Evaluation of functional capacity for exercise in children and adolescents with sickle-cell disease through the six-minute walk test

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Received 1 February 2013; accepted 10 April 2013
Available online 19 September 2013

Keywords
Sickle cell anemia; Acute chest syndrome; Exercise; Nutritional status

Abstract
Objective: To evaluate lung functional capacity (FC) for physical exercise in children and adolescents with sickle cell disease (SCD) through the six-minute walk test (6MWT).
Method: A cross-sectional prospective study was performed to evaluate the FC of 46 patients with SCD through the 6MWT. The following parameters were assessed: heart rate (HR), respiratory rate (RR), peripheral pulse oxygen saturation (SpO2), peak expiratory flow (PEF), blood pressure (systolic and diastolic), dyspnea, and leg fatigue (modified Borg scale) at rest, in the end of the test, and ten minutes after the 6MWT. The total distance walked was also recorded. For statistical analysis, the parametric variables were analyzed using the paired Student's t-test, analysis of variance (ANOVA), and Bonferroni multiple comparisons, with a significance level set at p < 0.05.

Results: The 46 patients were aged 9.15 ± 3.06 years, presented baseline Hb of 9.49 ± 1.67 g/dL, and walked 480.89 ± 68.70 m. SCD diagnosis was as follows: group 1- HbSS (n = 20)/HbSβ0-thalassemia (n = 3) and group 2 - HbSC (n = 20)/HbSβ+-thalassemia (n = 3). Regarding total distance walked, patients in group 1 walked a shorter distance than patients in group 2 (459.39 ± 57.19 vs. 502.39 ± 73.60 m; p = 0.032). There was no statistical difference regarding PEF in the three moments of evaluation. The SpO2 in ambient air and SpO2 with O2 differed between groups 1 and 2 (p < 0.001 vs. p = 0.002), as well as the RR (p = 0.001).

Conclusion: These patients showed a lower FC for exercise than that predicted for the age range in the literature. Patients diagnosed with HbSS/Sβ0-thalassemia had a lower performance in the exercise.
PALAVRAS-CHAVE
Anemia falciforme; Síndrome torácica aguda; Exercício; Estado nutricional

Avaliação da capacidade funcional para o exercício de crianças e adolescentes com doença falciforme pelo teste da caminhada de seis minutos

Resumo
Objetivo: Avaliar a capacidade funcional pulmonar (CF) para o exercício físico de crianças e adolescentes com doença falciforme (DF) pelo teste da caminhada de seis minutos (TC6').
Métodos: Estudo transversal prospectivo avaliando a CF pelo TC6' de 46 pacientes com DF. Foram avaliados: frequência cardíaca (FC), frequência respiratória (FR), saturação de pulso de oxigênio (SpO2), pico de fluxo expiratório (PFE), pressão arterial (PA) sistólica e diastólica, dispneia e cansaço em membros inferiores (escala de Borg modificada) em repouso, ao término e 10 minutos após o TC6' e a distância percorrida. Análise estatística: test t-Student pareado, análise de variância e comparações múltiplas de Bonferroni, significância p ≤ 0,05.
Resultados: Dos 46 pacientes, a média ± dp da idade foi 9,15 ± 3,06 anos, hemoglobina basal 9,4 ± 1,67 g/dL e distância percorrida 480,89 ± 68,70 m. Diagnóstico da DF: Grupo 1 - HbSS (n = 20)/HbSβ+-talassemia (n = 3); e Grupo 2 - HbSC (n = 20)/HbSβ+-talassemia (n = 3). O Grupo 1 apresentou menor distância percorrida do que o Grupo 2 (459,39 ± 57,19 vs 502,39 ± 73,60 m; p = 0,032). Não houve diferença estatística em relação ao PFE. A SpO2 em ar ambiente e a SpO2 com O2 (1 L/min) após o teste foi maior no Grupo 2 (p < 0,001 e p = 0,002, respectivamente). A FR foi maior no Grupo 1 ao final do TC6' (p < 0,001).

Introduction

Sickle cell anemia (HbSS) is the most common monogenic hereditary disease in Brazil, with an estimated prevalence of heterozygotes for HbS ranging from 2% to 8% in the general population. HbSS, the most severe form of sickle cell disease (SCD) is a hemoglobinopathy resulting from the single amino acid substitution of a glutamic acid for a valine at the sixth position of the beta globin chain, on chromosome 11, giving rise to hemoglobin S (HbS). This alteration in hemoglobin is responsible for the anomalous form of erythrocytes, leading to hemolytic anemia, endothelial vasculopathy, and vaso-occlusive phenomena, followed by tissue ischemia and necrosis, with subsequent organ dysfunction, which are responsible for the high mortality of SCD. SCD occurs when HbS combines with another hemoglobinopathy, such as C, D, β-thalassemia, or another HbS. The lung is a major target organ of acute and chronic complications in SCD; acute chest syndrome (ACS) is the second most frequent cause of hospitalization in this population, with high rates of morbidity and mortality. It is an acute complication usually triggered by a clinical picture of infection. It can be defined by a combination of signs and symptoms, which include dyspnea, chest pain, fever, cough, and a new pulmonary infiltrate. The proliferative vasculopathy that occurs in sickle cell disease is the main cause of the chronic pulmonary alterations that occur in these patients.

The chronic alterations and recurrent episodes of ACS decrease the functional capacity (FC) in patients with SCD. MacLean et al., when assessing lung function in children with SCD through spirometry, observed a restrictive pulmonary pattern and a progressive reduction in lung volume. Another prospective study, with patients aged 10 to 26 years, found alterations in pulmonary function, with a predominance of mixed or combined pattern.

Thus, the evaluation of FC should be part of outpatient monitoring of these patients. However, studies assessing and addressing the FC in children and adolescents with SCD are limited. A simple and effective method to evaluate the FC is to apply the six-minute walk test (6MWT), which provides information about functional status, oxygen consumption, exercise tolerance, and patient survival according to test performance. The 6MWT assesses the individual’s sub-maximal effort, similar to the effort made in some daily life activities, representing their FC to exercise.

Although the 6MWT has not been widely studied in patients with hemoglobinopathies, especially in pediatric patients, preliminary data suggest that there may be a good correlation among this test, maximum oxygen uptake, and severity of pulmonary hypertension in adults with SCD. There are no published articles in the literature evaluating the FC in children and adolescents with SCD; thus this study aimed to evaluate the FC to exercise in children and adolescents with SCD using the 6MWT.

Methods

This was a prospective cross-sectional study evaluating 46 children and adolescents with SCD aged between 6 and 18 years, confirmed by Hb electrophoresis (HbSS, HbSC, HbSβ+-talassemia, or HbSβ+-thalassemia major). The study was completed using the consensus criteria established by the American Academy of Pediatrics, consisting of an interview with parents or guardians, a medical history, clinical examination, physical-education history, and laboratory tests: complete blood count (Hb, platelet count, percentage), reticulocyte count, and ferritin. 

The patients were divided into two groups: Group 1 (G1) - HbSS (n = 20)/HbSβ+-talassemia (n = 3); and Group 2 (G2) - HbSC (n = 20)/HbSβ+-talassemia (n = 3). The patients had the following characteristics: Group 1 - 9,15 ± 3,06 years old; Group 2 - 9,67 ± 3,06 years old. The patients were assessed with the 6MWT, which consists of measuring the distance walked (in meters) in 6 minutes. The test was performed in a hospital setting: an inpatient room, an outpatient room, or a specialized room, followed by a physical examination with a clinical history, supplemented by a medical history, physical-education history, and laboratory tests. 

The patients were evaluated in a pre-test, with a 10-minute rest period, followed by a 6-minute walking test, and a post-test with a 10-minute rest period. The patients were assessed with the 6MWT, which consists of measuring the distance walked (in meters) in 6 minutes. The test was performed in a hospital setting: an inpatient room, an outpatient room, or a specialized room, followed by a physical examination with a clinical history, supplemented by a medical history, physical-education history, and laboratory tests.
18 years, distributed according to HbSS genotype, HbSβ*-
thalassemia, HbSC, and HbSβ*-thalassemia. The children
who were attended to at the pediatric hematology outpa-
tient clinic from April of 2009 to July of 2010 and met the
inclusion criteria were evaluated.

The FC of these patients was evaluated through the
6MWT, following the guidelines of the American Thoracic Society. The study was approved by the Ethics
Committee in Research of the Escola Paulista de Medicina/Universidade Federal de São Paulo (EPM/UNIFESP). Exclusion criteria were patients with hemodynamic instability or neurological or orthopedic diseases that limited exercise performance.

Basal hemoglobin (Hb) and history of hospitalizations for
pulmonary complications were collected from the patients’
medical records. The assessment of body mass (in kg) and
height (in m) was performed in a standardized manner, using
an anthropometric digital scale (Filizola®). The classification
of nutritional status was performed using Z-score distribu-
tion for weight/age, height/age and body mass index (BMI).

The WHO AnthroPlus 2007 software of the World Health Organization (WHO) was used to obtain the BMI and Z score values.

The 6MWT was performed in a 10-meter long corridor,
outdoors, with markings at every meter and indicators on the
ground indicating the beginning and end of the trajectory. It
was decided to perform the test in a 10-meter corridor due to
the promising results in the ‘’shuttle walk test’’, which
also uses this distance.

Patients received theoretical and practical training
regarding the objectives of the 6MWT and how they should
perform it. Each patient underwent two tests (with a
30-minute interval between them); the test with best per-
formance was considered if the difference between tests
was less than 10% in case of a difference higher than 10%,
a new test would be performed. No patient had to perform
more than two tests.

The 6MWT was administered by two trained physical ther-
apists. At the beginning of the test, the patient was at rest
for 15 to 20 minutes and had fasted for at least two hours. At
the end of six minutes, the patient stopped where he/she
was, and one of the therapists approached him/her with
a chair and assessment equipment in order to record the
total distance walked. The number of turns was counted
manually, and a stopwatch (Casio®) was used to mark the
time.

Water was offered to the patients before and after the
6MWT. All patients used oxygen during the test (nasal can-
nula 1 L/min), regardless of SpO₂ on ambient air, in order
to prevent hypoxemia during exercise, due to the risk of
a vaso-occlusive crisis caused by SCD.

All variables were assessed at rest, at the end of the test,
and at 10 minutes after it. The following parameters were
measured: systolic (SBP) and diastolic (DBP) blood pressure
with a BD® sphygmomanometer; respiratory rate (RR),
SpO₂, and heart rate (HR) with a portable pulse oximeter
(Dixtal®). The peak expiratory flow (PEF) was measured
using an Assess Peak Flow Meter® device; three measure-
ments were taken and the highest was considered. Dyspnea
and lower-limb fatigue were assessed by the modified Borg scale. All
variables were measured with the patient in the sitting position,
except for PEF, which was measured in the standing position.

To analyze the behavior of SCD during the 6MWT, the sample
was divided into two groups according to the disease
genotype. Group 1 consisted of patients with HbSS/HbSβ*
thalassemia and group 2 consisted of patients with HbSC/
HbSβ*-thalassemia, as patients in group 1 tend to have a
more severe clinical course than those in group 2.

Statistical analysis

Parametric variables were analyzed by paired Student’s t-
test and continuous measurements by ANOVA for repeated
measures. Multiple Bonferroni comparisons were made
between the two evaluation moments, and values were
considered statistically significant when p ≤ 0.05. Results
are shown as mean ± standard deviation (SD), median
(minimum-maximum), frequency, and percentage. The
statistical analysis was performed using the Statistical Package
for Social Sciences (SPSS) release 15.0.

Results

This study evaluated 46 patients with SCD with
the following demographic characteristics, expressed
as mean ± standard deviation (SD): age 9.15 ± 3.06 years;
basil Hb 9.49 ± 1.67 g/dL; weight 30.98 ± 11.30 kg;
height 1.34 ± 0.16 m; BMI 16.63 ± 2.40 kg/m²; percentile
height/age 49.29 ± 26.57; height/age 42.83 ± 25.92;
BMI/age 46.86 ± 24.70. The Z-scores for all anthropo-
metric indices were: weight/age 0.04 ± 1.03; height/age
0.22 ± 0.95; and BMI/age 0.20 ± 1.26. The total distance
walked during the 6MWT was 480.89 ± 68.70 m.

Patients in group 1 and group 2 were similar regarding
age, gender, and anthropometric variables; group 1 had
lower mean Hb values and higher frequency of pneumonia
and/or ACS than group 2 (Table 1). The distance walked
by patients in group 1 was significantly shorter than that of
patients in group 2 (459.39 ± 57.19 vs. 502.39 ± 73.60 m,
p = 0.032 - Table 1).

Analyzing the 46 patients, it was observed that the
cardiorespiratory variables (HR and RR) differed only at
the end of the 6MWT compared to the other moments in
time (p < 0.001). SBP and DBP decreased significantly ten
minutes after the end of the 6MWT, when compared to measurements
at the end of the test (p = 0.003, p < 0.001) (Table 2).

There was no statistical difference regarding PEF (L/min)
between the three moments in time, as well as in the eval-
uation of lower-limb stress and fatigue assessed by the Borg
scale (Table 3).

Table 4 presents the description of the variables mea-
sured during the 6MWT (at rest, end of the test and ten
minutes after the 6MWT) in groups 1 and 2. When per-
forming multiple comparisons of mean differences between
the moments when cardiorespiratory and respiratory vari-
ables were measured in Groups 1 and 2, it was observed
(means of measurements/standard error; p) at rest vs.
end of the 6MWT that there was an increase in HR (-10.83/2.50; p < 0.001), RR (-4.50/0.56; p < 0.001), SBP
(-3.85 / 1.50, p = 0.052) and DBP (-3.09/1.48, p = 0.119); rest
vs. ten minutes after the end of the 6MWT, a decrease in
HR (0.76/2.93, p = 1), RR (0.41/0.70, p = 1), SBP (1.41/2.03,
p = 1) and DBP (2.80/1.76, p = 0.343); end of the 6MWT vs.
Table 1  Demographic and clinical data and distance walked in the six-minute walk test by the HbSS/Spβ-thalassemia and HbSC/Spβ-thalassemia groups.

<table>
<thead>
<tr>
<th></th>
<th>HbSS / Spβ-thalassemia group 1</th>
<th>HbSC / Spβ-thalassemia group 2</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic data</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>9.21 ± 3.45</td>
<td>9.08 ± 2.69</td>
<td>0.887</td>
</tr>
<tr>
<td>Gender (%)</td>
<td>56.53 (male)</td>
<td>52.17 (male)</td>
<td>0.767a</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>30.85 ± 13.31</td>
<td>31.11 ± 9.16</td>
<td>0.939</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.34 ± 0.18</td>
<td>1.34 ± 0.14</td>
<td>0.956</td>
</tr>
<tr>
<td>Body mass index</td>
<td>16.37 ± 2.67</td>
<td>16.89 ± 2.13</td>
<td>0.472</td>
</tr>
<tr>
<td>Hb (mean g/dL)</td>
<td>8.26 ± 1.33</td>
<td>10.70 ± 0.90</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Hospitalizations due to pulmonary complications</strong></td>
<td></td>
<td></td>
<td>0.001b</td>
</tr>
<tr>
<td>PNM % (n)</td>
<td>47.82 (11)</td>
<td>34.78 (8)</td>
<td></td>
</tr>
<tr>
<td>ACS % (n)</td>
<td>26.08 (6)</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td>ACS and PNM % (n)</td>
<td>13.05 (3)</td>
<td>8.70 (2)</td>
<td></td>
</tr>
<tr>
<td>No complications % (n)</td>
<td>13.05 (3)</td>
<td>56.52 (13)</td>
<td></td>
</tr>
<tr>
<td>Distance walked (m)</td>
<td>459.30 ± 57.19</td>
<td>502.39 ± 73.6</td>
<td>0.032</td>
</tr>
</tbody>
</table>

Tests, Student’s t-test; ACS, acute chest syndrome; n, number; m, meters; PNM, pneumonias.

a chi-squared.
b likelihood ratio.

Table 2  Respiratory and cardiorespiratory variables of children and adolescents with sickle cell disease submitted to the six-minute walk test.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Rest</th>
<th>End of test (sixth minute)</th>
<th>Ten minutes after end of the test</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (bpm)</td>
<td>91.93 ± 13.0</td>
<td>102.76 ± 20.3a</td>
<td>91.17 ± 12.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SpO2 c/ O2 (%)</td>
<td>97.46 ± 1.9</td>
<td>97.20 ± 1.9</td>
<td>95.72 ± 3.0</td>
<td>0.053</td>
</tr>
<tr>
<td>SpO2 AA (%)</td>
<td>95.15 ± 3.3</td>
<td>-</td>
<td>95.72 ± 3.0</td>
<td>0.053</td>
</tr>
<tr>
<td>RR (rpm)</td>
<td>21.67 ± 4.4</td>
<td>26.17 ± 5.0a</td>
<td>21.26 ± 4.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>99.37 ± 11.6</td>
<td>103.22 ± 15.4</td>
<td>97.96 ± 11.6a</td>
<td>0.003</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>59.26 ± 10.0</td>
<td>62.35 ± 10.2</td>
<td>56.46 ± 7.9a</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

bpm, beats per minute; DBP, diastolic blood pressure; HR, heart rate; mmHg, millimeters of mercury; rpm, respirations per minute; RR, respiratory rate; SBP, systolic blood pressure; SpO2 AA, pulse oxygen saturation with ambient air; SpO2 w/ O2, pulse oxygen saturation with oxygen (1 L/min).

Test: analysis of variance with repeated measures, with two factors.

ten minutes after the end of the 6MWT, a decrease in HR (11.59% / 2.50%; p < 0.001), RR (4.91% / 0.56%, p < 0.001), SBP (5.26% / 1.59%, p = 0.004) and DBP (5.89% / 1.48%, p < 0.001). When comparing rest vs. ten minutes after the end of the 6MWT, there was an increase in SpO2 AA (-3.65% / 0.53%; p < 0.001). When comparing Groups 1 and 2 at rest vs. six minutes after the end of the 6MWT there was an increase in SpO2 with O2 (-1.57% / 0.47%, p = 0.002).

Discussion

This study demonstrated that 65.21% of patients had a history of hospitalizations for pulmonary complications (ACS and/or pneumonia). People with a history of recurrent ACS have lower peak maximum oxygen consumption (VO2) and greater possibility of chronic lung injury, which may have an important impact on FC for exercise.11 Pulmonary

Table 3  Modified Borg scale and peak expiratory flow of children and adolescents with sickle cell disease submitted to the six-minute walk test.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Rest</th>
<th>End of the test (Sixth minute)</th>
<th>Ten minutes after end of the test</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Borg D</td>
<td>0 (0-3)</td>
<td>0 (0-9)</td>
<td>0 (0-4)</td>
<td>-</td>
</tr>
<tr>
<td>Borg LLLL</td>
<td>0 (0-5)</td>
<td>1 (0-10)</td>
<td>0 (0-9)</td>
<td>-</td>
</tr>
<tr>
<td>PEF (L/min)</td>
<td>223.04 ± 65.92</td>
<td>231.63 ± 76.65</td>
<td>226.63 ± 67.06</td>
<td>0.074</td>
</tr>
</tbody>
</table>

Borg D, Borg of dyspnea; Borg LLLL, Borg of lower limbs; L/min, liters per minute; PEF, peak expiratory flow.

Test: analysis of variance with repeated measures, with two factors.

a Variables as median (minimum-maximum).
Table 4  Description of variables at the moments (at rest, end of the test, and ten minutes after the test) in the HbSS/HbSβ0-thalassemia and HbSC/HbS β+ -thalassemia groups.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Moment</th>
<th>Group 1 (n = 23)</th>
<th>Group 2 (n = 23)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>Rest</td>
<td>94.61</td>
<td>11.93</td>
</tr>
<tr>
<td></td>
<td>End of the test (sixth minute)</td>
<td>105.65</td>
<td>19.44</td>
</tr>
<tr>
<td></td>
<td>Ten minutes after end of test</td>
<td>94.39</td>
<td>12.13</td>
</tr>
<tr>
<td>SpO2 AA (%)</td>
<td>Rest</td>
<td>93.13</td>
<td>3.55</td>
</tr>
<tr>
<td></td>
<td>Ten minutes after end of test</td>
<td>94.09</td>
<td>3.41</td>
</tr>
<tr>
<td>SpO2 with O2 (%)</td>
<td>Rest</td>
<td>96.70</td>
<td>2.30</td>
</tr>
<tr>
<td></td>
<td>End of the test (sixth minute)</td>
<td>96.39</td>
<td>2.25</td>
</tr>
<tr>
<td></td>
<td>Ten minutes after end of test</td>
<td>23.30</td>
<td>4.33</td>
</tr>
<tr>
<td>RR (rpm)</td>
<td>End of the test (sixth minute)</td>
<td>28.30</td>
<td>5.34</td>
</tr>
<tr>
<td></td>
<td>Ten minutes after end of test</td>
<td>22.65</td>
<td>4.32</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>End of the test (sixth minute)</td>
<td>104.78</td>
<td>18.55</td>
</tr>
<tr>
<td></td>
<td>Ten minutes after end of test</td>
<td>98.70</td>
<td>12.54</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>End of the test (sixth minute)</td>
<td>57.39</td>
<td>10.96</td>
</tr>
<tr>
<td></td>
<td>Ten minutes after end of test</td>
<td>61.74</td>
<td>11.14</td>
</tr>
<tr>
<td>PEF (L/min)</td>
<td>End of the test (sixth minute)</td>
<td>223.04</td>
<td>64.77</td>
</tr>
<tr>
<td></td>
<td>Ten minutes after end of test</td>
<td>234.57</td>
<td>78.78</td>
</tr>
</tbody>
</table>

bpm, beats per minute; DBP, diastolic blood pressure; HR, heart rate; L/min, liters/minute; mmHg, millimeters of mercury; RR, respiratory rate; rpm, respirations per minute; SBP, systolic blood pressure; PEF, peak expiratory flow; SpO2 AA, pulse oxygen saturation with ambient air; SpO2 w/ O2, pulse oxygen saturation with oxygen (1 L/min).

complications were similar to those reported in literature: 86.95% of patients in group 1 had a history of hospitalization for pulmonary complications (pneumonia and/or ACS), whereas in group 2 the incidence was 43.48%. Clinical manifestations of SCD, in general, are more severe in patients with HbSS and HbSβ0-thalassemia, and ACS is more frequent in this group.6,23

The total distance walked in the 6MWT by healthy children is influenced by age, height, and weight: it is inversely proportional to weight and directly proportional to age and height.24 Although the nutritional status of the patients were within the mean normal values, differing from other studies in SCD where patients tend to be malnourished,25,26 the distance walked during the 6MWT was shorter than that predicted for age and height,17-29 meaning that factors other than weight and height, such as hemoglobin value and the occurrence of ACS, may be related to these findings.

When comparing the total distance walked, patients in group 2 walked a significantly longer distance than those in group 1. These results may be related to the fact that patients with HbSS and Sβ0-thalassemia have a clinically more severe form of the disease, with lower basal Hb values and greater number of hospitalizations for pulmonary complications, which may have also caused a significant difference in the comparison of the two groups regarding SpO2 and RR during the 6MWT.

Liem et al.11 evaluated FC in 30 children and adolescents with SCD undergoing exercise testing, and found FC limitation ranging from moderate to severe. FC for exercise was significantly lower in children with a history of recurrent ACS. and was related to the level of basal Hb (9.5 ± 1.6 g/dL), similar to values found in this study (9.49 ± 1.67 g/dL - Table 1).

Most children and adolescents adapt to the increased cardiac demand caused by chronic anemia, and generally have a 50% to 75% reduced exercise capacity.30 Chronic anemia can lead to lower tissue oxygenation, mainly during exercise, in which the use of oxygen is increased to meet the demand for energy. In SCD, some compensatory mechanisms prevent this from occurring, such as increased heart rate during exercise, increased systolic volume, and decreased peripheral vascular resistance, reducing the resistance of sickle erythrocytes in capillary transit and oxygen supply to the tissues, thus allowing close to normal saturation in the mixed venous blood.31,32 This could explain the present results of a significant increase in HR at the end of the 6MWT without significant changes in SpO2.

The study by Campbell et al.32 concluded that the exercise-induced SpO2 decrease was more related to the degree of anemia and hemolysis than to previous history of ACS and severe pain. Lambers et al.33 demonstrated that SpO2 varies little during the 6MWT in healthy children, whereas there is an increase in HR and RR. In the present study, a significant increase in HR, RR and SpO2 with O2 was observed at the end of the 6MWT.

SBP in patients with SCD is described as normal and DBP as decreased, resulting in a lower mean arterial pressure.34 The response observed in this study, a decrease in SBP and DBP
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ten minutes after the 6MWT, may be related to the decrease in HR and consequent decrease in cardiac output, maintaining vasodilatation for a period of time after the exercise, which was also described in other studies. 35,36

A subjective method of dyspnea and fatigue assessment is through the Borg scale. 21 The Borg scale can be used as an aid to the 6MWT, allowing for the evaluation of the degree of respiratory distress according to the patient’s perception through subjective indices. 12 In this study, there were no significant changes in respiratory distress of patients during the 6MWT, which may have been due to the oxygen supplied to patients (nasal cannula 1L/min) during the 6MWT.

When evaluating PEF, there was no statistical difference among the three moments in time (Table 3). Lower PEF in asthmatic children is related to disease symptoms and the risk of exacerbation. 37 In the present sample of children with SCD, there was no difference between groups 1 and 2 when PEF was evaluated at rest.

Regarding the variables analyzed during the test, it was observed that SpO2 in ambient air (AA SpO2) and SpO2 with 1 L/min of O2 were on average significantly higher in group 1 than in group 2. Significant differences were also found for RR, and higher values were observed in group 1 regardless of the time of evaluation. These findings may be related to the fact that pulmonary complications were more frequent in group 1.

This is a novel study; however, it has the limitation of using a 10-meter corridor to perform the 6MWT, whereas the ATS recommends a 30-meter corridor. 12 Despite the recommendation of the ATS, some studies 38-40 applied different lengths for the 6MWT. Sciubba et al. 41 stated that the length of the track is not the most important feature of the 6MWT. The standardization of the shuttle walk test recommends the use of a 10-meter corridor, 12 and there is a reference value for the distance traveled (544.28 ± 131.13 meters) for Brazilian children (mean age ± SD: 11.28 ± 1.85 years). 20 This study sample showed low predicted values for the distance walked in the 10-meter corridor, when compared to healthy Brazilian children.

It can be concluded that this sample of children and adolescents with SCD had FC for exercise below that predicted for the age range when compared to healthy children. Patients diagnosed with HbSS/Sp²-thalassemia had a worse performance regarding total distance walked, HR, and SpO2 after 6MWT when compared to patients with HbSC/Sp⁺-thalassemia. It is suggested that other studies should be conducted with similar designs for evaluation of FC in patients of this age group with SCD, as they show alterations in FC, which are related to the disease prognosis and quality of life.

Conflicts of interest

The authors declare no conflicts of interest.

References


23. Van Beers EJ, van Tuijn CF, Mac Gillavry MR, van der Giessen A, Schnog JJB, Biemond BJ, on behalf of the CURAMA study group. Sickle cell disease-related organ damage occurs irrespective