ORIGINAL ARTICLE

Effect of pulmonary rehabilitation on exercising tolerance in patients with advanced lung disease in waiting list for lung transplant

Efeito da reabilitação pulmonar na tolerância ao exercício de pacientes com doença pulmonar avançada em lista de espera para transplante de pulmão

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ABSTRACT

Introduction: patients with advanced lung disease (DPA) exhibit reduced tolerance to an effort, dyspnea, and fatigue. Pulmonary rehabilitation (RP) aims to improve exercising tolerance, controlling symptoms, minimize complications in the pulmonary disease, and improve the quality of life. **Objective:** to evaluate the effect of RP on exercise capacity, according to the distance traveled in the six-minute walk test (TC6M), in patients with DPA on the waiting list for lung transplantation. **Methodology:** patients on the waiting list for lung transplantation, referred to RP in the General Hospital of the Federal University of Minas Gerais were submitted to the TC6M, at the beginning and end of RP, and the degree of dyspnea was assessed using the Borg scale. The data were presented as mean and standard deviation of absolute values and compared using the Student's t-test. The p-values < 0.05 were considered statistically significant. **Results:** between January of 2011 and December of 2012, 17 patients completed the RP. The average age was 42 ± 12 years, 65% were females, the peripheral oxygen saturation on admission was 83 ± 17%, and 35% used oxygen 24 hours/day. Seven patients (41%) presented DPOC, six (35%) had pulmonary fibrosis, and four (24%) other DPA. There was a significant improvement in the distance walked in the TC6M at the end of RP (314 ± 131 m versus 427 ± 111 m; p = 0.0016), with an average increase of 118 m. **Conclusion:** the RP had a positive impact on the exercise capacity of patients on the waiting list for lung transplantation.

Key words: Lung Diseases/rehabilitation; Lung Transplantation; Respiratory Therapy; Breathing Exercises; Exercise Test.

RESUMO

Introdução: *pacientes com doença pulmonar avançada (DPA) apresentam redução da tolerância a esforços, dispneia e fadiga. A reabilitação pulmonar (RP) visa a melhorar a tolerância ao exercício, controlar sintomas, minimizar complicações da doença pulmonar e melhorar a qualidade de vida.* ***Objetivo:*** *avaliar o efeito da RP na capacidade de exercício, segundo a distância percorrida no teste da caminhada de seis minutos (TC6M), de pacientes com DPA em lista de espera para o transplante pulmonar.* ***Metodologia:*** *pacientes em lista de espera para transplante pulmonar, encaminhados à RP no Hospital das Clínicas da Universidade Federal de Minas Gerais foram submetidos, no início e no final da RP, ao TC6M e o grau de dispneia foi avaliado segundo a escala de Borg. Os dados foram apresentados como média e desvio-padrão dos valores absolutos e comparados usando o teste t de Student. Foram considerados estatisticamente significativos os valores de p<0,05.* ***Resultados:*** *entre janeiro de 2011 e dezembro 2012, 17 pacientes completaram a RP. A média de idade foi de 42±12 anos, 65% do sexo feminino, saturação periférica de oxigênio na admissão de 83 ±17% e 35% em uso de oxigênio 24h/dia. Sete pacientes (41%) apresentavam DPOC, seis (35%) fibrose pulmonar e quatro (24%) outras*

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DPA. Houve melhora significativa na distância percorrida no TC6M ao final da RP (314±131 m versus 427±111 m; p=0,0016), com aumento médio de 118 m. ***Conclusão:*** *a RP teve impacto positivo na capacidade de exercício dos pacientes em lista de espera para transplante de pulmão.*

Palavras-chave: *Pneumopatias/reabilitação; Transplante de Pulmão; Terapia Respiratória; Exercícios Respiratórios; Teste de Esforço.*

INTRODUCTION

Advanced lung disease (ALD) is defined as any serious lung disease, non-neoplasic, usually progressive and irreversible that, due to functional and structural pulmonary and systemic alterations, permanently limits the individual's everyday activities.[1] Patients with ALD can present dyspnea, hypoxia and/or hypercapnia, malnutrition and/or cachexia, anxiety and/or depression, and intolerance to efforts.[1-2] Lung diseases that most result in ALD are chronic obstructive pulmonary disease (COPD), which is the most frequent, bronchial asthma, bronchiectasis, pulmonary fibrosis, and diseases of pulmonary circulation.[1]

It is known that patients with ALD present decreased physical exercise tolerance associated with dyspnea and fatigue. In the later stages, many wait in the lung transplant waiting list while the illness is still in progress.[1-3]

A number of strategies, aimed at the improvement of symptoms and quality of life of these patients have been studied in the last decades, being pharmacological or not.[1] Pulmonary rehabilitation (PR), a non-pharmacological therapy, is defined as a multidisciplinary intervention program that involves therapeutic approaches, emotional support, education, and physical reconditioning,[1,3-5] with the aim of improving and controlling symptoms, decrease complications of base pulmonary disease, and assisting the patient to live a more active life with fewer restrictions. Previous studies consider that pre-transplant PR is essential to minimize the loss of pulmonary functional while patients remain waiting on the transplant.[2-5]

Considering the high degree of limitations in these individuals, this study aims to analyze the effect of PR on the tolerance to physical efforts in patients with ALD on the waiting list for lung transplantation.

METHODS

This was a retrospective analysis of patients with advanced lung disease on the waiting list for lung transplantation, submitted to pre-transplant PR at the University General Hospital of the Federal University of Minas Gerais (HC-UFMG) in Belo Horizonte, Minas Gerais.

The inclusion criteria were patients over 18 years old, with ALD, who went through lung pre-transplant PR from January 2011 to December 2012 in the Pulmonary Rehabilitation Sector of the HC-UFMG. Patients who did not consent to participate in the study and had not completed the PR program were excluded.

At the beginning of the PR program, and based on medical records and physiotherapeutic assessments, clinical information related to age, gender, diagnosis, comorbidities, peripheral oxygen saturation, use of supplemental oxygen, lung function (forced vital capacity-FVC-forced expiratory volume in the first second- FEV_1, FEV_1/FVC, total lung capacity-TLC-, diffusion of carbon monoxide), distance covered by a six-minute walk test (DWT6M), desaturation at the end of WT6M, heart rate, Borg dyspnea index,[6] and modified mMRC dyspnea index (modified Medical Research Council) were collected.[7]

The tests were performed in the Laboratory of Pulmonary Function of the HC-UFMG using Collins equipment, GS II and CPL models, and a Koko spirometer. The direction followed in the implementation and interpretation of tests was those recommended by the Guidelines for Pulmonary Function Tests from SBPT, from 2002.[8] In the case of WT6M, the procedure rules from the American Thoracic Society (ATS)[9] were followed with addition of the O_2 saturation (StO_2) measurement, before and during the test.

The spirometry reference values used were those from Pereira et al.[10], published for the Brazilian population; Knudson et al.[11] for spirometry in patients under the age of 25 years (62); Bates[12] for the measurement of absolute lung volumes; Crapo et al. for the carbon monoxide diffusion test[13]; and Enright et al.[9] for the WT6M. The results found in the functional tests were compared with normal values for individuals of the same height, age, and gender.

Patients with significant peripheral muscle atrophy and inability to perform the endurance training received the pre-PR training consisting of exercises for specific muscle strength gain (involving the biceps, triceps, quads, and iliopsoas muscles).[14] The training included sessions from two to four series of 12 repetitions with intensity between 50 and 85% of a maximum rotation, three times a week, for four weeks.[14]

Subsequently, the PR program itself began. The sessions took place three times a week, lasting 90 min-

utes and totaling 36 meetings. The following activities were carried out: stretching of muscles associated with breathing exercises and muscle strengthening in the upper limbs with 50% of the maximum load from the incremental test.[15] The load was increased (0.5 kg) according to the patient's tolerance (between eight and 12 sessions on average). The diagonal exercise mode was chosen: with the arm extended along the body, a movement starts from the greater trochanter of the major homolateral femur towards the ipsilateral contralateral shoulder and, with the arm in adduction, a movement starts from the contralateral iliac crest, performing abduction with an outstretched arm.[16,17]

In continuation of the physical training, already started in the pre-rehabilitation period, strengthening of the lower limbs was conducted with load increments according to the patient's tolerance (increase of 0.5 kg every three to six sessions). The treadmill mode was used for the aerobic training (Inbrasport Ergometric Treadmill, Porto Alegre, Brazil), with intensity at 80% of the heart rate obtained at the end of WT6M. Speed was increased 0.5 km/h every four sessions, according with the tolerance of each patient.

Complaints of dyspnea and/or muscle fatigue were limiting factors for the continuation of exercises. At the end of each session, patients remained seated for five minutes, relaxing and performing breathing exercises.

All patients used continuous oxygen therapy during the rehabilitation program, according to medical prescriptions, and were constantly monitored by means of pulse oximetry. An oxygen flow required to maintain $StO_2 \geq 92\%$ was used.

Patients were evaluated by the same physical therapist, before and after the 36 sessions. At the end of the PR program, patients repeated the WT6M and evaluation of dyspnea by the modified Borg scale.

Variables were input into a database developed in the Excel program and analyzed through the Statistical Package for the Social Sciences program, version 14.0 (SPSS Inc, Chicago, IL, USA). The evaluation of the distribution of symmetric variables was carried out using the Kolmogorov-Smirnov test. Continuous variables were expressed as mean and standard deviation while categorical variables were expressed as absolute and relative frequency. The comparison of outcomes, before and after the sessions of rehabilitation, was carried out through the Student's t-test for paired samples. Values of $p < 0.05$ were considered statistically significant.

The project was approved by the Research Ethics Committee from the Federal University of Minas Gerais by means of opinion paragraph ETIC 274 673 from 5/17/2013.

RESULTS

Between January 2011 and December 2012, 67 patients with ALD were sent to PR. The final sample constitution is presented in Figure 1.

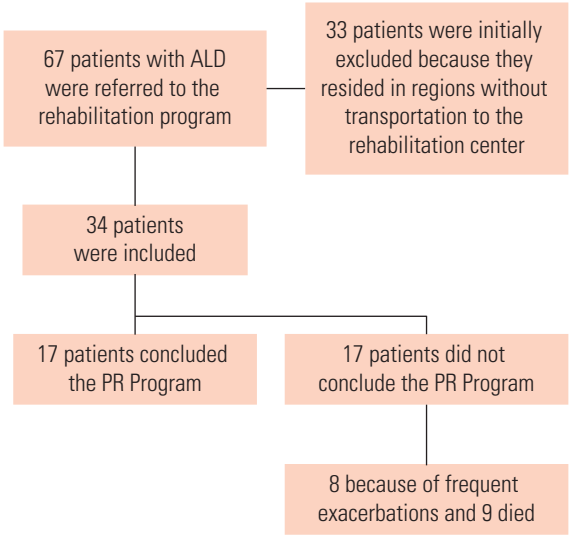

Figure 1 - Flowchart of the sample included in the study.

The clinical, demographic, and functional characteristics are presented in Table 1. The functional baseline data and indexes of dyspnea reveal the serious limitations of these patients.

The WT6M variables results, before and after the PR program, are presented in Table 2. After the end of the program, patients have achieved an average increase of 118 m in the total distance walked (WT6M), and the perception of dyspnea decreased significantly (Borg before PR: 6.5; after 5.3; $p = 0.02$). The final StO_2 after the program remained similar, with no statistically significant difference (81% vs. 83%). Patients walked greater distances, did not exhibit more significant desaturation with the increased effort, and referred reduced degree of dyspnea after this program. The initial and final heart rate did not differ when compared before and after PR (Table 2).

Table 1 - Clinical, demographic, and functional characteristics of patients with ALD submitted to pulmonary rehabilitation

Variables	Participants (n = 17)
Demographics	
Gender, female, n (%)	11(65)
Age, years, avg ± SD	42 ± 12
Anthropometrical	
BMI Kg/m2 (m), avg ± SD	24.2 ± 5.5
Diagnosis	
Idiopathic pulmonary fibrosis n (%)	6 (35)
Pulmonary emphysema n (%)	7(41)
Other n (%)	4(17)
Pulmonary function	
FVC, L, avg ± SD	1.67 ± 0.5
FVC,% predicted, avg ± SD	48 ± 13
FEV1, L, avg ± SD	0.88 ± 0.50
FEV 1% predicted, avg ± SD	29 ±14
TLC, L, avg ± SD	4.58 ± 2.21
TLC,% of predicted, avg ± SD	98 ± 34
DCM m, avg ± SD	34 ± 10
WT6MM	
DT6M, avg ± SD	301 ± 121
STO2%, avg ± SD (with O2?)	92 ± 2.7
Borg modified scale	**3.9 ± 2**
MRC dyspnea index avg ± SD	**3 ± 1**

avg: average; SD: standard deviation; n: number of patients; BMI: body mass index; Other: bronchiectasis and cystic fibrosis; FVC: forced vital capacity; L: liters; TLC: total lung capacity; DCM: diffusion of carbon monoxide; WT6MM: six-minute walk test; DT6M: distance travelled in the six-minute walk test; STO2%: peripheral oxygen saturation; MRC: *Medical Research Council.*

Table 2 - Variables in the six-minute walk test before and after the Rehabilitation Program

Programa de Reabilitação Pulmonar			
	Before	After	p
DT6M avg ± SD	301,2 (±121,1)	427,1 (±111,4)	0,001
Initial STO2 avg ± SD	93,6 (±2,6)	95,1 (±1,7)	0,07
Final STO2% avg ± SD	81,0 (±11,6)	83,6 (8,1)	0,30
Initial HR avg ± SD	94,6 (±15,9)	90,8 (±14,1)	0,44
Final HR avg ± SD	132,5 (±22,7)	135,5 (±22,1)	0,50
Initial Borg avg ± SD	3,9 (±2,7)	2 (±2,1)	0,04
Final Borg avg ± SD	6,5 (±1,9)	5,3 (±2,3)	0,02

DT6M: distance travelled in the six-minute walk test; avg: average; SD: standard deviation; STO2: peripheral oxygen saturation; HR: heart rate. Source: study data.

DISCUSSION

The main result in this study showed significant improvement in the distance walked in the WT6M, in patients with ALD and on the waiting list for lung transplantation. Because this is a debilitated population, functional parameters were significantly compromised. The results from the WT6M after the PR program shows that patients were not separated as presenting obstructive and restrictive disorders because these patients, according to the definition criteria, fit the diagnosis of ALD.

ALD patients show alterations in pulmonary ventilation, gas exchanges, and peripheral muscle mechanics, which are factors that contribute to a limitation in the ventilatory reserve.[1] This condition, associated with the increased demand that occurs during exercising, generates imbalance between the supply and consumption of oxygen.[1] This maladjustment is experienced as dyspnea and fatigue. PR, while training muscles in the lower and upper limbs, improves exercise tolerance and reduces ventilation demand and oxygen consumption for the same amount of exercise, thus decreasing the dyspnea and increasing tolerance to stress. Besides exercising, the following should be pointed out: the importance of energy conservation methods and psychological, pharmaceutical, and nutritional support with a doctor who, along with the physical work, contributes to the success of the program.[5]

The benefits of PR in patients with COPD, pulmonary fibrosis, and pulmonary arterial hypertension have been well documented.[18-24] PR improves exercise tolerance, reduces dyspnea, improves the quality of life, and reduces the use of health resources in COPD patients.[5]

In the last decade, the role of PR in pulmonary fibrosis has been described with more evidence. In 2008, Holland et al.[19], in a study on the short-term benefits of exercise training in the interstitial lung disease, verified the improvement in exercise capacity observed by an increase of 35 meters in WT6M, reducing dyspnea and improving the quality of life. In 2010, Salhi et al.[22] concluded that patients with restrictive pulmonary disease with low exercise tolerance, muscle weakness, and poor quality of life are good candidates for PR. After 24 weeks of PR, there was an alteration in WT6M from 390 ± 140 m to 463 ± 146 m.

Frankel et al.[23], in 2012, demonstrated that PR improves WT6M in patients with advanced lung fibrosis when performed in high frequency and intensity. Patients increased by 89 meters the distance walked in the WT6M ($p < 0.0001$) after PR. In our study, although the diseases have not been separated, with 35% of the sample consisting of patients with restrictive disease, a significant increase in exercise tolerance, translated into increased distance walked in the WT6M after

PR without dyspnea worsening was observed.[23] Despite the group being composed of patients with significantly impaired pulmonary function, it was found that patients walked a distance greater than 300 m in the WT6M even before PR, therefore, presenting a reasonable exercise capacity despite the important desaturation to exercise and dyspnea.

A study recently published in Brazil by an important lung transplant group in Porto Alegre, Rio Grande do Sul, using a methodology similar to that of the present study on the evaluation of patients with advanced lung disease, also on the waiting list for transplant, showed significant increase in distances walked in the WT6M after PR (367 ± 136 vs. 439 ± 114 m; average increase of 72 m).[3]

The sample size is among the limitations of this study, which was undermined by the loss of participants. In addition, it is necessary to consider that the heterogeneity and small number of patients in each subgroup did not allow more detailed analysis of alterations in the WT6M separately.

Despite these restrictions, the results found here show that PR improves exercise tolerance and reduces dyspnea in patients with ALD and on the waiting list for lung transplantation. One should also consider that these patients can remain on the waiting list for long periods, and PR can maintain their health status, exercise capacity, and quality of life while waiting for the transplant.

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