Inspiratory Muscle Training in Patients with Chronic Obstructive Pulmonary Disease[1,2]

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SUMMARY To investigate the effects of inspiratory muscle resistive loading training (IMT) on exercise performance in chronic obstructive pulmonary disease (COPD), 13 patients undergoing standard pulmonary rehabilitation were divided into control (n=6) and experimental (n=7) groups. Prior to training, we measured inspiratory muscle strength and endurance, resting pulmonary function, and exercise performance on a bicycle ergometer (a progressive test and an endurance test at two thirds of maximal work load). We then determined their resistive loads for training by measuring their 10-min maximal sustainable resistance. Training by patients in the experimental group involved inspiring against a predetermined resistive load. The control subjects breathed through a sham training tube, so that studies were performed in double-blind fashion. The training consisted of 15-min sessions twice daily for 4 wk. The IMT dramatically improved inspiratory muscle endurance—represented as either sustainable inspiratory pressure (SIP) or endurance time at 60% of maximal inspiratory mouth pressure (P_{Imax}) at functional residual capacity. The SIP of the trained group increased from 29 ± 11 to 46 ± 11% of P_{Imax} ($p < 0.005$). Training slightly increased inspiratory muscle strength ($p < 0.05$), as determined by P_{Imax}. In contrast, resting pulmonary function and performance of both progressive and constant-load exercise remained unchanged. We conclude that 4-wk IMT in a pulmonary rehabilitation setting improves inspiratory muscle endurance in patients with COPD without changing pulmonary function or exercise performance.

AM REV RESPIR DIS 1985; 131:251–255

Introduction

In patients with chronic obstructive pulmonary disease (COPD), large amounts of pressure work are required to overcome high airway resistance, so that the O_2 cost of breathing becomes significant, particularly during exercise (1). In addition, hyperinflation of the lung puts the inspiratory muscles at a mechanical disadvantage (2), although these muscles compensate in part for this by shortening their optimal length (3). Therefore, the inspiratory muscles, especially the diaphragm, are susceptible to fatigue (4, 5). This is clinically important because respiratory muscle fatigue may lead to exertional dyspnea, limit exercise performance, and contribute to the development of acute and chronic respiratory failure (6, 7).

In 1976, Leith and Bradley (8) first reported that respiratory muscles could be specifically trained in normal persons. They used maximal normocapnic hyperpnea to improve respiratory muscle endurance. Later, Gross and coworkers (9) proposed that inspiratory resistive breathing training might improve inspiratory muscle function in quadriplegics. Since then, both methods have been used to evaluate the effects of inspiratory muscle training (IMT) on patients with pulmonary diseases (10–14).

Several previous studies have reported that respiratory muscle training improves exercise tolerance in patients with COPD (10, 12–14). None of these studies have been performed double-blind, a consideration crucial for proper evaluation of variables, such as exercise performance, that depend on subject motivation. In this double-blind study, we sought to clarify the effects of resistive load IMT on the lungs, on inspiratory muscle function, and on exercise performance in patients suffering from COPD.

Methods

This study was approved by an institutional committee for protection of human subjects.

Subjects

The selection criteria for our patients with COPD were those of the American Thoracic Society (15). Our patients were free from other significant illness, clinically stable during the study, and able to exercise maximally without adverse cardiovascular effects.

Thirteen outpatients with COPD were studied after they gave informed consent. During this study, they were also participating in a hospital rehabilitation program that included 20 min of moderate cycle ergometer exercise 3 times each week. They were randomly assigned to either a control or an experimental group by a third party not otherwise involved in the study. The physical characteristics of these patients are shown in table 1. Seven subjects (3 men and 4 women) were assigned to the experimental group, and the remaining 6 (4 men and 2 women) were assigned to the control group.

To safeguard patients, studies were done under medical supervision at Bloomington Hospital.

Tests

Before the actual study, all subjects were familiarized with experimental techniques so that learning or habituation would not produce spurious results. On separate visits, the tests described subsequently were completed to evaluate resting pulmonary function, inspiratory muscle strength and endurance, and exercise performance both before and after training. The resistive loads for training were also determined before training.

Resting pulmonary function tests. The forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), 12-s maximal voluntary ventilation (12-s MVV), and forced expiratory flow between 25 and 75% of FVC (FEF_{25-75}) were measured twice on a computerized spirometer (Model-9000IV; Gould Instruments, Cleveland, OH) by a respiratory therapist. The better result of 2 trials in each subject was used for data analysis.

Exercise tests. During these tests, the electrocardiogram (EKG) and arterial O_2 saturation were monitored continuously by a patient monitor electrocardiograph (General Electric) and an ear oximeter (Model 47201A; Hewlett-Packard, Waltham, MA). A needle was placed in a heated hand vein for sampling of arterialized venous blood (16). During the third minute at each work load, samples were withdrawn for determination of pH and P_{CO_2} (ABL-3; Radiometer, Copenhagen) and lactate by an enzymatic technique (17).

(Received in original form May 21, 1984 and in revised form September 17, 1984)

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Progressive exercise tests were performed on a bicycle ergometer (Monark) to determine each subject's maximal work load ($\dot{W}max$). Subjects rested on the bicycle until stable baseline readings of heart rate and arterial O_2 saturation were made. Resting minute ventilation ($\dot{V}E$), oxygen uptake ($\dot{V}O_2$), and CO_2 production ($\dot{V}CO_2$) were also assessed. The subject then started pedaling at 50 cpm as set by metronome. The initial work load was 0 kp. It was increased by either 0.25 or 0.50 kp every 3 to 5 min until the subject became exhausted. In only one experiment did arterial O_2 saturation drop below 85% and thus serve to terminate the study. No subject had to cease exercise because of chest pain, abnormalities in the EKG, cyanosis, or hypotension or hypertension (2, 18, 19). Blood pressure, heart rate, and expired gas measurements were taken in the third minute at each work load.

During the collection of expired gas, the subject inspired humidified air through a mouthpiece connected to a humidification apparatus to prevent dryness of the mouth and upper airway (20). The expired gas was collected in a Tissot spirometer for measurement of $\dot{V}E$. Mixed expired gas concentration was then measured by O_2 and CO_2 analyzers using the S-3A O_2 analyzer (Applied Electrochemistry Inc., Pasadena, CA) and the Beckman LB-2 (Beckman Instruments, Fullerton, CA) for later calculations of $\dot{V}O_2$ and $\dot{V}CO_2$. Before and after each experiment, both analyzers were calibrated with a gas mixture established as standard by micro-Scholander analysis.

The endurance exercise test was conducted 15 min after the progressive exercise test. Subjects worked at two thirds of their previously defined $\dot{W}max$ and pedaled at 50 cpm until they became too fatigued to continue. Again, in only one experiment did arterial O_2 saturation drop below 85% and serve to terminate the test.

Determination of inspiratory muscle strength. We used maximal inspiratory mouth pressure (PIMmax) as a measure of strength of all inspiratory muscles (5). The patient breathed through a Daniel's valve (R-Pel, Inc.) with the inspiratory port occluded by a rubber cork. Verbal encouragement was given, and the PIMmax in cmH_2O was recorded via a pressure transducer (Statham P23AA; Statham Instruments, Hato Rey, PR) on a dynograph (Beckman Type RB), which was calibrated by a manometer preceding each experiment. The PIMmax was measured both at functional residual capacity (FRC) and residual volume (RV). The tests were repeated 3 times, and the best performance was used in data analysis.

Measurements of inspiratory muscle endurance. To determine inspiratory muscle endurance, a device similar to that proposed by Nickerson and Keens was used (21). The apparatus consisted of a two-way Daniel's valve with the inspiratory port connected to a chamber. Inside the chamber was a plunger mounted over a large opening. When the pressure difference between the chamber and atmosphere was greater than a certain threshold pressure, the plunger lifted and air entered, allowing the subject to take a breath. The threshold pressure could be varied by adding weights to or removing them from the plunger. In this test, patients lifted a plunger with threshold pressure approximately equal to 60% of PIMmax at FRC for as many inspirations as possible, and time to exhaustion was recorded. After this, the sustainable inspiratory pressure (SIP), which was the highest percentage of PIMmax a subject could generate in each breath for 10 min, was determined by 10% decrements or increments in PIMmax until the subject could tolerate the load for 10 min, with 15-min rest periods between runs to allow recovery from a previous trial. Neither the respiratory rate nor the ratio of inspiratory time to total time were constrained.

Resistive load for training. The resistive loads for the training program were determined by clinical observations. Patients inspired against a resistive load while seated. We used 1-inch Plexiglas® rods and created different resistances by varying the hole size drilled in the rods. Bore sizes included diameters of 2.5, 3, 3.5, 4, 5, or 6 mm, which produced resistances of 45, 35, 25, 7.5, 6, or 5 $cmH_2O/L/s$, respectively, at a constant air flow of 0.2 L/s.

Each patient tried 3 progressively higher resistances for 10 min each, with rest periods of 20 min between runs. The initial selection of resistance was chosen to induce inspiratory mouth pressure approximately equal to SIP minus 10%, SIP, or SIP plus 10%. During these runs, the patients chose their own breathing frequencies and breathing patterns arbitrarily to ease their breathing. If the patient could not tolerate the resistive load or showed respiratory alternans (i.e., abdomen moved outward for a few breaths, then did not move at all for a few breaths) or abdominal paradox (i.e., abdomen was displaced inward during inspiration), the test ceased (20). The highest resistive load that could be sustained for 10 min without showing respiratory alternans or abdominal paradox was used as the training load for the patients.

TABLE 1

CHARACTERISTICS OF 13 PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Group	Subject No.	Sex	Age (yr)	Height (cm)	Weight (kg)	FEV_1 (% pred)
C	3	M	58	175	95.0	30
	4	F	61	165	60.9	48
	5	M	62	170	78.2	68
	10	F	61	170	85.5	34
	12	M	57	172.5	65.0	40
	13	M	50	187.5	77.0	20
Mean ± SE			58 ± 2	173.3 ± 3.1	76.9 ± 5.2	40 ± 8
E	1	F	52	162.5	54.1	22
	2	M	58	165	56.8	18
	6	M	79	172.5	57.7	40
	7	F	47	160	55.0	
	8	F	74	152.5	60.5	48
	9	M	67	170.0	68.2	75
	11	F	55	147.5	84.1	55
Mean ± SE			62 ± 4	161.4 ± 3.4*	62.3 ± 4.0*	43 ± 8

Definition of abbreviations: FEV_1 = forced expiratory volume in one second; C = control group; E = experimental group.
* $p < 0.05$.

Training Protocol

After familiarizing themselves with resistive breathing techniques, subjects in the experimental group trained for 4 wk at home by breathing against the predetermined inspiratory resistive load in 15-min sessions twice daily. While wearing noseclips, subjects inspired through their resistive load, which was attached by a short rubber tube to the inspiratory port of a Daniel's valve. Patients in the control group breathed through the same kind of tube with a rod that had a resistance less than 2 $cmH_2O/L/s$ (hole diameter, 10 mm), although their training resistive loads had also been estimated.

Any subject who stopped training for 3 consecutive days because of an illness was considered detrained. All of the subjects were asked to keep diary records of their training programs.

Statistical Analysis

Paired *t* tests were used to analyze the changes within a group. Comparisons of the results between 2 groups were analyzed by unpaired *t* test, except those not normally distributed, such as inspiratory muscle endurance time at 60% of PIMmax and work time at two thirds of $\dot{W}max$. These latter were analyzed by Wilcoxon's rank sum test (22). A p value less than 0.05 was considered significant. Because we did not expect IMT to decrease inspiratory muscle strength or endurance or exercise performance, *t* tests were one-tailed.

Results

There was no age difference between the 2 groups (table 1). The average body weight and average body height of subjects in the control group were higher than those in the experimental group because of the sex-based differences. All

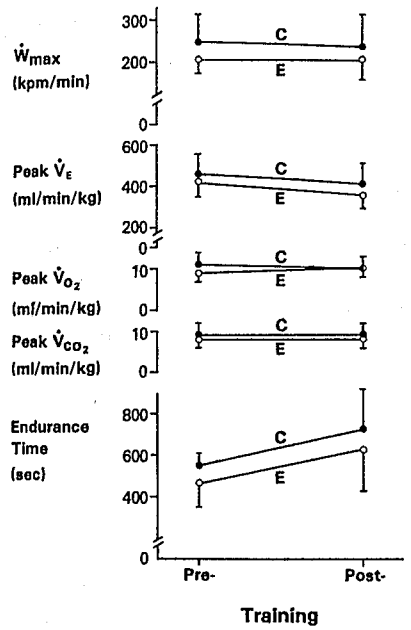

Fig. 1. Mean results of pulmonary function tests before and after 4 wk of inspiratory muscle resistive training (E; n = 6) or sham training (C; n = 6). All tests showed similar values before and after training in both groups. The units are percentages of the predicted values. The results are represented as mean ± SE.

of the patients were highly motivated and cooperative. The average training period was 28 days. Only 1 subject in the experimental group was considered to be detrained because of an upper respiratory infection, and later restarted the training program. The training loads varied from 17 to 62% of PIMmax at FRC (mean ± SE, 35 ± 7%).

The results of pulmonary function tests are illustrated in figure 1. One subject in the experimental group refused to participate in the resting pulmonary function tests. No significant changes of FVC, FEV_1, FEF_{25-75}, and 12-s MVV were found in either the control group or the experimental group after 4 wk.

Inspiratory muscle strength was unchanged in the control group at both RV and FRC after 4 wk of sham training. In contrast, the experimental group showed slight but significant increases ($p < 0.05$) in strength after training (table 2). Changes in inspiratory muscle endurance as measured by SIP are illustrated in table 3. Prior to training, there was no difference between control and trained groups (p = NS). Four weeks later, SIP of the control group was not changed, whereas that of the experimental group was significantly improved by a mean of 59% (table 3). Similar changes occurred in endurance time at 60% of PIMmax at FRC (table 4), with the increase in the experimental group averaging 69%.

The results of progressive exercise tests are shown in figure 2. The IMT did not significantly influence progressive exercise performance in patients with COPD. There was no significant difference between sham and trained groups even when we normalized the data by dividing the values by body weight. Peak exercise heart rate was also unchanged by training, averaging 120 ± 5 beats/min before and 121 ± 7 beats/min after sham training in the control group (p = NS), and 121 ± 8 before and 123 ± 5 beats/min after training in the experimental group (p = NS). Endurance work time at two thirds of $\dot{W}$max is also shown in figure 2. No significant increases in endurance time after IMT were found. Because individual subjects differed greatly in the degree of airway obstruction, we wondered if only those with especially mild or especially severe obstructive disease were aided by training. We could find no correlative relationship between disease severity and improvement in ventilatory endurance or exercise performance.

A variety of technical problems prevented blood analysis in various patients at various work levels (during progressive exercise). At the highest work rate available for comparison (225 kpm/min), 5 subjects in the control group exhibited identical arterialized venous pH, P_{CO_2}, and lactate before and after sham training. In like fashion, 6 subjects in the experimental group, at the highest work rate that could be compared (156 kpm/min), displayed before and after training similar values for pH (7.382 ± 0.014 versus 7.363 ± 0.013; p = NS), P_{CO_2} (36.7 ± 1.2 versus 38.2 ± 1.6 mm Hg; p = NS), and lactate (14.9 ± 2.5 versus 14.0 ± 1.4 mg%; p = NS).

Discussion

In our study, we found that 4 wk of inspiratory resistive loading training, added to a pulmonary rehabilitation program, markedly improved inspiratory muscle endurance and slightly elevated inspiratory muscle strength, but it did not im-

TABLE 2

EFFECTS OF INSPIRATORY MUSCLE TRAINING ON PIMmax AT RESIDUAL VOLUME IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Control Group			Experimental Group		
Subject No.	Before	After	Subject No.	Before	After
3	66	66	1	56	56
4	50	55	2	50	50
5	38	38	6	42	44
10	60	65	7	15	20
12	67	53	8	50	52
13	41	41	9	76	82
			11	60	66
Mean ± SE	54 ± 5	53 ± 5		50 ± 7	53 ± 7†

Definition of abbreviations: PIMmax = maximal inspiratory mouth pressure.
* Units are in cmH_2O.
† $p < 0.05$ (paired *t* test within the experimental group).

TABLE 3

EFFECTS OF INSPIRATORY MUSCLE TRAINING ON SUSTAINABLE INSPIRATORY PRESSURE IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE*

Control Group			Experimental Group		
Subject No.	Before	After	Subject No.	Before	After
3	20	30	1	0	10
4	50	50	2	20	40
5	60	50	6	20	40
10	80	80	7	30	40
12	20	20	8	20	30
13	20	20	9	90	100
			11	20	60
Mean ± SE	42 ± 10	42 ± 9		29 ± 11	46 ± 11†

* Units are % of PIMmax at FRC.
† $p < 0.005$.

TABLE 4

EFFECTS OF INSPIRATORY MUSCLE PRESSURE ON THE ENDURANCE TIME AT 60% OF PIMmax AT FRC IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE*

Control Group			Experimental Group		
Subject No.	Before	After	Subject No.	Before	After
3	60	22	1	15	13
4	138	197	2	80	133
5	600	303	6	44	246
10	600	600	7	92	130
12	98	65	8	62	174
13	58	66	9	600	600
			11	227	600
Mean ± SE	259 ± 100	209 ± 82		160 ± 78	271 ± 89†

* Units are in seconds.
† $p < 0.05$.

prove exercise tolerance or pulmonary function in patients with COPD.

After 4 wk of resistive breathing training, we failed to find increases in Ẇmax, peak $\dot{V}_E$, peak $\dot{V}_{O_2}$, and peak $\dot{V}_{CO_2}$. These results conflict with the findings of both Pardy and coworkers (13), and Sonne and Davis (14). However, the results of the study of Pardy and coworkers (13) actually failed to show changes in progressive exercise performance after training when the whole group was considered. In addition, patients in their Group B, who showed improvement in exercise performance after training in their study, increased the 12-min walking distance at the end of the control period without any training, whereas those in group A did not. This implied that the patients in Group B had potential for improvement even without training. Our results might also have differed from those previous studies because we employed a double-blind design, which should help protect against unintentional bias of data. We were concerned that subjects in both of our groups remain unaware of the group in which each was placed. We did not poll subjects for fear of directing their scrutiny to this question, so our knowledge here is not systematic. It was, however, our clear impression that subjects in the experimental group knew they were in the experimental group, and that the majority of the subjects in the control group thought that they were in the experimental group as well. Three of the 6 control subjects spontaneously told us how much the training had helped them, but no one ever stated that they thought themselves a control group member.

It has been suggested that inspiratory muscle fatigue might limit exercise in patients with COPD (23). We expected to see improvement of exercise performance if inspiratory muscle strength and endurance were enhanced. Although inspiratory muscle endurance of patients with COPD was improved after IMT in our study, their exercise performances were unchanged. There are several possible explanations for this. First, although inspiratory muscle endurance was improved at rest, it might not be equally improved during exercise. In exercise, recruitment of nonrespiratory muscles might affect the blood supply to respiratory muscles and compromise inspiratory muscle function (24, 25).

It is also possible that the training load or the training period in this study might not be large enough to produce a training effect. A constant resistive load without readjustment was used throughout the 4-wk training period in our study. We could not rule out the possibility that we might observe positive training effects on exercise performance if we conducted a longer training period and/or readjusted the resistive load during training. Indeed, 6 wk of training in one previous study increased both short- and long-term maximal ventilation and exercise performance (10). However, that study failed to include control subjects.

An additional point of view is that the respiratory muscles of patients with severe pulmonary diseases are extremely susceptible to fatigue. Thus, although inspiratory muscle endurance is enhanced after inspiratory muscle training in these patients, their ventilatory demands during exercise may still be excessive for their diminished ventilatory capacities. In COPD, airway resistance is much higher than normal, especially in the latter phase of expiration. It is likely that expiratory muscles as well as inspiratory muscles need to be trained. Finally, it simply may be that other factors limit exercise performance in these patients (23), perhaps stemming from systemic malnutrition, deficits in gas exchange, or in locomotory muscle function.

Our study showed that specific inspiratory muscle training for 4 wk by means of inspiratory resistive loading did not alter FVC, FEV_1, FEF_{25-75}, and 12-s MVV in patients with COPD (figure 1). These results are comparable with 2 previous studies (13, 14) that also failed to find changes in resting pulmonary function in patients with COPD after resistive loading training.

It is known that inspiratory muscle endurance is influenced not only by the generated force (i.e., PIM) but also by the ratio of inspiratory time to total time (26), and that alternate contribution of respiratory muscles may delay muscle fatigue (24). As a compromise between comfort and cooperation of our subjects, and admittedly better controlled but more complicated evaluations, we let our subjects choose their own breathing pattern to ease their breathing during the assessment of inspiratory muscle endurance. Although we did not notice any changes in their breathing frequencies before and after training, we are unable to rule out the possibility that changing breathing pattern in these patients, or perhaps simply greater tolerance of hypoventilation, produced spurious increases in their measured inspiratory muscle endurance.

In summary, this study suggests that

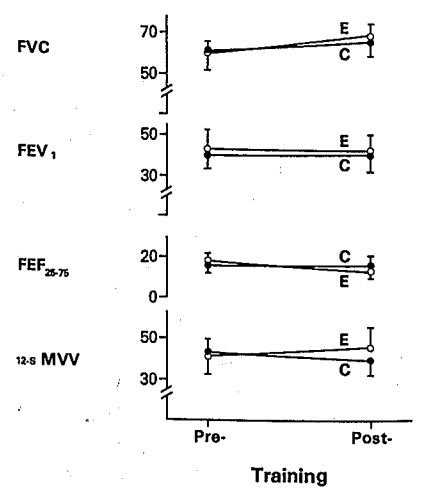

Fig. 2. Responses to progressive exercise and endurance time of constant load exercise in control (C; n = 6) and experimental (E; n = 7) groups before and after 4 wk of inspiratory muscle resistive loading training. Maximal work rate achieved (Ẇmax), and peak exercise ventilation ($\dot{V}_E$), oxygen uptake ($\dot{V}_{O_2}$), and CO_2 production ($\dot{V}_{CO_2}$) were unchanged by either actual (Group E) or sham training (Group C). Endurance time during constant-load work was similarly unchanged by training. The results are represented as mean ± SE.

4 wk of inspiratory resistive loading training is unable to improve pulmonary function and exercise tolerance in patients with COPD, although their inspiratory muscle endurance is enhanced. We think that further studies are required to reevaluate the effects of IMT before clinical application to patients with COPD.

Acknowledgment

We thank the subjects for their enthusiastic participation. We also appreciate the assistance of Ms. Susie Carter, Debby Fee, Michele Matejek, Sandy Roberts, Mr. Ed Getts, and other respiratory therapists in Bloomington Hospital.

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