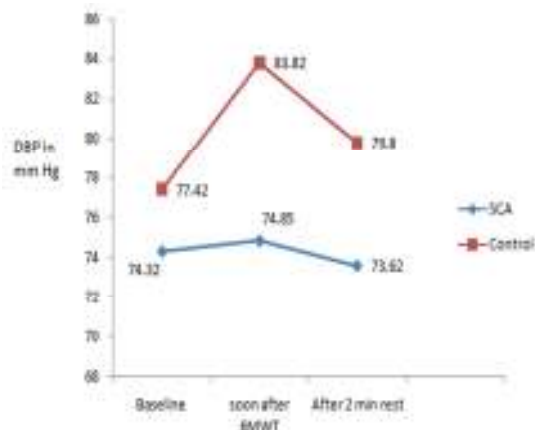


Fig: 2 DBP

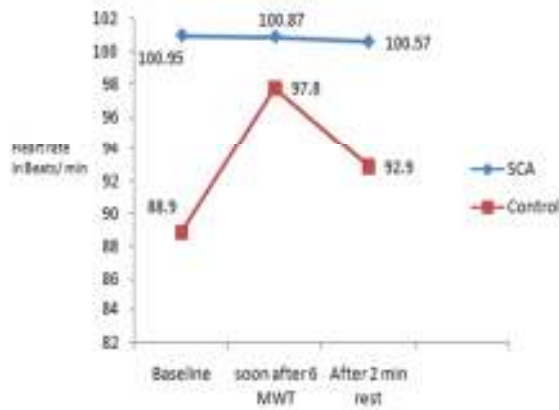


Fig: 3 Heart rate

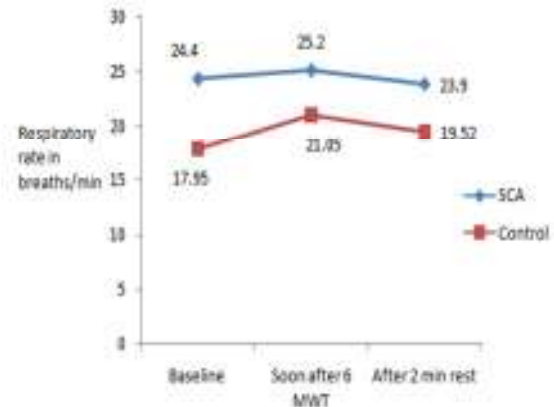


Fig: 4 Respiratory rate

Discussion

The results indicate a change in the cardiopulmonary responses on performance of 6MWT. So, the changes in relation to distance covered in SCA patients suggests that the anemic state itself may to a slight extent alter the ability of cardiopulmonary system to respond to stress induced by exercises. Moreover, as the oxygen to the working cells is sharply limited, the production of carbon dioxide is equivocally reduced or curtailed.

Lower levels of distance covered on completion of six minute walk test (6MWD) in SCA group may be related to exhaustion of skeletal muscle when compared to the control group. The reason for this is attributed to depleted hemoglobin levels. It has been observed in the study that hemoglobin level of SCA patients was 8.41gm % whereas in control it was 11.46 gm % & these values would have resulted in differences in distance covered when SCA and control were compared. This study is in line with the work done by R.K. Kapoor. [14]

Liem RI, et al, in 2009, in their study on, "Functional capacity in children and young adults with Sick cell disease undergoing evaluation for cardiopulmonary disease", commented that cardiopulmonary disease is associated with decreased functional capacity among adults with Sick cell disease and they also had used six minute walk test as a cardiopulmonary exercise testing. [15] In view of this, six minute walk test was used for the study and found that SCA individuals had exercise limitations

In this study the exercise limitations in SCA group may be related to reduced hemoglobin content, & sickle cell RBC's & endothelial dysfunction which leads to reduced oxygen carrying capacity and there by exhibiting compensatory mechanisms by these patients. [5]

The differences in the SCA and the control group is due to decreased quantity of available hemoglobin in SCA group, which is proved by the facts of reduced hemoglobin levels when compared with that of control group. Therefore, the availability of hemoglobin for oxygen transport is in itself limited in SCA patients. So, such patients have to be cautiously exercised in order to prevent any untoward effects. It also emphasizes that, while exercising, the level of hemoglobin should be incorporated in the assessment Performa's since it is also important parameter when cardiopulmonary exercise testing is being done.

On performance of 6 MWT, reduced values in SBP, DBP, HR and saturation levels can be considered as an indicator of dysfunction in the cardiopulmonary and vascular status of SCA patients, and if these dysfunctions are not intervened it could further deteriorate the patient. So proper exercise intervention has to be administered to regain back the cardiovascular changes to almost near normal and if such training is employed in SCA patients then their functioning capabilities could be improved to certain extent, so that their quality of life could be improved in the long run.

Pulmonary component in term of respiratory rate was concerned, it is clearly evident from the results that SCA patients had higher respiratory rate when compared to controls.

Thereby, indicating that the cardiovascular compromise due to sickle cell anemia has been compensated by the pulmonary system by increases in respiratory rate. But the quantification of compensatory mechanisms of cardiovascular and pulmonary systems is not exactly notified and is also beyond the scope of the present study.

The rate of perceived exertion on Modified Borg Scale is higher in SCA group when compared to control group is attributed to the sickling of RBCs in SCA. The problems may further increase during the sickle cell crises period and such patients are bound to develop easy fatigability, thereby contributing to exercise limitation.

The factors triggering the increase in respiratory rate are not exactly cleared by this study, but the possibility of alteration in mechanical properties of lungs may be the reason for increases and alteration in the composition of the blood may mediate the increases in the respiratory rate. So, the observed increase in the respiratory rate reflects an increase work load of breathing in anemic subjects when compared to healthy counterparts. But, this relative increase in work of breathing was not reflected on the subjective appreciation when examined on Modified Borg Scale, since it was a light activity but the things would have been different, if they were exercised heavily on a treadmill or on cycle ergo meter. Reduced cardiovascular responses in SCA are compensated by increasing the respiratory rate.

The strength of this study was it elicited that there exist exercise limitations in SCA patients. The study was able to underline the fact that 6 MWT can be applied without untoward effects in SCA patients

The limitations of the current study is that the changes observed during the performance of each minute of six minute walk test was not considered but graphical representations for both groups have helped to overcome this problem to certain extent.

Conclusions

This study suggests that there is a reduction in the 6MWT values when compared to control group emphasizing that SCA patients have exercise intolerance. It is concluded, that the cardiovascular responses are blunted in anemic patients due to depleted cardiac reserves which in turn are compensated by increased respiratory rates.

Conflict of interests: There are no conflicts of interests

Finance: It was a self financed study

Acknowledgements: The authors thank the management of V.S.P.M 's College of physiotherapy, & Mr.More for statistical support.

References

- [1] World Health Organization-Sickle cell anemia, report by the Secretariat, 24th April 2006.
- [2] Sickle cell disease available from University of Maryland Medical Center, 2011, what is sickle cell anemia available from <http://umm.edu/health/medical/reports/articles/sickle-cell-disease>
- [3] Sickle cell history available from <http://www.innvista.com/health/ailments/anemias/sickle-cell-history/>
- [4] SD Zavar, et al ,Non-invasive Detection of Endothelial Dysfunction in Sickle Cell Disease by Doppler ultrasonography, JAPI , Vol. 53, August 2005
- [5] Davies CTM, Cheuveneka AC, Venharpen JPM. Iron deficiency anemia: Its effect on maximum aerobic power and response to exercise in African males aged 17-40 years. Clinical Science 1973; 44: 555-561.
- [6] Gardner GW, Edgerton VR, Senevirathne B, Bernard RJ, Ohina Y. Physical work capacity and metabolic stress in subjects with iron deficiency anemia. American Journal of Clinical Nutrition 1977; 30: 910-917.
- [7] Viteri FE, Torun B. Anemia and physical work capacity. Clinical Hematology 1974;3: 609-626.
- [8] Cumming GR, Everatt D, Hastman L. Bruce treadmill test in children: Normal values in clinical population. American Journal Cardiology 1978; 41: 69-75.
- [9] Riopel DA, Taylor AB, Hohn AR. Blood pressure heart rate, pressure rate product and electrocardiographic changes in healthy children during treadmill exercise. American Journal of Cardiology 1979; 44: 697-704.

- [10] Bhav S, Pherwani AV, Desai AG, Dattani KK. Cardio-respiratory response to stress test in normal Indian boys and adolescents. *Indian Pediatrics* 1989; 26: 882-887.
- [11] Cardiopulmonary responses to exercise in woman with sickle cell anemia, Leigh A. Callahan, et al. *American journal of respiratory and critical care medicine* volume 165 2002.
- [12] Orah S. Platt et al, Mortality in Sickle cell anemia-life expectancy and risk factors for early death, *The New England journal of Medicine*, volume 330:1639-1644, June 9,1994
- [13] American Thoracic Society Guidelines for six minute walk test, *American journal of respiratory and critical care medicine* volume 166, March 2002
- [14] R.K. Kapoor, Ajay Kumar, Mahesh Chandra, et al, Cardiovascular responses to treadmill exercise testing in anemia- *Indian Pediatrics*, Volume 34, July 1997
- [15] Liem RI, et al, Functional capacity in children and young adults with Sickle cell disease undergoing evaluation for cardiopulmonary disease, *American Journal of Hematology*, October 2009, 84(10):645-9