

Program of combined physical exercise reduces the perception of pain in a patient with sickle cell anemia. Case report

Programa de exercício físico combinado reduz a percepção da dor em paciente com anemia falciforme. Relato de caso

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DOI 10.5935/1806-0013.20170114

ABSTRACT

BACKGROUND AND OBJECTIVES: Sickle cell anemia is one of the most common hereditary hematological disease in the world. Among many clinical manifestations, the main characteristic of this disease is the painful crises. Considering the increasing number of individuals with sickle cell anemia in Brazil, the increase in life expectancy of these individuals, who are advised to restrict physical activity, it is important to investigate this subject since exercises have been listed as relevant in health promotion. The objective of this study was to analyze the perception of pain, some physiological responses and the quality of life of a patient with sickle cell anemia undergoing a program of physical exercises (aerobic and resistance).

CASE REPORT: Female patient, 56 years old, diagnosed with sickle cell anemia as a child, and in the course of this research did not make routine use of drugs in the control of the disease. On physical and ergo-spirometric examination, and during four-month of combined exercise, she did not present critic clinical condition, only some characteristic difficulties such as musculoskeletal pain, low cardiorespiratory resistance, and early fatigue.

CONCLUSION: The results suggested that a program of combined and regular exercises produced important changes in the patient, in several aspects related to her health, including the reduction of musculoskeletal pain and increased general physical fitness, contributing to the improvement of the perception of quality of life.

Keywords: Health promotion, Musculoskeletal pain, Physical exercise, Physiology, Quality of life, Sickle cell disease.

RESUMO

JUSTIFICATIVA E OBJETIVOS: A anemia falciforme é uma das doenças hematológicas hereditárias mais frequentes no mundo. Dentre as diversas manifestações clínicas, a principal característica dessa doença são as crises dolorosas. Considerando o crescente número de indivíduos com anemia falciforme no Brasil, o aumento da expectativa de vida desses indivíduos, e que ainda recebem orientação para restringirem práticas de esforços físicos, investigações sobre o tema se tornam relevantes, uma vez que o exercício físico tem sido elencado como estratégia na promoção da saúde. O objetivo deste estudo foi analisar a percepção da dor, algumas respostas fisiológicas e a qualidade de vida de uma portadora de anemia falciforme submetida a um programa de exercício físico combinado (aeróbio e resistido).

RELATO DO CASO: Paciente do sexo feminino, 56 anos de idade, diagnosticada com anemia falciforme quando criança, e no decorrer desta pesquisa não fez uso rotineiro de fármacos para o controle da doença. No exame físico e ergoespirométrico, e durante o período de intervenção de quatro meses de exercício físico combinado, não apresentou quadro clínico crítico, apenas algumas dificuldades características, como: dores osteomusculares, baixa resistência cardiorrespiratória e fadiga precoce.

CONCLUSÃO: Os resultados sugeriram que um programa de exercício físico combinado e regular produziu alterações importantes para a paciente, em diferentes aspectos relacionados à sua saúde, dentre elas destacam-se a diminuição da dor osteomuscular e aumento da aptidão física geral, contribuindo para a melhora da percepção da qualidade de vida.

Descritores: Anemia falciforme, Dor musculoesquelética, Exercício físico, Fisiologia, Promoção da saúde, Qualidade de vida.

INTRODUCTION

Sickle cell anemia (SCA) is a hemoglobinopathy arising from the replacement of a glutamic acid by a valine at the sixth position of the beta globin, giving rise to hemoglobin S (HbS). The gene responsible for encoding this protein is located on chromosome 11. In the case of absence or decreased oxygen tension, HbS undergoes polymerization, changing the morphology of the red blood cells (sickling), carrying less oxygen and having difficulties to properly circulate through the small blood vessels, resulting in the obstruction of the capillary blood flow and their early destruction¹. Sickle cell anemia is one of the most common hereditary hematological disease in the world. In Brazil, it has a significant

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Submitted in Apryl 05, 2017.

Accepted for publication in July 17, 2017.

Conflict of interests: none – Sponsoring sources: none.

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epidemiological importance due to its prevalence; 2 to 8% of the population and its morbidity and mortality, therefore it has been singled out as a public health issue². However due to the advances in treatment, the infant mortality rate has decreased significantly in recent decades, however, the number of adults with SCA with late complications increased³.

The pathophysiological mechanism of the disease can cause several acute and chronic clinical manifestations, such as acute chest syndrome, pulmonary hypertension, heart failure and stroke⁴. Among the characteristic manifestations of the disease, vaso-occlusive crises are frequent, causing pain in bones, muscles, and joints as a result of the obstruction of the microcirculation of the sickled erythrocytes⁵. The intense physical effort is one of the factors that can contribute to this process⁶ which can worsen the complications and cause sudden death of these patients. However, Harmon et al.⁷ found that the absolute number of deaths in people with SCA due to physical exercise (PE) is small and that mortality occurred with practitioners of intense physical exercise. Thus, there are some recommendations for the practice of physical exercises in order to reduce the risks and injuries of the disease, such as: control the intensity and duration of exercises and hydration during the performance^{8,9}. Following the recommendations, the study of Barbeau et al.¹⁰ showed that regular exercise with moderate intensity (60-75%) can decrease the risk of the inflammatory reaction related to exercise and increase the vasodilator reserve, decreasing the risk of vaso-occlusive crisis.

Systemic deficiencies caused by the disease can lead to a more sedentary lifestyle, which in turn may result in an overall loss of muscle strength and cardiorespiratory capacity. Ivo and de Carvalho¹¹ reported that patients with SCA had dyspnea when walking, climbing stairs or ramps, or performing vigorous physical activities, which indicates a loss of functional capacity in this population. As a result of these alterations, limitations, and pain, it is also common to see a variable impact on the quality of life (QoL) of these patients¹².

As a consequence of the inherent risks in the practice of misguided physical exercises and incipient information in the scientific literature, professionals are still reluctant to recommend physical exercises. Studies on the effects of physical exercises in patients with SCA showed beneficial effects on pain, strength and QoL in children^{13,14}. However, little is known about the possible effects on adults, especially, the combined physical exercise. Considering the increasing number of cases of SCA in Brazil, the increase in life expectancy of these individuals and the progressive reduction in functional capacity due to complications, specifically the painful crises, investigations on the subject become relevant, both for patients who will directly benefit from the effects of physical exercises and for health professionals, who can identify therapeutic strategies for these patients.

The objective of this study was to analyze the perception of pain, some physiological responses and the QoL of an SCA patient undergoing a combined physical exercise program.

CASE REPORT

Female patient, 56 years old, diagnosed with SCA as a child. She underwent a multidisciplinary treatment with the family, to bet-

ter understand the disease, signs of severity, and proper measures to prevent and treat her crises. During this survey, and in the six previous months, she did not take any drugs routinely to control the disease, only when she had the painful crises. Her hemoglobin test showed a moderate anemia (9.7 g/dL), according to the World Health Organization (WHO)¹⁵. In the physical examination and ergospirometry test, she did not present critical clinical conditions (ulcers, bacterial infections or any other renal, ophthalmologic, neurologic, cardiovascular and pulmonary complications)¹⁶, only some difficulties characteristic of the disease as musculoskeletal pain (mainly in the lower limbs and the lumbar region), low cardiorespiratory resistance and early fatigue in the ergospirometry test. Apart from that, she had a physically active life according to the data obtained by the International Physical Activity Questionnaire (IPAQ).

Before the beginning of the activities, it was applied the pain questionnaires (Brief Pain Inventory - BPI)¹⁷ and level of physical activity by IPAQ, brief forms¹⁸. Also, we had anthropometric evaluations (body mass, height, and body mass index - BMI), and physical fitness test (flexibility of upper/lower limbs, motor coordination, agility, upper and lower limbs and abdominal strength, and static balance¹⁹). The ergospirometry test was performed on a treadmill to measure the cardiorespiratory capacity, using the Bruce Protocol adapted, with progressive load until maximum voluntary exhaustion. During the test, the heart rate (HR) was monitored using a frequency counter (POLAR[®] T31), blood pressure (Premium sphygmomanometer and stethoscope) and the subjective perceived exertion (The Borg Rating of Perceived Exertion scale - RPE)²⁰. During the assessment, the level of hemoglobin was also measured by capillary blood collection and by hemoglobinometer (Agabe[®]).

In addition, for the analysis of the effect of the physical exercise pre-and post-program on the patient's QoL (qualitative character), a semi-structured interview was elaborated aiming at the self-perception of the improvement or worsening in relation to: pain, sleep, mood, self-esteem, health, pleasure, stimulation, posture and exercises.

The physical exercise program adopted lasted for four months (48 sessions). The training was a combined approach (aerobic and resisted in the same session)²¹, and the overload was applied in accordance with the results obtained in the tests and by the RPE during the program. Three weekly sessions of 60 minutes each, consisting of 30 minutes of aerobic training (at HR between the anaerobic threshold 1 and the anaerobic threshold 2 [110-125 bpm]) and 30 minutes of resisted exercise, with three sets of 10 to 12 repetitions, for the large muscle groups, alternating exercises for the lower and upper members. The sequence adopted throughout the experiment was aerobic followed by resisted training, and the subject accomplished the 48 scheduled sessions of physical exercises (100% attendance).

The general characteristics of the patient, the absolute results and the respective classifications of the functional tests (physical fitness), before and after the period of the physical exercises can be observed in table 1. It is worth to highlight the increase in the diastolic blood pressure (DBP) after the training protocol and slight decrease in the hemoglobin value. In addition, the

Table 1. Values of body mass index, heart rate, blood pressure, biochemical tests, and functional fitness before and after the PE program

Variables	Before		After		Δ%
Body mass index (kg/m ²)	21.7		21.4		-1.38
Heart rate at rest (bpm)	70		68		-2.86
Systolic blood pressure (mmHg)	120		120		0.00
Diastolic blood pressure (mmHg)	70		90		28.57
Hemoglobin (g/dL)	9.7		9.4		-3.09
Tests	Before	Classification	After	Classification	Δ%
Flexibility of lower limbs (cm)	61.1	Good	61.3	Good	0.33
Coordination (sec.)	8.26	Very good	7.45	Very good	-9.81
Agility (sec.)	18.8	Very good	16	Very good	-14.89
Strength resistance of upper limbs (rep/t)	20	Poor	22	Regular	10.00
Flexibility of upper limbs (cm)	+ 4.0	Very good	+ 7.50	Very good	87.50
Abdominal resistance (rep/t)	13	Good	15	Good	15.38
Strength resistance of lower limbs (rep/t)	17	Regular	21	Very good	23.53
Static balance (sec.)	30	Very good	30	Very good	0.00

Before = period before physical training; After = period after physical training; Δ% = percentage of change in before and after evaluation; Rep/t: repetitions per time.

results indicated that the patient showed improvement in all the variables after the PE program, except in static balance, which remained the same. The aspects that had higher differences were: flexibility of upper limb, strength resistance of lower limb, abdominal resistance and agility.

The results of the HR, the RPE, maximum consumption of oxygen (VO₂max.), and total time during the ergospirometry test are shown in table 2. We can see a decrease in the VO₂max results e longer permanence in the test after the PE program. Moreover, for the same workload, the subject had a lower HR and RPE in relation to the initial data.

In relation to pain, in the BPI, the patient reported that the main sites of pain in both assessments were concentrated in the lower limbs and the lumbar spine. However, in the assessment after the PE program, she reported a decrease in the pain scale intensity and reduction of pain interference in her daily activities to walk, work, in her social activities, sleep, and mood (Table 3).

Table 3. Pain perception-Brief Pain Inventory before and after the physical exercise program

Pain	Before	After	Δ%
Average intensity	7	5	- 20
At the time of interview	8	4	- 40
Relief with exercise	-	80%	-
Pain interference	Before	After	Δ%
General activity	7	4	- 30
Disposition	6	2	- 40
Ability to walk	3	0	- 30
Work	8	5	- 30
Relationship with other people	0	0	0
Sleep	2	1	- 10
Mood	2	0	- 20

Before = period before physical training; After = period after physical training; Δ% = percentage of change before and after evaluation.

Table 2. Data obtained in the ergospirometry test: heart rate, Borg scale, VO₂ maximum and total time of the test before and after the physical exercise program

Phases	Before	After
Adaptation	HR: 75 bpm	HR: 70 bpm
1 st (3 min)	Easy (9) - 83 bpm	Very easy (7) - 78 bpm
2 nd (3 min)	Relatively easy (11) - 92 bpm	Easy (9) - 89 bpm
3 rd (3 min)	Slightly tiring (13) - 107 bpm	Relatively easy (11) - 100 bpm
4 th (3 min)	Tiring (16) - 118 bpm	Slightly tiring (13) - 112 bpm
5 th (3 min)	Exhaustion - 129 bpm	Exhaustion - 123 bpm
VO ₂ maximum (mL/kg/min)	21.7	20.31
Total time (min)	12.48	14.10

Before = period before physical training; After = period after physical training; HR = heart rate; bpm = beatings per minute; VO₂max = maximum oxygen uptake.

In relation to the qualitative assessment of the QoL, the subject reported pain reduction in the lumbar spine, a significant improvement in her posture, much more disposition in daily activities, and a significant increase in strength or muscle resistance. *"I feel that I am improving, I don't feel so tired during work or even with the activities at home, and I regret when I do not come to the session because I feel my body heavier"*.

DISCUSSION

SCA clinical manifestations vary among patients, while some have severe conditions with several complications, others evolve only with mild symptoms^{22,23}. In relation to the patient in this case, despite living a physically active life as seen in the IPAQ, the early diagnosis and proper professional and family follow-up were very important and probably contributed to a controlled clinical condition, without the need for routine use of drugs, providing a longer life expectancy. In fact, authors state that the early diagnosis, added to the expertise of a multidisciplinary team and the participation of the family has a crucial role in the reduction of complications associated with the disease, as well as prolonging the life of patients^{24,25}.

Pain is a common clinical manifestation of SCA and patients usually seek for medical care²⁶. In fact, Martins, Moraes and Silveira²⁷ in a study conducted in a blood bank in Brazil, showed that the most prevalent care for patients with SCA is due to pain crises, accounting for a total of 64.4% of the cases.

In this study, the main discomfort related to pain reported by the subject was in the lower limbs and in the lumbar region, corroborating with Taylor et al.²⁸ study on the multiple dimensions of chronic pain in adults with sickle cell disease, being the hip region the most affected by chronic pain, followed by the spine. With regard to the hemodynamic variables, the subject had systolic and diastolic blood pressure within the normality limits, however, we noticed an increase in the diastolic blood pressure (DPB) after the PE program. The increase in DPB to 90 mmHg characterizes the cut-off point between normotension and hypertension^{29,30}. In this case, the proposal for a combined exercise intervention may have been responsible for the increase in DPB (however, within the normal range), at the end of the PE period, probably due to a greater total peripheral vascular resistance and the systolic parietal stress caused by resisted exercise³¹.

The results obtained in the ergospirometry confirmed that the cardiorespiratory capacity of the subject, defined by the VO_2 peak, was lower when compared to a person without the disease, as in the study of Liem et al.³². Van Beers et al.³³, also affirmed that the cardiorespiratory responses are below average in 83% of patients with SCA. Moreover, the oxygen uptake efficiency seems to be lesser between adults with SCA submitted to sub-maximum effort tests³⁴.

Some studies analyzed the mechanisms responsible for the intolerance to exercises in patients with SCA and found out that some factors can contribute, such as the reduction of oxygen carrying capacity related with the low hemoglobin level, the functional and structural heart adaptations resulting from the chronic anemia and pulmonary dysfunctions^{9,32,33}.

The patient presented a VO_2 max and HR below the expected for her age and physical condition³⁵, both before and after the combined PE intervention. This condition can be attributed, in part, to the left ventricular systolic dysfunction (due to an HR max lower than expected), and/or the decrease in the hemoglobin level. However, despite the decrease in the relative VO_2 max, the subject had an increase in the total time of the test (13%), on the same protocol (Bruce adapted). So, one can assume that the low hemoglobin level may have led to the decrease of total oxygen content, but, on the other hand, it may have improved blood flow and, consequently, increased the cardiac output after the training period³⁶.

Regarding the cause of SCA, there are no clear indications in the literature that PE have the potential to change hemoglobin S concentration or to revert the sickling process. In the present study, we found a reduction of 0.3 g/dL in plasma hemoglobin concentration after the PE program. However, such difference does not present great biological relevance. Furthermore, it was not measured if this discrete reduction was on sickle hemoglobin (HbS) or normal hemoglobin (HbAA). However, there was no severe symptom of the disease during the experiment, suggesting that a combined, and guided PE program does not bring risks or harm to patients with SCA.

The functional capacity can influence the performance of daily activities. In this context, the subject reported that most of the time her functional capacity was influenced by pain. Lobo, Marra and Silva³⁶ showed that the results of the physical aspects domain that include the impact of physical health in the performance of daily activities and/or professional were also significantly affected by pain.

In this scope, physical fitness parameters were also assessed, and the absolute values demonstrated that after the PE program there was an improvement in all the variables, except for static balance which remained the same. Moreover, in the strength resistance tests of upper and lower limbs, the classification went from poor to good, and from regular to good, respectively. We did not find studies in the literature that used similar tests in SCA patients. However, the responses found become relevant, especially within the context of the patient's QoL since it is influenced by physical aspects, as well as emotional and social³⁷.

Therefore, this case demonstrates that although the cardiorespiratory conditions did not improve by the combined PE protocol, it was observed a trend to the improvement in the aspects of physical fitness, pain and in the perception in the QoL. This is an important point to emphasize since this patient was physically active (according to the IPAQ classification), which can lead to the assumption that better results could have been observed in case of sedentary individuals.

It is important to point out the inherent risks of the practice physical exercises not controlled and supervised by qualified professionals, mainly by people with severe SCA complications. The risks go from worsening of disease complications to sudden death, which raise the fear by doctors to recommend physical exercises for SCA patients⁹. In General, physical exercises induce metabolic changes (production of lactic acid, reactive oxygen species, and other circulating cytokines)^{38,39}, changes in tempera-

ture and dehydration during exercise, which can stimulate the polymerization of HbS⁴⁰ and trigger the vaso-occlusive crisis⁹. However, current results support the safety and potential benefits of the practice of PE by SCA patients, as reported by Tinti et al.¹⁴ and Balayssac-Siransy et al.⁴¹, provided that some specific recommendations are followed^{8,9}. First, before the beginning of PE program, it is recommended to conduct the stress test to identify the intensity of exercise the patient may put up with stand without fatigue, pain or other symptoms. Subsequently, it is recommended to patients to start exercising gradually, avoiding intense efforts and stopping the exercise in the case of fatigue. Also, it is important to pause every 20 minutes for hydration and prevent excessive lactic acid buildup^{8,9}.

CONCLUSION

It is expected that the results of this study will contribute to the planning of preventive interventions and promotion of health in patients with SCA through a multi-professional assistance, including the presence of physical education professionals, aiming at the reduction and improvement of pain, improvement of physiological conditions and resistance to efforts, thus improving the perception of the QoL, providing individuals with SCA better conditions to perform daily activities as a result of the practice of PE.

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