Effects of Muscle Training on Breathing Pattern in Patients With Severe Chronic Obstructive Pulmonary Disease

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OBJECTIVE: During physical exertion, the ventilatory response of patients with severe chronic obstructive pulmonary disease (COPD) is more rapid and shallow than that of healthy subjects. There is evidence that exercise training can alter breathing pattern in COPD patients. The purpose of the present study was to observe the effects of physical training on patients with severe COPD and to determine whether or not any possible changes were maintained over time.

MATERIAL AND METHODS: Patients with severe COPD without bronchial reversibility were enrolled in a randomized controlled trial of a peripheral muscle training program carried out in a hospital setting. All enrolled patients were clinically stable, without exacerbation, and were randomly assigned to a training program of high (group A) or low (group B) intensity.

RESULTS: Thirty-five men with severe COPD in stable condition (mean [SD] forced expiratory volume in 1 second at 41%[7%]) were enrolled in the study. The mean age was 64(5) years. Group A underwent training at 70(22) W and group B at 35(10) W, such that the estimated total work was 8050(2882) kJ in group A and 4044(1205) kJ in group B. Breathing pattern changes were detected in exercise tests only for group A patients, but the changes were not maintained 12 months after the end of the program.

CONCLUSIONS: Intense training produces changes in the breathing pattern of patients with severe COPD. The changes are not specific to the task performed, not dependent on lactate production, and not maintained over the long term.

Key words: *Chronic obstructive pulmonary disease (COPD). Ventilation. Exercise test.*

Efectos del entrenamiento muscular sobre el patrón ventilatorio en pacientes con enfermedad pulmonar obstructiva crónica grave

OBJETIVO: Durante el esfuerzo físico la respuesta ventilatoria de los enfermos con enfermedad pulmonar obstructiva crónica (EPOC) grave es más rápida y superficial que la de los sujetos sanos, y existen indicios de que el entrenamiento físico podría cambiar el patrón ventilatorio de estos pacientes. El propósito del presente estudio fue comprobar los efectos que el entrenamiento físico de los pacientes con EPOC grave tiene sobre el patrón ventilatorio, así como determinar o no el mantenimiento de los posibles cambios producidos en el tiempo.

MATERIAL Y MÉTODO: Se realizó un estudio aleatorio y controlado con pacientes con EPOC grave sin reversibilidad bronquial. En estos pacientes se efectuó una intervención mediante entrenamiento físico. Los pacientes fueron remitidos al hospital para entrenamiento muscular periférico, todos ellos en situación clínica estable, sin exacerbación, y fueron asignados a dos programas diferentes de entrenamiento físico.

RESULTADOS: Se estudiaron 35 pacientes varones con EPOC grave, estables (volumen espiratorio forzado en el primer segundo del 41 ± 7%), con una edad media de 64 ± 5 años, divididos en dos grupos con diferente potencia media estimada de entrenamiento (grupo A: 70 ± 22 W; grupo B: 35 ± 10 W) y trabajo total desarrollado (grupo A: 8.050 ± 2.882 kJ; grupo B: 4.044 ± 1.205 kJ). Sólo se objetivaron cambios en el patrón ventilatorio durante el ejercicio realizado durante la prueba de esfuerzo en el grupo A, que no se mantuvieron a los 12 meses de finalizado el programa.

CONCLUSIONES: El entrenamiento intenso produce cambios en el patrón ventilatorio de los pacientes con EPOC grave que son inespecíficos de la tarea e independientes de la producción de lactato, y que no se mantienen a largo plazo.

Palabras clave: *Enfermedad pulmonar obstructiva crónica (EPOC). Ventilación. Prueba de esfuerzo.*

Introduction

The exercise capacity of patients with chronic airflow limitation—or chronic obstructive pulmonary disease (COPD)—is often reduced, particularly in those with functional limitation at maximal effort.[1] The

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symptom that most often limits physical exercise in such patients is dyspnea.[2] Patients with COPD develop altered ventilatory mechanics leading to dynamic hyperinflation,[3] and there is solid evidence supporting the hypothesis that such hyperinflation contributes to reducing exercise tolerance.[4,5] The ventilatory response of such patients during physical exercise is faster and more superficial than it is in healthy controls, contributing to greater dynamic hyperinflation.[6]

Muscle training of patients with COPD has been shown to improve response to exercise, capacity, and stamina and also to enhance cell metabolism in skeletal muscles.[7] Certain indications suggest that training might also change respiratory pattern in COPD patients, improving efficiency.[8] Our aim was to determine the effects that skeletal muscle training has on the respiratory pattern of patients with severe COPD and to observe whether possible changes are preserved over the long term.

Material and Method

This randomized controlled trial enrolled severe COPD patients (limitation defined by a ratio of forced expiratory volume in 1 second [FEV_1] to forced vital capacity [FVC] less than 70% of predicted with FEV_1 less than 50% of predicted). The enrolled patients' bronchial obstruction was not reversible and they had not smoked in the 6 months before enrollment. The intervention consisted of a physical exercise program. The patients were referred to hospital for the program in stable condition, without exacerbation, and were assigned randomly to 2 muscle training regimens. Exclusion criteria were a history of ischemic heart disease or other diagnoses that would contraindicate performance of a stress test. The study was approved by the hospital's Ethics Committee and all patients signed informed consent forms.

Once enrolled in the trial, all patients underwent physical examination, electrocardiography, and spirometry. Spirometry was performed in accordance with the recommendations of the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR),[9] using a Pneumoscreen II (Erich Jaeger GmbH, Hochberg, Germany). FEV_1 and FEV_1/FVC were recorded 15 minutes after inhaling 200 μg of salbutamol. No subjects had bronchial reversibility.

During a second visit, each patient underwent progressive exercise testing on a treadmill, limited by symptoms according to the protocol of Balke and Ware[10] to estimate maximum oxygen consumption ($\dot{V}O_{2max}$) and peak minute ventilation. Ventilation and gas exchange were measured during the test using an Oxycom α (Erich Jaeger GmbH).

The patients were randomly assigned to one of 2 treatment groups. Group A underwent more intense training under supervision on a treadmill for 8 weeks, 4 days per week, beginning at a level equal to the anaerobic threshold reached plus 25% of the difference between that intensity and the maximum intensity (Δ 25%), which was then increased in keeping with the patient's tolerance. Group B underwent less intense training, in a self-supervised program, walking 3 or 4 km in 1 hour, monitored by a pedometer for 8 weeks, 5 days per week.

Before and after training patients in both groups performed a cycle ergometer test at 50% of the $\dot{V}O_{2max}$ measured during the previous progressive exercise test. This continuous exercise test was thus carried out below the patient's anaerobic threshold, such that oxygen uptake increased less than 50 mL/min during the interval between 4 and 10 minutes of testing and that there was no increase of lactic acid concentration above 2.5 mmol/L in circulating blood.

Immediately after the muscle-training period, we studied changes in respiratory function variables in both groups. Later we studied whether changes persisted over time (12 months) in both groups. Patients in both groups were given periodic physical examinations (every 3 months) and all were encouraged to continue exercising. Twelve months after ending the training program, the patients underwent another submaximal continuous exercise test for recording ventilatory function variables. We compared the 12-month results within each group to the results obtained before and just after the peripheral muscle training program. We also compared the 12-month results between groups.

Mean results recorded before and after muscle training were compared using a Student *t* test for paired data, after confirming that differences were normally distributed. Means for each group were compared using a Student *t* test for unpaired data, and a *t* test for unequal variances was used for two-tailed comparisons. Means were considered significantly different when the probability of a type I error was less than 0.05 for a two-tailed test. Statistical analysis was carried out using the SPSS package (version 7.5; Hispanoportuguesa SPSS, SL, Madrid, Spain) on a personal computer.

Results

Thirty-five men with severe but stable COPD (mean FEV_1 41% [SD 7%]), with a mean age of 64 (5) years were studied. Patient characteristics were similar, as were lung function variables at rest and during exercise, with the exception of mean estimated intensity of training (group A: 70 [22] W; group B: 35 [10] W) and total work (group A: 8050 [2882] kJ; group B: 4044 [1205] kJ). The patients' exercise capacity was moderately reduced, as estimated by oxygen uptake in the progressive exercise test. Table 1 shows patient characteristics.

Exercise test performance changed after muscle training in relation to type of training undergone (Table 2). Breathing pattern changes were seen during continuous exercise testing in group A in expiratory minute ventilation ($\dot{V}_E$), the ratio of $\dot{V}_E$ to maximal voluntary ventilation (MVV) expressed as a percentage, respiratory rate, tidal volume, and the ratio of physiological dead space to tidal volume. Changes in breathing pattern observed immediately after the muscle training period in the high intensity training group were not maintained over time; a year after finishing the training program, those changes had disappeared and the breathing pattern in group A was similar to what it was before the study as well as similar to the pattern in the low intensity group (group B) after training.

TABLE 1
Patient Characteristics and Lung Function Variables*

Variable	Self-Supervised (n = 17) Mean (SD)	Supervised (n = 18) Mean (SD)
Age, years	63.4 (4.8)	65.8 (5.7)
Height, cm	163.3 (4.8)	164.9 (5.7)
Weight, kg	69 (8.1)	68.5 (12.6)
FEV_1, mL	1087 (160)	1090 (161)
FEV_1, %	41 (7.1)	40.4 (7.5)
FEV_1/FVC, %	45 (8.3)	47 (8.7)
FVC, mL	2596 (484)	2560 (690)
PaO_2, mm Hg	67.5 (5.4)	62.8 (8.5)
$PaCO_2$, mm Hg	37.9 (2.6)	37.7 (3.3)
DLCO, $mmol \cdot min^{-1} \cdot kPa^{-1}$	4.8 (1.6)	5.2 (1.7)
DLCO% predicted, %	62.2 (19.7)	66.7 (21.5)
KCO, $mmol \cdot min^{-1} \cdot kPa \cdot L^{-1}$	1.2 (0.4)	1.1 (0.4)
KCO% predicted, %	77.6 (33.9)	77.7 (29)
$\dot{V}O_2max$, mL/min	1247 (264)	1200 (350)
$\dot{V}O_2max$ % predicted, %	59.1 (11.6)	61 (18.1)
Mean training intensity, W	35.1 (10.4)†	69.8 (22.3)†
Total work, kJ	4044 (1205)†	8050 (2882)†

*FVC indicates forced vital capacity; FEV_1, forced expiratory volume in 1 second; DLCO, carbon monoxide diffusing capacity; KCO, DLCO divided by alveolar volume; $\dot{V}O_{2max}$, peak oxygen uptake. †$P<.0001$.

TABLE 2
Changes Observed in Respiratory Variables During Continuous Exercise Testing, Before and After the Muscle Training Program in the High and Low Intensity Groups*

Variables	High Intensity			Low Intensity		
	Before	After	*P*	Before	After	*P*
$\dot{V}_E$, L/min	29.4 (5.7)	27.5 (5.8)	<.05	27.4 (6.2)	26.5 (6.5)	NS
$\dot{V}_E$/MVV, %	65.4 (11.8)	60.7 (9.2)	<.05	65.3 (14.5)	61.9 (11.2)	NS
RR, min^{-1})	27.2 (4.0)	24.1 (4.3)	<.01	25.8 (4.2)	26.1 (7.8)	NS
V_T, mL	1090 (211)	1156 (204)	<.05	1077 (237)	1062 (313)	NS
V_D/V_T	0.37 (0.10)	0.34 (0.10)	<.05	0.36 (0.09)	0.37 (0.12)	NS
Lactic acid in blood, mmol/L	2.17 (0.27)	2.18 (0.28)	NS	2.23 (0.40)	2.29 (0.38)	NS

*Results are expressed as means with SD between parentheses. $\dot{V}_E$ indicates expiratory minute ventilation; $\dot{V}_E$/MVV, ventilatory reserve, or $\dot{V}_E$ as a percentage of maximal voluntary ventilation; RR, respiratory rate; V_T, tidal volume; V_D/V_T, ratio of physiologic dead space to tidal volume.

Discussion

Two interesting findings come from this study of muscle training in patients with severe COPD. First, we saw that high intensity muscle training in such patients changes breathing pattern during submaximal exercise, with breathing becoming slower, deeper, and in consequence, more efficient (with less dead space). Patients who trained at a lower intensity, on the other hand, showed no such change. Second, those beneficial effects on breathing pattern during exercise disappeared after the high intensity training came to an end, such that the patient returned to a situation that was similar to the one that prevailed before the muscle training program began.

These findings suggest that high intensity muscle training, as opposed to less intense exercise, seems to induce beneficial changes in breathing pattern during exercise. Unlike normal subjects, COPD patients can increase tidal volume only slightly in response to ventilatory demand, given that COPD patients breathe at high lung volume levels, such that increasing that volume further would suppose a disproportionate decrease in static and dynamic compliance, an increase of respiratory muscle effort, and more work of breathing.[11,12] Because total lung capacity does not change with exercise, the only way to increase minute ventilation is to increase respiratory rate.[13,14] Our patients who trained at high intensity increased minute ventilation and decreased respiratory rate during exercise, whereas those who underwent less intense training did not.

Dyspnea is the symptom that is mostly responsible for limited exercise capacity in patients with COPD.[2] Several studies have shown that some patients benefit from muscle training. Among treatments, muscle training has proven to be a valid tool for improving symptoms of dyspnea, quality of life, and capacity for exercise in these patients.[15,16] However, the mechanisms that reduce dyspnea have not been fully elucidated, and

it has been suggested that increased "tolerance" to exercise must be responsible for improvements. Our results indicate that a possible mechanism would be a change in breathing pattern and the foreseeable reduction in dynamic hyperinflation. This effect seems to be independent of the intensity.

An interesting finding from our study is that the changes observed seem to be independent of the type of task that was performed, given that the submaximal exercise tests were carried out on a cycle ergometer, even though the patients trained on a treadmill. We observed changes in variables measured during the first exercise test (before muscle training) and the second (after training) (Table 2). The breathing pattern changes seen during continuous exercise in the high intensity group (group A), in terms of both $\dot{V}_E$ and $\dot{V}_E$/MMV, as well as respiratory rate and tidal volume or the ratio of physiological dead space to tidal volume (all of which take place without changes in lactic acidemia), suggest that such changes in ventilatory pattern do not depend on the amount of lactic acid produced and allow us to say that the effort made by the patients was submaximal. On the other hand, the patients who trained at low intensity (group B) had no changes in ventilatory variables.

Patients with COPD have altered ventilation and pulmonary mechanics during exercise, with a prolonged time of exhalation and higher respiratory rate leading to dynamic hyperinflation with increased end-expiratory pressure and greater work of breathing. This is to say, the pulmonary hyperinflation of these patients increases inspiratory work and the sensation of dyspnea, although this pattern is essential if a COPD patient is to increase ventilation to adapt to the demands of exercise.[17]

Changes in breathing pattern occurring after physical exercise have been demonstrated before now,[5,18] as have changes in ventilatory efficiency.[19,20] Our findings, however, are the first to demonstrate that the changes related to the intensity of muscle training disappear over time.

Based on these findings, we think that muscle training in severely ill COPD patients is a tool that will help improve exercise tolerance, owing to decreased perception of dyspnea related to decreased dynamic hyperinflation in response to exercise, which must be intense and continued over the long term.

In conclusion, intense training produces changes in the breathing pattern of patients with severe COPD (in the form of deeper and less rapid breathing). The changes lead to greater efficacy and less ventilatory demand in these patients when they engage in submaximal exercise. This effect does not depend on the reduction of lactic acid and is unrelated to task. However, once these effects on ventilatory pattern are achieved, they are not maintained 12 months after ending intense training, such that the characteristics of breathing pattern regress to similar levels as those that existed in these patients before participation in the intense physical training program.

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