Targeted resistive ventilatory muscle training in chronic obstructive pulmonary disease

MICHAEL J. BELMAN AND REZA SHADMEHR
Division of Pulmonary Medicine, Cedars-Sinai Medical Center, and The University of California, Los Angeles, California 90048

BELMAN, MICHAEL J., AND REZA SHADMEHR. *Targeted resistive ventilatory muscle training in chronic obstructive pulmonary disease.* J. Appl. Physiol. 65(6): 2726–2735, 1988.—To overcome the problem of altered breathing strategy during resistive ventilatory muscle training (VMT), we used a single-orifice inspiratory resistance together with a target feedback device (TFD) in patients with chronic obstructive pulmonary disease (COPD). In a preliminary study (*study A*), we showed that the resistance plus TFD was effective in controlling breathing strategy. We subsequently used the resistor plus TFD in a 5-wk study (*study B*) of VMT in 17 COPD patients who were randomized into high-intensity (HI) and low-intensity (LI) training groups. Compared with the LI group, the HI group showed significant increases in static maximal inspiratory pressure (21.3 vs. 5.0 cmH_2O), maximal sustained ventilatory capacity (MSVC, 3.2 vs −0.1 l/min, sustained maximal mouth pressure (12.1 vs. 0.6 cmH_2O), mean mouth pressure (6.9 vs. 3.9 cmH_2O), peak inspiratory flow rate (12.3 vs. 4.0 l/min), and maximal sustained work rate (12.2 vs. 4.2 $cmH_2O \cdot l^{-1} \cdot min^{-1}$). We conclude that targeted VMT with control of breathing strategy improves both ventilatory muscle strength and endurance.

diaphragm; exercise therapy; breathing strategy

TWO METHODS of ventilatory muscle training have been used in the past. The first is the hyperpneic method in which patients rebreathe at high minute ventilations for prolonged periods. This method improves ventilatory muscle endurance as measured by the maximal sustained ventilatory capacity (MSVC) (6, 22, 23, 24). The second method is the resistive method in which patients breathe through inspiratory resistances of varying magnitude, usually at normal breathing frequencies. Several reports have documented that after resistive training, there is an improved ability to breathe through smaller inspiratory orifices (1, 10, 20, 27). It is assumed, but not proven, that in these studies the use of a smaller orifice implies a higher inspiratory resistance and improved ventilatory muscle endurance.

Breathing strategy is an important determinant of resistive breathing endurance (4, 5, 11, 21, 25) and alterations in breathing pattern result in improved ability to breathe through smaller orifices in patients with COPD (8). Furthermore, a change in breathing strategy results in a reduction in perceived effort (21). The important variables that influence breathing endurance include inspiratory mouth pressure, inspiratory time, duty cycle, breathing frequency, and inspiratory flow rate (21). Because breathing strategy was not monitored in previous studies (1, 10, 26, 27, 30, 31), it is not clear if patients improved their ability to breathe through smaller orifices as a result of improved ventilatory muscle endurance, or because of changes in breathing strategy. The change in breathing strategy is self defeating not only because it results in spurious improvements in breathing endurance, but by reducing the load on the respiratory muscles, the intensity of the training stimulus is decreased and may even be below the threshold necessary to induce a training effect (8). To prevent these problems, we designed a target feedback device (TFD), which both sets and provides feedback on pressure and respiratory timing targets.

In a previous study, we attempted to examine the transferance of the training effect of resistive training to the ability to increase the level of sustained hyperpnea (8). Because of alterations in breathing strategy, we were unsuccessful in improving resistive breathing function and, therefore, could not evaluate hyperpneic endurance. This question is of importance as it is believed that specificity of ventilatory muscle training dictates that hyperpneic training (high velocity, low tension contractions) should be used if the goal of training is increased ventilatory levels during exercise (20). However, devices for hyperpneic training are cumbersome and generally complex. It would, therefore, be advantageous to develop a simpler system that would simultaneously allow the training of both strength (high tension, low velocity of contraction) and endurance of the ventilatory muscles.

The purpose of this study was to evaluate the use of targeted resistive breathing training as a means of improving ventilatory muscle strength and endurance in patients with chronic obstructive pulmonary disease (COPD).

METHODS

The study was approved by the Institutional Review Board and informed consent was obtained from each patient. The study was carried out in two parts. In *part A*, the preliminary study, the utility of the TFD was investigated in five patients with severe COPD. In *part B*, the TFD was used with a resistive training device (RTD) to investigate its usefulness in training strength and endurance of the ventilatory muscles in COPD pa-

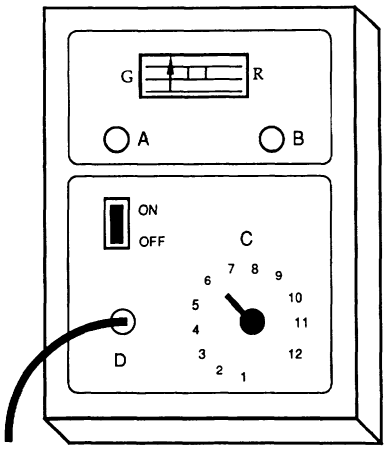

FIG. 1. Target device. *A*, green inspiratory timing light; *B*, red light, which comes on when maximal pressure target is reached; *C*, knob to set pressure target; setting on this dial determines threshold pressure, which must be reached to silence the buzzer; *D*, connection between target feedback device and resistive breathing device. Analog scale is represented by arrow, which moved from the green (G) to the red (R) end as pressure increased. During *study A*, goal was to reach a plateau target pressure represented by 2 vertical lines to the right of midpoint of scale. In *study B*, goal was to raise pressure to move arrow to the extreme right (red zone) of scale. When this was achieved, *red light B* came on.

tients. A similar experimental set-up was used in both studies.

Target Feedback Device

Patients performed resistive breathing through a RTD (PFLEX, Healthscan, New Jersey), which was connected to a small portable TFD (Fig. 1) by means of a small tube (*D*). Mouth pressures developed during resistive breathing were measured by a strain gauge pressure transducer in the TFD and compared with a preselected target pressure. The plateau target pressure could be selected by means of *knob C* (Fig. 1), which had a range of 5–65 cmH_2O. Respiratory timing was regulated by means of a green light (*A*), which remained lit for 2.1 s. The total breath time (TT) was set at 4.8 s (TI/TT = 44%, breathing frequency = 12.5 breaths/min). These settings were arbitrary, but in our experience, this breathing pattern is well tolerated by COPD patients. Patients were instructed to inspire at the onset of this light and maintain the target pressure until the light went out. To ensure that the pressure target was reached, a buzzer sounded if, with inspiration, the preselected target pressure was not achieved. On the analog scale, this corresponds to the two vertical lines to the left of the midpoint of the scale. Since there is a time lag between the onset of inspiration and the achievement of the target pressure, a delay of 0.4 s was allowed until the buzzer sounded. On this device, unlike the threshold device used by Clanton and associates (12), inspiratory flow rate and mouth pressure are not independent variables. At a given orifice size and target mouth pressure, the inspiratory flow rate required to sustain the target mouth pressure is readily predicted from the pressure flow properties of the resistive load ($\dot{V} = Pm/R$). The use of this device directs the patient to maintain a constant pattern of breathing as described by the target Pm, TI, and TT. The TFD was used for both testing in the laboratory as well as for training in the home.

Experimental Setup

The patients breathed through a one-way valve (Hans Rudolph, no. 1400). Between this and the PFLEX, a pneumotachometer (Fleich no. 3) was placed to measure airflow. Moth pressure was recorded continuously via a differential pressure transducer (Validyne ± 140 cmH_2O) connected to an orifice in the mouthpiece of the RTD. Flow and pressure signals were transmitted to a microcomputer (IBM AT) via an analog to digital converter (Data Translation board 2801). These signals were used for the determination of tidal volume (VT), frequency of breathing (f_b), peak inspiratory flow rate (PIFR), peak mouth inspiratory pressure (Pm_{max}), mean inspiratory pressure ($\bar{P}m$), inspiratory time (TI), mean inspiratory flow ($\dot{V}I$), and the duty cycle (TI/TT). In addition, the external work rate (WR) required to breathe through the RTD was calculated by integration of the product of instantaneous mouth pressure and the rate of volume change during inspiration.

$$WR = f_b \int_{TI} Pm \times \dot{V}dt$$

Pressure time index (PTX) was calculated by the formula

$$PTX = \frac{\bar{P}m \cdot TI}{MIP \cdot TT}$$

where MIP is the maximal static inspiratory pressure and $\bar{P}m$ is the mean inspiratory mouth pressure.

The fractional end-tidal CO_2 (FET_{CO_2}) was monitored continuously by means of a mass spectrometer (Perkin-Elmer, model 1100), and the O_2 saturation (Sa_{O_2}) was measured by a pulse oximeter (Biox, 11A).

Part A. Preliminary Studies

Preliminary studies were done on five patients with COPD (3) mean forced expired volume in 1 S (FEV_1) = 0.69 ± 0.10 liters, mean forced vital capacity (FVC) = 2.33 ± 0.32 liters, mean arterial P_{O_2} (Pa_{O_2}) = 66 ± 2 Torr, mean arterial P_{CO_2} (Pa_{CO_2}) = 43 ± 1 Torr to test the effectiveness of the device in regulating breathing pattern. These patients performed resistive breathing maneuvers through the RTD. Nose clips were worn during all breathing trials. Participants were given two to three preliminary trials of 4 min each to familiarize themselves with the timing device. This was easily accomplished by all subjects within the prescribed time. An initial target pressure of 5 cmH_2O was chosen and then increased progressively by 2.5–5 cmH_2O. Patients breathed for 4 min at each of the target pressures. It was clear that they had difficulty in maintaining an adequate ventilation when breathing through small orifices of the RTD (holes 4 and smaller) and therefore they were tested only at *holes 1*, *2*, and *3*. The breathing pattern of one subject is shown in Fig. 2. The ability of the patients to track the pressure and timing targets was measured as the ratios Pm/target Pm, TI/target TI, TT/target TT,

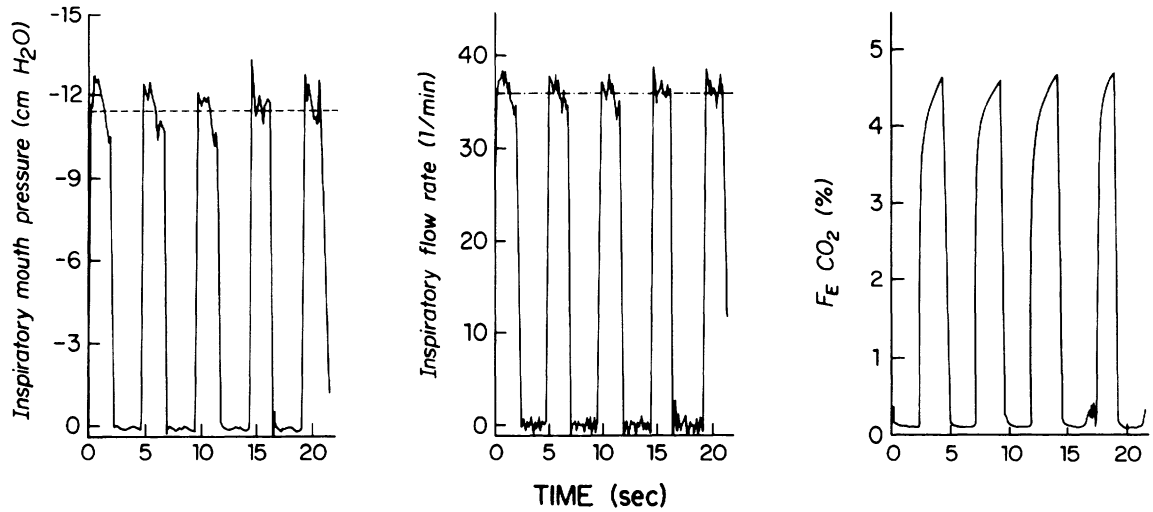

FIG. 2. Pressure and flow patterns and expired CO_2 fraction (FE_{CO_2}) patterns generated during targeted breathing. · · · · On pressure tracing illustrates target pressure during this run (11 cmH_2O). Note reproducibility of pressure and flow tracings and ability of patient to achieve target pressure.

TABLE 1. *Ratio of actual Pm, TI, TT, and V̇I to respective target values*

Patient No.	Pm/ Target Pm	TI/ Target TI	TT/ Target TT	V̇I/ Predicted V̇I
1	1.11	0.98	1.01	1.18
2	1.03	1.02	0.99	0.99
3	1.08	0.93	1.00	1.13
4	0.99	1.01	0.98	0.95
5	1.03	0.93	0.99	1.06
Mean ± SE	1.05±0.02	0.97±0.02	0.99±0.01	1.06±0.04

Pm, mouth pressure; TI, inspiratory time; TT, total breath time; V̇I, mean inspiratory flow. Predicted V̇I derived from relationship between flow and pressure for the relevant orifice.

and the mean V̇I/predicted V̇I on a breath-by-breath basis and averaged for a given test. The mean values for all tests performed by each patient are given in Table 1. The ability of the patients to maintain a consistent breathing pattern was measured as the coefficient of variation (CV) of $\overline{Pm}$, TI, TT, and V̇I for a given test. The results for all tests were averaged and shown in Table 2. These data indicate that the patients could successfully follow simultaneous pressure and timing targets during resistive breathing. The relationship between WR and mean mouth pressure for *orifices 1* through *3*, while using the target device is shown in Fig. 3. With increasing pressure, there is an increase in WR, but there are noteable differences between orifices. The

TABLE 2. *Coefficient of variation for index of breathing strategy*

Patient No.	Pm	TI	TT	V̇I
1	0.10	0.11	0.13	0.08
2	0.10	0.15	0.07	0.11
3	0.13	0.04	0.03	0.09
4	0.09	0.04	0.05	0.11
5	0.09	0.08	0.07	0.10
Mean ± SE	0.10±0.01	0.08±0.03	0.07±0.02	0.10±0.01

See Table 1 footnote for definition of abbreviations.

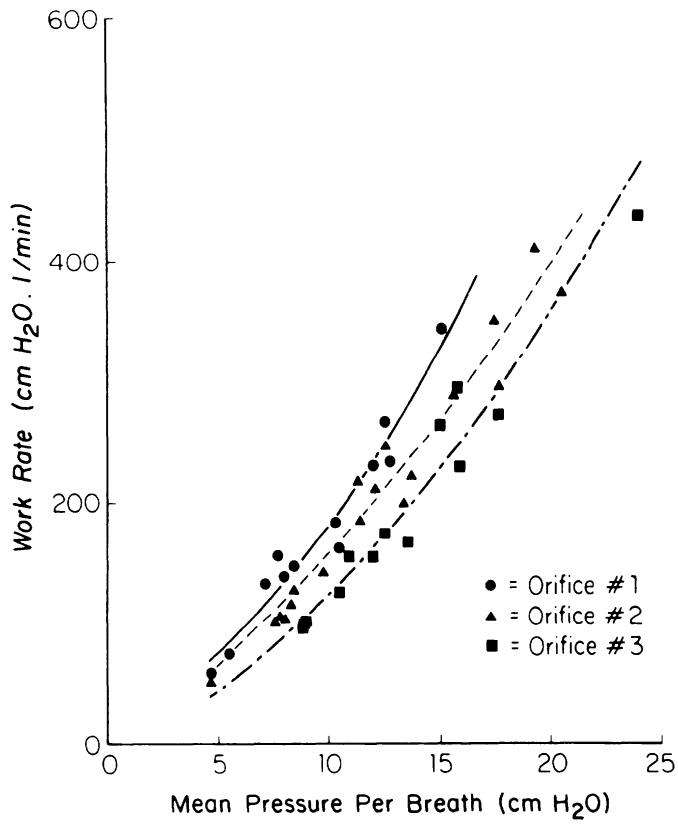

FIG. 3. Relationship between work rate and mean mouth pressure for 5 chronic obstructive pulmonary disease (COPD) bindings while breathing through *holes 1* through *3*. Correlation coefficient for each curve is highly significant ($P < 0.0001$)

rate of increase in work is much greater for *hole 1* (largest diameter) compared with *hole 3* (smaller diameter) when target pressures are increased. This is due to the higher level of ventilation required to maintain a given Pm at the smaller resistive load. Furthermore, at a constant target pressure, there is a reduction in WR as hole size is decreased.

In Fig. 4 we show the relationship between WR and ΔFET_{CO_2}. These data show that FET_{CO_2} rises when breath-

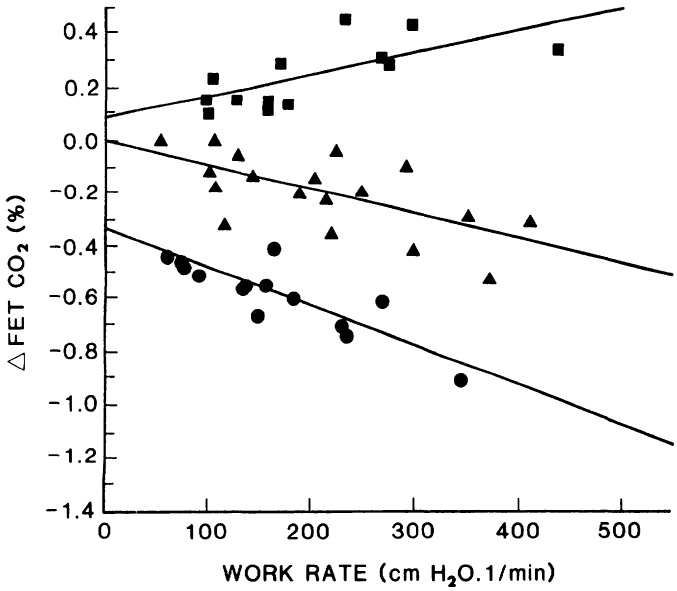

FIG. 4. Relationship between change in fractional end-tidal CO_2 (FET_{CO_2}) and work rate for 3 largest orifices of resistive training device (RTD). Each regression line is significant ($P < 0.01$). See Fig. 3 for definition of symbols. See text for further explanation.

ing through *hole 3*, and decreases when breathing through *hole 1* as work rate increases. *Hole 2* provides relative stability of the FET_{CO_2}, despite increases in WR. By using *orifice 2* of the PFLEX (diam 0.46 cm), we could provide a wide range of work rates and pressure targets, while simultaneously permitting the patients to maintain FET_{CO_2} within physiological limits.

On the basis of these findings, we concluded that using only one orifice of the RTD is suitable for ventilatory muscle training.

Part B. Ventilatory Muscle Training Study

Patients. Twenty patients (11 men and 9 women), none of whom had participated in the validation study, with clinical and functional evidence of moderate-to-severe COPD were recruited for this study. Criteria for inclusion were *1*) presence of COPD as defined by the American Thoracic Society, and *2*) improvement in FEV_1 of <20% after inhaled isoproterenol. Criteria for exclusion were *1*) evidence of coronary artery disease, cardiac arrhythmias, congestive heart failure, and *2*) orthopedic problems such as shoulder girdle and spinal abnormalities, which would interfere with performance of the breathing maneuvers. The patient characteristics are shown in Table 3. Of the 20 patients recruited, 3 failed to complete the training because of intercurrent illness. Patients were stratified by sex and subsequently randomized into two groups: *1*) the high-intensity (HI group), in which the pressure target during training was raised as tolerated, and *2*) the low-intensity group (LI), in which the pressure target was kept at low levels (7.5–10 cmH_2O) throughout the training.

Procedure. MEASUREMENTS OF LUNG FUNCTION. Before and after the training program, patients underwent measurements of spirometric data, maximum voluntary ventilation (MVV), and lung volumes by standard methods (2, 15). Lung volumes were measured by the technique of helium dilution (14).

MEASUREMENTS OF VENTILATORY MUSCLE FUNCTION. *1) MIP.* MIP was measured at functional residual capacity (FRC). During measurement of the MIP, an 18-gauge needle was placed in the mouthpiece to prevent oral pressure artifacts (9). Before obtaining these measurements, patients were given several practice attempts at performing these respiratory maneuvers.

2) Unloaded ventilatory muscle endurance. This was measured as MSVC in a rebreathing circuit (6, 23, 24). This system allows continuous monitoring of the patient's ventilatory level, while simultaneously providing a visual target to encourage maximal performance. Concentrations of O_2 and CO_2 are maintained within physiological limits. The initial target level was set at 90% of the MVV and adjusted to encourage maximal performance. The test was conducted for 10 min, and mean ventilatory levels were calculated each minute. The mean of the last 8 min was defined as the MSVC. Each patient performed a practice maneuver of the MSVC, before the base-line test to overcome the small learning effect.

3) Loaded ventilatory muscle endurance. A. REGULATION OF BREATHING PATTERN. The patients performed resistive breathing through the RTD which was connected to the TFD as previously described. In brief, the function of the TFD is to provide timing and pressure targets when the patient breathes through the RTD. Because we were interested in both strength and endurance training of the ventilatory muscles, we used a different breathing strategy in *study B* compared with *study A*. The TT was maintained at 4.8 s with a TI of 2.1 s. However, the HI group patients were instructed to reach as high Pm as possible with each breath. With each breath, the patient attempted to light the red light (B), which occurred when the indicator reached the red zone at the extreme right of the analog scale (see Fig. 1). By adjusting knob C, the maximum pressure target could be adjusted in increments of 5 cmH_2O to a maximum of 65 cmH_2O.

As in *study A*, the buzzer came on 0.4 s after the onset of the green light, but it sounded for only 0.5 s, although the patients were encouraged to maintain the TI for the full 2.1 s. Because of a relatively rapid decay in pressure after peak inspiratory pressures were reached, the breathing pattern resembled a sawtooth rather than a square wave pattern as seen in *study A* (Fig. 5).

The breathing pattern used in the training study constrained the breathing frequency, TI, and the pattern of pressure generation. If the Pm_{max} were not reached, the red light would not be lit and if the pressure decay were too rapid (< 0.5 s), the buzzer would sound.

This breathing pattern was designed to stress the ventilatory muscles so as to increase both strength and velocity of contraction. As the target Pm_{max} is raised, the patient is required to increase the inspiratory flow rate to achieve the target Pm. Furthermore, because of the use of a single fixed orifice, a unique peak flow rate is required to match the target Pm_{max}. Thus although inspiratory flow rate is not displayed, it is constrained via control of the other components of the breathing pattern.

B. MEASUREMENT OF RESISTIVE BREATHING ENDUR-

TABLE 3. *Pulmonary function tests before and after training in the LI and HI group*

Patient No.	Sex	Age, yr	FVC		FEV_1		FRC		MVV		Pa_{O_2}		Pa_{CO_2}	
			Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
						LI group								
1	M	77	3.39	3.38	0.79	0.73	6.03	6.15	39	43	61	58	42	38
2	F	71	2.50	2.53	0.57	0.62	2.88	2.99	29	29	59	58	35	36
3	M	57	4.10	2.28	0.90	0.78	4.45	3.75	43	36	54	62	38	42
4	M	52	2.24	1.96	0.52	0.47	4.44	5.59	27	17	51	63	41	48
5	M	58	3.13	3.05	1.05	1.18	5.36	5.14	50	54	64	63	51	46
6	F	73	2.53	2.50	0.97	0.98	3.75	3.68	18	38	61	79	35	37
7	M	62	3.07	3.23	1.75	1.90	4.60	4.78	50	63	73	75	39	38
8	M	68	2.85	2.55	0.60	0.59	3.99	3.97	41	38	69	66	35	34
9	F	55	2.00	2.03	0.70	0.78	3.83	4.09	41	41	67	65	40	34
Mean ± SE		64±3	2.87±0.21	2.61±0.17	0.87±0.13	0.89±0.14	4.37±0.31	4.46±0.34	38±3	40±5	62±2	65±2	40±2	39±2
						HI group								
1	M	55	3.66	4.44	0.82	1.00	6.70	5.23	38	52	58	59	33	30
2	F	64	2.24	2.30	0.88	0.89	3.13	3.22	31	32	83	76	41	44
3	M	67	3.10	2.85	1.11	1.11	2.68	2.97	59	59	66	73	42	42
4	F	77	1.89	1.83	0.88	0.78	3.00	3.05	33	32	67	59	32	38
5	M	51	3.08	3.30	1.02	0.99	3.51	3.99	45	45	62	72	44	46
6	M	68	2.21	2.99	0.74	0.92	3.95	5.11	41	54	61	62	47	48
7	F	65	2.38	2.22	1.15	1.09	2.73	3.45	52	63	65	67	35	39
8	F	66	2.38	2.41	1.20	1.23	2.87	3.36	70	94	66	84	35	37
Mean ± SE		64±3	2.62±0.21	2.79±0.29	0.97±0.06	1.00±0.05	3.57±0.47	3.80±0.32	46±5	54±7	66±2	69±3	39±2	41±2

LI, low-intensity group; HI, high-intensity group; FVC, forced vital capacity; FEV_1, forced expired volume in 1 s; MVV, maximal voluntary ventilation; Pa_{O_2}, arterial P_{O_2}; Pa_{CO_2}, arterial P_{CO_2}.

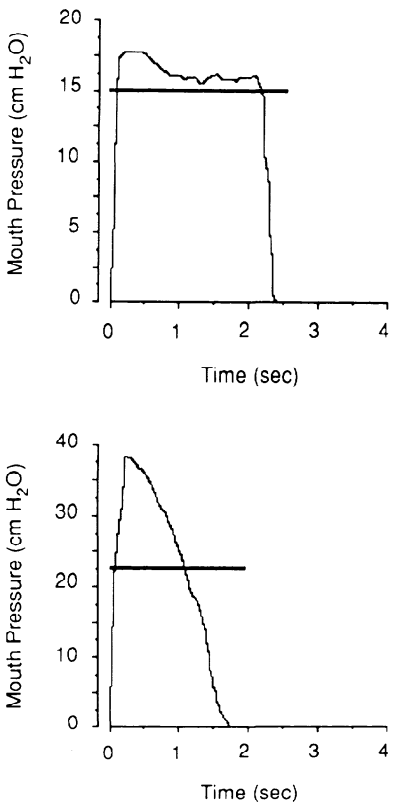

FIG. 5. A comparison of breathing pattern in *study A* (*top*) vs. high-intensity trainers in *study B* (*bottom*).

ANCE. This was measured with the RTD connected to the target feedback device. An initial practice session was performed with the target pressure set at ~7.5 cmH_2O, a level which can be easily reached by all patients. Subsequently the subjects performed a practice maximal test. The target pressures was set initially at ~50% of the previously measured MIP. The patient was encouraged to perform maximally and the target was adjusted accordingly. Using the information of Pm_{max} achieved during the practice test, the maximal effort test was repeated for a duration of 10 min on a subsequent day.

In previous studies (4, 5), the end point of the endurance test was recognized by the failure of the subjects to maintain the plateau of the square-wave breathing pattern. We found that our patients were unable to maintain a square wave pattern of breathing, when simultaneously aiming for maximal pressures. In this case after reaching the target pressure, the Pm decayed despite continuation of the inspiratory effort. Furthermore, we found that during performance of the prolonged tests, the patients' attention frequently wanders and a decline in achieved pressures may be due to inattention or other technical factors rather, than a true failure of the ventilatory muscles as a pressure generator. We, therefore, decided to use a fixed time test (10 min) and instructed the patients to achieve as high a pressure as possible with each breath. Thus during loaded breathing, we measured ventilatory muscle endurance as the mean Pm_{max}, $\bar{P}m$, WR, and PTX that could be sustained for 10 min using a fixed breathing strategy.

The testing sequence is as follows: *day 1*: spirometry, lung volumes, and arterial blood gas measurements; prac-

tice session for MIP measurement; *day 2*: practice MSVC for 10 min, practice using the target feedback device at 5–7.5 cmH_2O for 10 min, second practice of measurement of MIP; *day 3*: MSVC for 10 min, MIP measurements; three trials done and the highest values chosen as the pretraining values; practice maximal resistive breathing trial with the TFD; *day 4*: base line maximal resistive breathing test with TFD with measurement of the breathing strategy.

After training, the tests were repeated with the exception of the practice maximal pressures and practice maximal resistive breathing test with the TFD.

RESISTIVE VENTILATORY MUSCLE TRAINING. Both HI and LI groups trained for 6 wk, using the RTD and TFD. The training was performed daily for two 15-min sessions at home for 6 days and 1 day/wk under supervision in the pulmonary laboratory. During all training sessions the patients wore nose clips. In patients with resting hypoxemia, supplemental O_2 was provided during the training. The HI group was encouraged to increase the pressure target as tolerated and each week in the laboratory performed a maximal resistive effort test during which time the respiratory variables were measured as noted above. The LI group was maintained at a low Pm_{max} of 7.5–10 cmH_2O and this level was also used at the weekly testing session in the pulmonary laboratory. Criteria for exclusion from the study were *1*) missing more than 3 consecutive days of training, and *2*) overall compliance of <90% of total possible training days. The patients were issued a daily log sheet and recorded the time and duration of training.

Of the 20 patients initially recruited, 2 patients suffered intercurrent illnesses and were forced to stop the training. One patient experienced a pneumothorax for which she was admitted to the hospital and treated by tube thoracostomy. This resolved without further complication, but the patient was subsequently dropped from the study. One patient missed 1 wk of training because of illness 1 wk after starting. She was subsequently restarted and completed a further 6 wk training program. Examination of the patient logs revealed that the overall compliance was 98.7% of the total possible training sessions.

Statistical Analysis

All data in this report are expressed as the means ± SE. Relationships between work rate, pressure, and FET_{CO_2} were evaluated by regression analysis. The pre- and posttraining values for the high and low intensity groups were compared by means of a two-way analysis of variance with repeated measures (BMDP, 2V) (16). Confidence intervals (95%) were calculated for changes in key variables.

RESULTS

Lung Function

The patient characteristics are described in Table 3. They show that the two groups were comparable with respect to the severity of their obstructive ventilatory defect. The HI group had a lower FRC, but this was not significantly different from the LI group. The mean Pa_{O_2} was 62 ± 2 Torr (range 51–73 Torr) and the mean Pa_{CO_2} was 40 ± 2 Torr (range 35–51 Torr). After training, there was no significant differences in the spirometric or lung volume measurements (Table 3).

Breathing Strategy

We evaluated the consistency of the breathing pattern during the maximal resistive breathing test by means of a comparison of the Pm_{max}, TI, and PIFR during the first and last minute of the maximal sustained pressure test before and after training (Table 4). These data showed no significant differences in these indexes in the HI and LI group for both the pre- and posttraining tests.

Ventilatory Muscle Function

The percent change in several variables measured during resistive breathing is illustrated in Fig. 6 and Table 5. Significant differences were found in the MIP and MSVC, which showed an increase in both groups but with a significantly larger difference in the trained group. The $\bar{P}m$, Pm_{max}, WR, and PIFR increased in both groups, but with a significantly greater increase in the trained group (Table 5). For TI, VT, PTX and $\dot{V}I$, there were increases in both the HI and LI groups after training, but no differences between groups (Table 5). The 95% confidence intervals for changes in several of the key indexes are also shown in Table 5. Evaluation of the sequence of change in the MIP's during the training in the HI group is shown in Fig. 7. This shows a continued increase throughout the training program. The pattern of increase in the WR in the HI group is illustrated in Fig. 8.

In both HI and LI groups, the FET_{CO_2} remained relatively stable. No patient showed the development of FET_{CO_2} greater than resting base-line levels. Similarly, no patient developed hypocapnia (FET_{CO_2} < 3.5%). Patients with resting Pa_{O_2} levels <60 Torr were provided with supplemental O_2 during training and no hypoxemia developed (Sa_{O_2} < 87%).

DISCUSSION

We found that resistive ventilatory muscle training by means of a fixed orifice with a target feedback device was successful in improving both ventilatory muscle strength and endurance in patients with COPD.

Study A

The training device was well accepted by the patients. All patients were able to follow the timing and pressure signals after short practice attempts, as shown by the ratio of achieved to target values for Pm, TI, and inspiratory flow. Furthermore, the consistency of the breathing pattern was demonstrated by the relatively small coefficients of variation of the indexes of breathing pattern (Tables 1 and 2) in *study A* and by the fact that the Pm_{max}, TI, and PIFR were similar in the first and last minute of the maximal resistive breathing test in *study B* (Table 4). In *part A* of the study we found empirically

TABLE 4. *Comparison of Pm_{max}, TI, and PIFR during 1st and 10th min of resistive breathing*

	Pm_{max}, cmH_2O		TI, s		PIFR, l/min	
	1st min	10th min	1st min	10th min	1st min	10th min
LI						
Before	35.8±1.0	36.3±1.0	1.59±0.03	1.74±0.06	68.4±1.6	68.6±1.6
After	35.1±1.0	33.7±1.0	1.58±0.4	1.58±0.05	67.9±1.7	67.3±1.7
HI						
Before	42.0±1.0	41.3±1.1	1.50±0.03	1.49±0.05	76.8±1.8	78.7±1.8
After	50.5±1.1	49.2±1.1	1.51±0.04	1.42±0.04	87.5±1.9	87.3±1.9

Values are means ± SE. Pm_{max}, peak mouth pressure; TI, inspiratory time; PIFR, peak inspiratory flow rate; LI, low-intensity group; HI, high-intensity group.

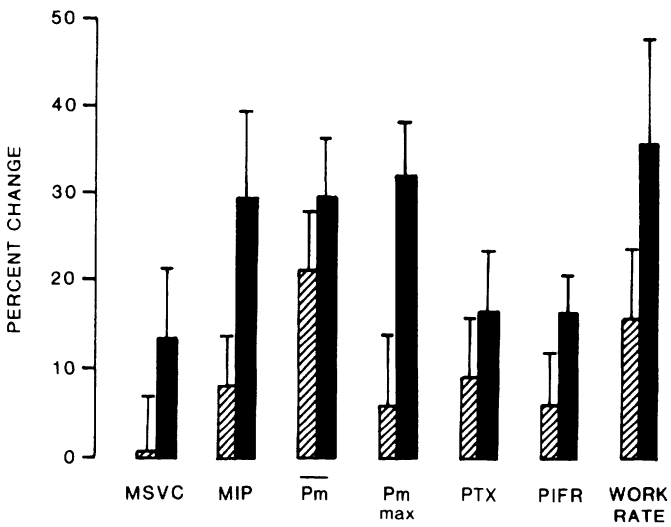

FIG. 6. Percent change (mean ± SE) in tests of ventilatory muscle function and indexes of breathing strategy in high- and low-intensity groups before and after training. MSVC, maximal sustained ventilatory capacity; MIP, maximal inspiratory pressure; $\bar{P}m$, mean mouth pressure; Pm_{max}, peak mouth pressure; PTX, pressure-time index; PIFR, peak inspiratory flow rate. ▨, Low-intensity group; ■, high-intensity group.

that *orifice 2* of the PFLEX provided a wide range of Pm and work rates (0–500 cmH_2O liters/min), which covered the values achieved by these patients with moderate-to-severe COPD. Furthermore, with a fixed breathing frequency of approximately 13 breaths/min, no patient developed hypo or hypercapnia. The use of one orifice facilitates the use of a TFD. As the orifice size is fixed, there is a unique mean flow rate required to achieve each target pressure. This is demonstrated by the fact that the flow rates achieved with use of the RTD plus TFD were consistent at each target pressure. Thus even though no flow targets are provided, it can be regulated through control of other indexes of breathing strategy provided that the orifice size is not changed.

By using the target device and measuring the breathing strategy during both the testing and training, we have overcome the problem of many previous studies in which the outcome measure was the ability to breathe through a smaller orifice (1, 10, 26, 27). As has been demonstrated, resistive breathing endurance may improve when breathing through a smaller orifice, not necessarily as a result of improved ventilatory muscle function, but as a result of a change in breathing strategy (8). Long slow inspirations can be performed easily through small orifices. As the Pm developed is low, the degree of discomfort is lessened (21). Such a breathing pattern also reduces the tension applied to the ventilatory muscles and probably is suboptimal for the induction of a true training response (8, 12).

Study B. Ventilatory Muscle Strength

Static ventilatory muscle strength was measured as the MIP. Although there was a small increase in MIP in the LI group, the HI group showed a significantly larger gain. An increase in MIP has not been a consistent finding in previous studies of resistive training (8). Whereas, increases were found in studies in normal humans and children with cystic fibrosis (1, 12), both Chen and associates and Pardy and associates (10, 26) failed to find increases in patients with COPD. The inconsistency of changes in MIP in these studies may be related to the lack of an optimal training stimulus, because of inadequate monitoring of breathing strategy (1, 10, 26, 27).

Ventilatory Muscle Endurance

Unloaded. We measured ventilatory muscle endurance during both loaded and unloaded conditions. The MSVC has been used as the standard index of sustained hyperpnea during unloaded conditions (23). The HI group showed a small but significant increase in this index. This is the first demonstration of the efficacy of resistive training as a means of improving endurance for isocapneic hyperpnea. The magnitude of change (+13%) was smaller than that seen in previous studies (25–30%) (6, 23), but important in that it demonstrates that there is the potential for transference of the effects of resistive to endurance training. During the resistive breathing the $\dot{V}I$ was higher than expected with minute ventilations of 15–20 liters/min. During unloaded hyperpnea it is possible to reach higher levels of ventilation. Nevertheless, these intermediate ventilatory levels, together with the inspiratory resistive load were sufficient to increase the MSVC. Under conditions of unloaded breathing, hypocapnea would probably have resulted. However, the stable FET_{CO_2} values indicate that the $\dot{V}CO_2$ rose proportionately during the resistive breathing to offset the increased CO_2 excretion of the hyperpnea.

Ventilatory Muscle Endurance

Loaded. During loaded breathing we found that the mean Pm_{max}, $\bar{P}m$, and WR increased in the HI group

TABLE 5. *Changes in measures of ventilatory muscle function and breathing strategy*

Variable	Protocol	Before	After	Mean Change and 95% CI of Change	*P* Value Treatment Effect
MSVC, l/min	LI	16.7±2.6	16.6±2.6	0.1±1.61	0.036
	HI	23.0±2.3	26.2±2.1	3.2±1.73	
MIP, cmH_2O	LI	63.0±5.0	68.0±5.1	5.0±4.95	0.0064
	HI	68.0±2.0	89.3±5.4	21.3±7.95	
Pm, cmH_2O	LI	18.4±1.3	22.3±1.6	3.9±1.15	0.0376
	HI	23.1±2.2	29.9±2.1	6.9±2.19	
Pm_{max}, cmH_2O	LI	35.1±3.0	35.7±2.9	0.6±0.81	<0.0001
	HI	37.9±3.0	50.0±3.1	12.0±3.13	
PIFR, l/min	LI	67.1±2.7	71.1±4.2	4.0±5.3	0.054
	HI	75.0±5.2	87.3±3.7	12.3±4.7	
Work rate, $cmH_2O \cdot l^{-1} \cdot min^{-1}$	LI	25.7±2.8	29.9±2.4	4.2±1.7	0.0012
	HI	33.1±4.8	45.3±5.7	12.2±3.1	
PTX	LI	0.19±0.01	0.21±0.02		0.471
	HI	0.19±0.01	0.23±0.02		
TI, s	LI	1.71±0.11	1.46±0.10		0.4
	HI	1.53±0.09	1.40±0.12		
VI, liters	LI	1.17±0.06	1.24±0.09		0.4
	HI	1.25±0.06	1.39±0.13		
$\dot{V}$I, l/min	LI	14.9±0.8	15.5±1.1		0.4
	HI	16.0±0.8	17.5±1.6		

Values are means ± SE. CI, confidence interval; MSVC, maximal sustained ventilatory capacity; MIP, maximal inspiratory pressure; PIFR, peak inspiratory flow rate; PTX, pressure-time index; VT, tidal volume. See footnotes of Tables 1 and 3 for definition of other abbreviations.

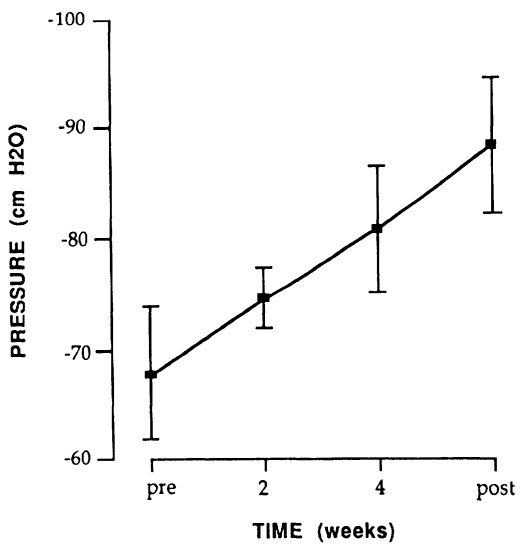

FIG. 7. Maximal inspiratory pressure measured at biweekly intervals in the high-intensity group during training.

compared with the LI group. These increases are indicative of an improvement in sustained power output by the ventilatory muscles. For reasons described in the methods section (see MEASUREMENT OF BREATHING ENDURANCE) we preferred to use a fixed time test with an increasing pressure target rather than a fixed pressure with measurement of endurance time. In this way, the test resembles a maximal sustained work rate test such

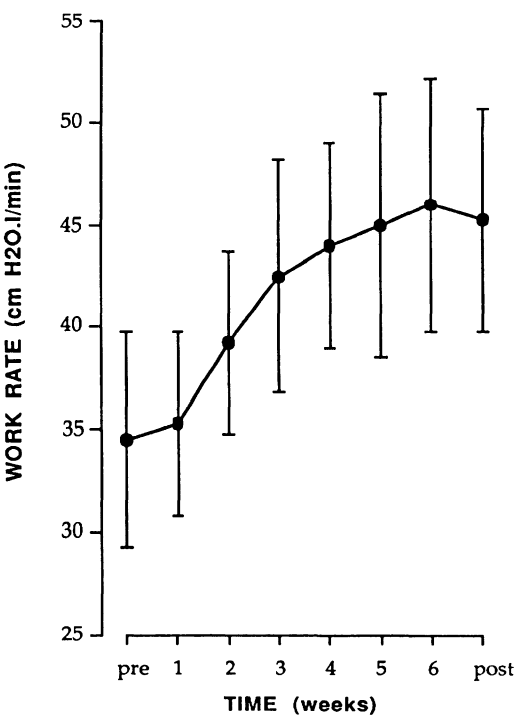

FIG. 8. Average work rate sustained by high-intensity group during training.

as the MSVC. However, in this case, the target is the Pm_{max} rather than a preset ventilatory level.

The increase in the PTX posttraining was twice as large in the HI group compared with the LI group, but was not significant. However, the magnitude of change in the PTX was smaller than the change in WR. There is disagreement in the literature regarding the relationship among WR, PTX, and O_2 cost of breathing ($\dot{V}O_{2resp}$) (13, 17, 21, 25). However, previous investigators (13, 25) have recently emphasized the fact that the $\dot{V}O_{2resp}$ and WR are closely correlated. They are proportional to the PTX only when inspiratory flow rates are relatively constant. In their studies, increasing the inspiratory flow rate increased the slope of the relationship between WR and PTX so that at higher mean flow rates there was a proportionately larger increase in $\dot{V}O_{2resp}$ or WR than PTX. At equivalent values of PTX, $\dot{V}O_{2resp}$ or WR were greater at higher inspiratory flow rates than at low flow rates. Thus it is understandable that as mean inspiratory flow rates increase there will be a larger increase in WR than PTX. It should be noted that in our study the increase in the mean flow rate was twice as large in the HI compared with the LI group. This probably accounted for the relatively larger change in WR compared with PTX.

In addition to the increased endurance, the HI group demonstrated a significantly larger increase in PIFR, a change consistent with an increase in maximal velocity of contraction of the ventilatory muscles (18). This change is of more than theoretical benefit to COPD patients, as it may permit the development of increased ventilatory muscle power during exercise (19). With an increase in PIFR, it is possible to shorten TI and reach similar or higher VT and minute ventilations. Furthermore a shorter TI allows a longer expiratory duration (TE), which would permit the patient to reach a lower lung volume and consequently a more advantageous diaphragmatic configuration before the next inspiration. These changes may help overcome the impairment of ventilatory muscle function induced by exercise hyperpnea, which include a decrease in maximum force secondary to an increase in inspiratory flow rate and end expiratory lung volumes. The former factor acts through the force-velocity relationships and the latter through the length-tension relationships (21, 25). Thus despite the increase in PIFR, a factor which tends to reduce endurance of ventilatory muscle (11, 13, 25), these patients were able to maintain a higher sustained ventilatory muscle power output.

The control (LI) and treated (HI) groups were managed in an identical manner as possible. They both used the same breathing pattern during the training. Both groups were told that the treatment may be helpful, and the number of visits and interaction with the research was identical. We felt that the latter factor was important to control as it has been well documented that the "laying on of hands" may play a role on influencing outcome in COPD patients. Thus the only difference in approach was that the HI group was instructed to increase the pressure target as tolerated. It is clear that use of the resistive device involves a learning effect in that the LI group did show an improvement in several of the outcome measures. However, with respect to the Pm_{max}, $\bar{P}m$, PIFR, and WR, the HI group showed a significantly greater increase in comparison with the LI group. This shows that the training per se was responsible for this change rather than just repetition of the resistive breathing. Thus by means of this device it is possible to ensure that an increased load is applied to the respiratory muscles during resistive training. The pattern of gradual increases during several weeks in the MIP and WR in the HI group, supports the development of a true training effect rather than a learning effect. In the latter situation, abrupt increases with an early plateau would be expected as the technique of resistive breathing was mastered.

The relative improvements in the resistive breathing maneuvers as measured by the WR, Pm_{max}, and $\bar{P}m$ were larger than the index of endurance (MSVC). Because muscles respond differently to different training stimuli (12, 20), it is not surprising that high tension, low repetition activity, as was performed here, mainly improved strength. Endurance training (high repetition, low tension), will increase endurance activities and in limb skeletal muscle is associated with an increase in oxidative mitochondrial enzymes (20). In previous studies of ventilatory muscles, endurance training improved the MSVC (6, 22–24), but MIPs were not measured. In the study of Leith and Bradley (23) however, endurance training increased the MSVC, but did not affect vital capacity, which was improved only by specific strength training manuevers.

Because specificity of training is an important principle in muscle physiology, it is important to train the ventilatory muscles in a manner that would be expected to improve hyperpneic endurance and, thus, exercise hyperpnea (20). However, as we and others have shown (21), increased strength is related to increased endurance and, therefore, a combination of strength and endurance training regimens may be additive. In this study, more emphasis was placed on strength, but in future studies a more equitable balance could be attained by increasing fb and, thus, $\dot{V}I$. With a higher sustained $\dot{V}I$ during training and consequently a greater endurance training intensity larger increases in the MSVC may be achievable. As emphasized recently by Grassino (20), improved coordination may also improve ventilatory muscle performance. We believe this is the basis for much of the improvement of the LI groups as they had considerable practice at performing the breathing maneuvers. However, the training stimulus was low (low Pm_{max} target) and the increases in Pm_{max}, $\bar{P}m$, and WR were significantly smaller than those found in the HI group.

In this study we did not examine exercise capacity after training. This is a complex issue because many patients with COPD stop exercising for reasons other than ventilatory muscle fatigue (24, 26). Improvement in their ventilatory muscle function may not be reflected in an improved exercise capacity as was shown by Pardy and co-workers (26). This does not, however, detract from the fact that ventilatory muscle training and improved ventilatory muscle function may be of benefit in other ways. This includes an increased resistance to

respiratory failure, more rapid weaning from mechanical ventilation, and reduced perception of dyspnea. These issues need to be explored in future studies.

In summary, we found that targeted resistive training with the use of a RTD and a TFD, successfully improved ventilatory muscle strength and endurance in patients with COPD. While improvements in some of the indexes of breathing strategy were found in the LI-trained group, a factor which emphasizes the importance of including sham treatments in future studies of this nature, the HI group showed significantly greater increases in ventilatory muscle strength and endurance. Many studies of ventilatory muscle training in the rehabilitation of patients with COPD have been done (1, 10, 10, 26, 27). As discussed above, the results are inconclusive because of the failure to correctly measure the training stimulus and the improvements in ventilatory muscle function. The availability of this simple technique to improve ventilatory muscle function should facilitate further studies to evaluate the functional benefits of ventilatory muscle training in COPD.

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