ORIGINAL ARTICLE

Domiciliary Positive Expiratory Pressure Improves Pulmonary Function and Exercise Capacity in Patients with Chronic Obstructive Pulmonary Disease

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Background/Purpose: This study assessed how positive expiratory pressure (PEP) affected pulmonary function, functional capacity, and subjective cough difficulty in individuals with chronic obstructive pulmonary diseases (COPD).

Methods: This was a prospective, randomized, controlled study. Subjects were recruited from an outpatient department at a university hospital. Thirty-two patients with COPD were allocated to either PEP + FET (forced expiratory technique) group ($n = 16$) or FET only group ($n = 16$). Subjects in PEP + FET and FET groups were in a clinically stable condition before and during the study. Subjects in the PEP + FET group received PEP breathing using a mouth adjunct to FET, and the FET group was administered FET for 4 weeks only. Patients received weekly follow-up during the study period. Pulmonary function, 6-minute walk tests, and subjective cough difficulty scores were measured before and after the 4-week interventions.

Results: Subjects in the PEP + FET group had a significantly increased diffusing capacity (DLCO) compared to preintervention ($p < 0.05$) and after intervention in the FET group ($p < 0.05$). DLCO significantly increased in the PEP + FET group from 18.0 ± 7.3 to 20.1 ± 7.2 mL/min/mmHg. The 6-minute walking distance (6MWD) also increased significantly from 516.8 ± 94.1 to 570.6 ± 60.4 m in the PEP + FET group ($p < 0.001$) after intervention, compared to that for the FET group ($p < 0.05$). Additionally, the PEP + FET group had significantly lower cough difficulty scores compared to those at baseline and in the FET group.

Conclusion: Four-week PEP therapy as an adjunct to FET further enhanced DLCO and 6MWD, and reduced cough difficulty compared to FET only in COPD patients with mucus hypersecretion. [*J Formos Med Assoc* 2007;106(3):204–211]

Key Words: chronic obstructive pulmonary disease, forced expiratory technique, positive expiratory pressure, 6-minute walk test

Chronic obstructive pulmonary disease (COPD) is a major and increasing global health problem that has become a leading cause of fatality.[1] COPD has multiple components which, in addition to a systemic component, include pulmonary inflammation, airway remodeling and mucociliary dysfunction. These latter features contribute to development of chronic, progressive airflow limitation. The mucociliary dysfunction component of COPD is caused by mucus hypersecretion combined with decreased mucus transport, and are important pathophysiologic features that require

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Received: March 12, 2006
Revised: September 1, 2006
Accepted: November 7, 2006

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prompt treatment.[2] Mucus hypersecretion results from autonomic nerve dysfunction and various chemical mediators, resulting in airflow limitation.[3] In COPD, considerable controversy exists regarding the importance of mucus hypersecretion. Long-term mucus impaction in small airways causes ventilation/perfusion mismatch, pulmonary hyperinflation, increased work while breathing, and exercise intolerance. Thus, airway mucus clearance is essential for COPD patients and should be optimized with appropriate therapeutic intervention. Although airway clearance modalities have been widely utilized in cystic fibrosis[4–6] and bronchiectasis,[7] few studies have focused on COPD patients with mucus hypersecretion.

The forced expiratory technique (FET) is a form of chest physiotherapy that can be self-administered to enhance mucus clearance from the airways of cystic fibrosis patients.[6] During FET, huffing is combined with postural drainage, breathing exercises and, when necessary, coughing to encourage mucus clearance from peripheral airways to central airways and easy expectoration of sputum. The FET can be self-administered without assistance. Therefore, FET has been proposed as an effective method for home physiotherapy for patients with chronic inflammatory airway diseases such as cystic fibrosis and bronchiectasis.[8] However, FET can induce early closure of airways, thus leading to bronchoconstriction and impairment of cough function.[9] Moreover, flattening the diaphragm in COPD patients combined with lung hyperinflation frequently results in inefficient diaphragmatic breathing during FET. Therefore, maneuvers to prevent airway closure and lung hyperinflation during FET alone can increase the efficacy of FET in clearing mucus from the airways of COPD patients.

In 1984, Falk et al[10] developed the positive expiratory pressure (PEP) mask technique for the removal of airway secretions. The clinical and physiologic utility of PEP has been accepted in recent years.[11] Previous studies have demonstrated that the PEP mask is at least as effective as conventional postural drainage and percussion in mobilizing secretions in patients with cystic fibrosis.[12] McIlwaine et al[13] also demonstrated that PEP has a better long-term effect on pulmonary function than flutters. The pressure generated by applying PEP therapy distal to an obstruction through collateral pathways may enhance FET efficacy in promoting movement of secretions toward large airways[14] and reduced pulmonary hyperinflation and airway instability[15,16] in patients with COPD and mucus hypersecretion. Thus, we hypothesize that PEP as an adjunct to FET is more efficient than FET only.

This study evaluated the effects of modified PEP techniques combined with FET in COPD patients with mucus hypersecretion in terms of pulmonary function, exercise tolerance, and subjective expectoration difficulty scores after 4 weeks of treatment. This study also investigated the relationship between pulmonary function and oxygenation change during exercise after PEP intervention.

Subjects and Methods

Subjects

Thirty-seven ambulatory outpatients with COPD who met the diagnostic criteria of the American Thoracic Society (ATS)[17] were recruited from July 1999 to July 2000. All enrolled subjects met the following criteria: (1) under regular medication treatment and clinically stable, i.e. without acute asthmatic attacks or airway infections in the 2 months prior to the study; (2) producing at least 25 cc of sputum in 24 hours; (3) able and willing to self-administer treatment daily; and (4) cooperative and motivated, with good medication compliance and willing to attend regular follow-up at an outpatient clinic for 3 months. Subjects who met one of the following criteria were excluded: (1) have other major diseases, such as heart disease, orthopedic, and/or neurologic problems; (2) poor compliance with medications and/or home bronchial hygiene program; (3) requiring oxygen and/or continuous positive airway pressure therapy at home; and (4) on a regular chest physiotherapy program.

Study subjects were randomly divided into two groups: (1) PEP adjunct to FET (PEP+FET) group; (2) FET only (FET) group. All enrolled subjects were numbered by a computer-generated randomized method. Thirty-seven patients were initially enrolled in this study. Five patients were dropped out of the study: two had poor compliance (one in each group), and two in the PEP group and one in the FET group deteriorated during the study period. Therefore, 32 subjects ($n=16$ in each group) finished the 4-week intervention program. The protocol was approved by the Ethics Committee at Chung Gung Memorial Hospital and informed consent was obtained from each subject prior to participation.

Interventions

FET

This method consisted of forced expirations from mid-lung volume to low-lung volume followed by a short period of relaxation and breathing control.[18] Each cycle of FET comprised six forced expirations with a short period of relaxation after three expirations. The sequence of deep breathing and six forced expirations was repeated six times while in a sitting position.

PEP and FET

The PEP system (Thera PEP; DHD Healthcare Co., NY, USA) consists of a mouthpiece and a one-way valve to which expiratory resistance (orifice) is attached. An expiratory airway pressure indicator is inserted into the system to visually confirm pressure range of 10–20 cm H_2O.[19] Resistance was adjusted so that the patient was expiring against a pressure of 10–20 cm H_2O, reaching an inspiration-to-expiration ratio of 1:3 to 1:4, or longer. One minute of PEP breathing in the sitting position was followed by forced expirations and a short period of relaxation and controlled breathing. Each session had 10 cycles of PEP breathing. The number of forced expirations in the two regimens was thus identical. The pressure level of PEP was individualized and adjusted according to the patient's condition during the study period.

Subjects performed the treatment program at home twice daily, once in the early morning and once at night before sleep for 4 weeks. All patients were requested to perform the techniques properly under the supervision of physical therapists on the first 3 study days. Subjects were contacted by phone every 3 days to confirm their adherence to the program and their (PEP and FET) techniques were rechecked at an outpatient clinic weekly.

Measurements

Pulmonary function tests, 6-minute walk tests (6MWT), and cough difficulty scores (CDS) were assessed before and after the 4-week period. The technicians and physicians in this study were blind to the treatment regimen. Subjects maintained their regular medication regimen and dosage but refrained from using short-acting bronchodilators for 8 hours, long-acting bronchodilators for 24 hours, and smoking for 8 hours before all tests. All subjects were asked not to drink coffee or tea on the mornings of the test days.

Pulmonary function tests

Pulmonary function tests were performed according to ATS guidelines.[17] The pulmonary functions (PFs), including forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), forced expiratory flow from 25% to 75% ($FEF_{25-75\%}$), peak expiratory flow (PEF), residual volume (RV), total lung capacity (TLC), functional residual capacity (FRC), and diffusing capacity (DLCO) were measured by plethysmography (Sensor Medics, CA, USA). DLCO was examined by a single breath method with a single carbon monoxide sample obtained after the subject held their breath for 10 seconds. Three trials were performed, and the best trial was recorded. Volume measurement accuracy was set at less than ±3% deviation with a 3L calibration syringe; a leaking test was performed daily.[20] The gas analyzer linearity and timer were also tested and had less than 1% deviation.[21] Reproducibility of two acceptable tests was within 0.2 L in volume measurements and within 10% in DLCO measurements.

6MWT

To minimize the learning effect during the walking test, all subjects were asked to practice the 6MWT 1 week prior to the study. The 6MWT was performed in accordance with the ATS Statement.[22] All subjects completed two 6MWTs and the farthest of the two walking distances (WD) was utilized for analysis. The modified Borg scale was evaluated at rest and immediately after exercise, and expressed as RBorg and EBorg, respectively.[23] During walking tests, subjects were monitored with a continuous pulse oximeter (3301; BCI International Co., WI, USA). Oxygen saturation (O_2SAT) was recorded and printed every 6 seconds at rest (RO_2SAT) and during exercise (EO_2SAT), as determined by pulse oximetry. The intrarater reliability of the 6MWT and modified Borg scale were examined for 15 patients with chronic obstructive lung disease (FEV_1 48.2 ± 3.6% predicted) on 2 consecutive days. Intraclass correlation coefficients (ICC) of 0.99 (95% confidence interval [CI], 0.98–0.99; $p < 0.001$) in WD, 0.89 (95% CI, 0.71–0.96; $p < 0.001$) in RBorg, and 0.58 (95% CI, 0.12–0.84; $p < 0.01$) in EBorg were obtained.

Cough difficulty assessment

A subjective assessment of "the degree of cough difficulty score" was determined using a scale with the following five fixed points: 1 point, "very easy"; 2 points, "easy"; 3 points, "no change"; 4 points, "with difficulty"; and, 5 points, "very difficult." In this study, the ICC of intrarater reliability of CDS for 14 COPD patients was 0.95 (95% CI, 0.85–0.98; $p < 0.001$).

Data analysis

Data were analyzed using commercially available software (SYSTAT 10.0; SPSS Inc., Chicago, IL, USA). Mann-Whitney *U* tests were used to detect significant differences in basic characteristics and baseline data for each intervention (i.e. PFs, 6MWTs, and CDS). To examine the effects of the interventions on PFs, 6MWTs, and CDS, Wilcoxon matched pair tests were used to test for significant differences between baseline and postintervention data within groups, and the Mann-Whitney *U* tests were utilized for postintervention data between groups. The level of significance was set at 0.05.

Results

No significant differences existed between the two groups for age, gender, height, weight, and PFs. Mean age was 59.1 ± 11.6 years in the PEP + FET group and 64.6 ± 9.5 years in the FET group. Mean FEV_1 was 48.1 ± 15.5% and 52.9 ± 16.7% of predicted values in the PEP + FET group and FET group, respectively (Table 1).

Baseline parameters

No statistically significant differences existed between baseline data for PFs (FVC, FEV_1, $FEF_{25-75\%}$, PEF, RV, TLC, FRC, and DLCO) (Table 2), 6MWTs

Table 1. Characteristics of patients with chronic obstructive pulmonary disease in the PEP + FET and FET groups*

	PEP + FET (*n* = 16)	FET (*n* = 16)	*p*
Age (yr)	59.1 ± 11.6 (26–75)	64.6 ± 9.5 (40–79)	0.148
Male/female (*n*)	13/3	12/4	0.975
Height (m)	1.63 ± 7.4 (1.47–1.75)	1.59 ± 9.0 (1.41–1.73)	0.439
Weight (kg)	66.3 ± 10.5 (50–82)	62.8 ± 12.1 (44–84)	0.440
FVC (% predicted)	68.8 ± 15.5 (44–92)	70.1 ± 17.9 (43–98)	0.801
FEV_1 (% predicted)	48.1 ± 15.5 (22–74)	52.9 ± 16.7 (27–69)	0.392
FEV_1/FVC (%)	55.0 ± 11.3 (41–76)	58.6 ± 9.0 (44–77)	0.283

**Data are presented as mean ± standard deviation (range). PEP = positive expiratory pressure; FET = forced expiratory technique; FVC = forced vital capacity; FEV_1 = forced expiratory volume in 1 second; FEV_1/FVC = ratio of FEV_1 to FVC.*

Table 2. Changes to pulmonary functions in the PEP + FET and FET groups*

	PEP + FET		FET	
	Baseline data	Posttreatment	Baseline data	Posttreatment
FVC (L)	2.2 ± 0.8 (1.2–4.6)	2.4 ± 0.9† (1.2–5.1)	1.9 ± 0.6 (1.1–3.2)	2.1 ± 0.6‡ (1.2–3.3)
FEV_1 (L)	1.2 ± 0.5 (0.5–2.4)	1.4 ± 0.6† (0.6–3.0)	1.2 ± 0.4 (0.7–2.1)	1.2 ± 0.4 (0.7–2.0)
$FEF_{25-75\%}$ (L/sec)	0.7 ± 0.4 (0.2–1.4)	0.8 ± 0.4‡ (0.3–1.9)	0.7 ± 0.3 (0.3–1.2)	0.7 ± 0.3 (0.3–1.3)
PEF (L/sec)	3.4 ± 1.2 (1.4–5.5)	4.1 ± 1.5§ (2.1–7.8)	3.4 ± 1.6 (1.6–7.3)	3.8 ± 1.3 (1.7–6.4)
TLC (L)	6.6 ± 1.7 (4.5–10.9)	6.3 ± 1.0 (4.6–7.7)	6.0 ± 1.1 (3.8–7.8)	5.7 ± 1.2 (3.5–7.8)
RV (L)	4.3 ± 1.6 (2.6–9.0)	3.8 ± 1.0 (2.4–5.4)	3.8 ± 0.9 (2.1–5.3)	3.3 ± 0.9§ (1.8–4.7)
FRC (L)	4.5 ± 1.5 (2.6–8.8)	4.4 ± 1.0 (2.7–6.3)	4.1 ± 1.0 (2.1–5.7)	3.7 ± 1.0‡ (2.1–5.3)
DLCO (mL/min/mmHg)	18.0 ± 7.3 (6.3–35.5)	20.1 ± 7.2$^{\ddagger\|\|}$ (6.0–35.3)	16.4 ± 5.5 (6.7–27.3)	16.0 ± 4.0 (8.8–25.1)

*Data are presented as mean ± standard deviation (range); $^{\dagger}p < 0.001$ vs. baseline; $^{\ddagger}p < 0.05$ vs. baseline; $^{\S}p < 0.01$ vs. baseline; $^{\|\|}p < 0.05$ vs. FET group. PEP = positive expiratory pressure; FET = forced expiratory technique; FVC = forced vital capacity; FEV_1 = forced expiratory volume in 1 second; $FEF_{25-75\%}$ = forced expiratory flow in 25–75% forced expiratory volume; PEF = peak expiratory flow; TLC= total lung capacity; RV = residual volume; FRC = functional residual capacity; DLCO = diffusion capacity.

Table 3. Changes during the 6-minute walk test in the PEP + FET and FET groups*

	PEP + FET		FET	
	Baseline data	Posttreatment	Baseline data	Posttreatment
6MWD (m)	516.8 ± 94.1 (320–640)	570.6 ± 60.4†‡ (450–667)	498.8 ± 61.8 (332–609)	526.4 ± 57.7§ (406–638)
RBorg	2.3 ± 0.7 (1–4)	1.8 ± 0.4$^{\|\|}$ (1–2)	2.2 ± 1.0 (1–4)	1.8 ± 0.7$^{\|\|}$ (0.5–3)
EBorg	5.1 ± 1.1 (4–7)	4.2 ± 1.0§ (3–7)	4.8 ± 1.2 (3–7)	4.1 ± 1.3§ (3–7)
RO_2SAT (%)	95.7 ± 1.5 (92–97)	96.3 ± 1.1 (93–97)	95.7 ± 1.2 (93–98)	96.1 ± 1.3 (93–98)
EO_2SAT (%)	88.9 ± 7.7 (66–97)	90.6 ± 7.2 (70–98)	91.1 ± 5.4 (80–97)	91.4 ± 5.0 (82–97)

*Data are presented as mean ± standard deviation (range); $^{\dagger}p < 0.001$ vs. baseline; $^{\ddagger}p < 0.05$ vs. FET; $^{\S}p < 0.01$ vs. baseline; $^{\|\|}p < 0.05$ vs. baseline. PEP = positive expiratory pressure; FET = forced expiratory technique; 6MWD = 6-minute walking distance; RBorg = Borg score at rest; EBorg = Borg score at end of exercise; RO_2SAT = oxygen saturation at rest; EO_2SAT = oxygen saturation at end of exercise.

(6MWD, RBorg, EBorg, RO_2SAT, EO_2SAT) (Table 3) and CDS.

Effects of PEP on PFs

FVC, FEV_1, $FEF_{25-75\%}$, and PEF significantly increased in the PEP + FET group from 2.2 ± 0.8 to 2.4 ± 0.9 L ($p < 0.001$), 1.2 ± 0.5 to 1.4 ± 0.6 L/second ($p < 0.001$), 0.7 ± 0.4 to 0.8 ± 0.4 L/second ($p < 0.05$), and 3.4 ± 1.2 to 4.1 ± 1.5 L/second, respectively (Table 2). FVC in the FET group also significantly increased from 1.9 ± 0.6 to 2.1 ± 0.6 L ($p < 0.05$), and the RV and FRC decreased from 3.8 ± 0.9 to 3.3 ± 0.9 L ($p < 0.01$), and 4.1 ± 1.0 to 3.7 ± 1.0 ($p < 0.05$), respectively. However, the difference between groups for PF parameters was not significantly different.

DLCO improved significantly in the PEP + FET group from 18.0 ± 7.3 to 20.1 ± 7.2 mL/min/mmHg ($p < 0.05$). Additionally, PEP + FET was more effective than FET alone in reducing DLCO ($p < 0.05$).

Effects of PEP on 6MWT

The 6MWD increased from 516.8 ± 94.1 to 570.6 ± 60.4 m in the PEP group ($p < 0.001$), and from 498.8 ± 61.8 to 526.4 ± 57.7 m in the FET group ($p < 0.01$); furthermore, PEP + FET was more effective than FET alone in increasing 6MWD ($p < 0.05$). Table 3 presents the Borg scores during the 6MWTs before and after treatments. There was a significant decrease in subjective Borg breathlessness sensation at rest ($p < 0.05$) and at the end of the 6MWT ($p < 0.01$) in both groups. However, the differences in Borg scores between the two groups did not reach statistical significance. No significant difference existed for O_2SAT during 6MWT within and between groups.

Effects of PEP on CDS

Patients in both groups had reduced CDS (Figure). Additionally, statistical analyses detected a significant difference in postintervention CDS between groups (3.3 ± 0.7 and 2.3 ± 0.6 in PEP + FET and FET groups, individually, $p < 0.01$).

Discussion

Mucus hypersecretion with viscid mucus plugs in the airway of COPD patients contributes to respiratory insufficiency. Good airway hygiene is essential to COPD management. This study demonstrated that 4-week regimens of regular physiotherapy, either PEP + FET or FET alone, improves FVC, WD, subjective breathlessness sensation, and CDS in COPD patients with mucus hypersecretion. Application of external PEP significantly improved the clinical efficacy of FET for long-term treatment of COPD by improving PFs, including FEV_1, $FEF_{25-75\%}$, PEF, DLCO, and sputum expectoration difficulty.

Ventilatory limitations in COPD patients are caused by airway inflammation that generates bronchospasms, airway hyperresponsiveness, and mucus hypersecretion. Mucus in the airways aggravates airway hyperresponsiveness in COPD patients[1] and lung atelectasis. Medical treatment, including anti-inflammatory agents, attenuates airway inflammation but does not eliminate airway hyperresponsivenesss. The instability of airways leads to early closure of the small airways and air becoming trapped in the lungs. In patients with mucus hypersecretion, early closure of the small airways can further hamper clearing of airway mucus. Therefore, facilitating mucus clearance is an essential part of maintenance treatment in COPD patients with mucus hypersecretion. Furthermore mucus clearance increases effective ventilation and reduces airway hyperresponsiveness. However, maintenance of airway stability is promising for effective mucociliary clearance in small airway diseases.[15] This study demonstrated that FET improves ventilation volume, air trapping, exercise tolerance and subjective dyspnea sensation. However, as advanced stages of COPD are characterized by airway instability, the effectiveness of FET may be hampered by airway collapse.[4] Applying PEP therapy via the mouth to COPD patients can prevent airway closure during forced expiration in FET. Additionally, PEP allows increased amounts of air to enter through collateral channels, facilitating reinflation of collapsed alveoli.[14,24,25] Moreover, Laube et al[26] concluded that aerosol administration with nebulizer and PEP device also results in a proportional redistribution of aerosol to the peripheral airway, compared with nebulizeration without the PEP device,

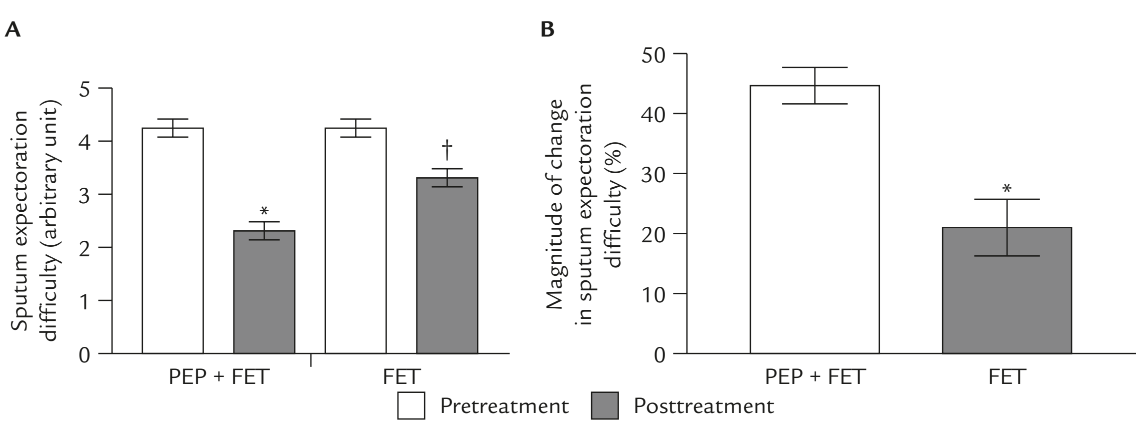

Figure. (A) Improvement in sputum expectoration difficulty (cough difficulty) in the PEP + FET and FET groups. (B) Magnitude of change in cough difficulty in the PEP + FET and FET groups. Results are presented as mean ± standard error of the mean. PEP = positive expiratory pressure; FET = forced expiratory technique. *$p < 0.001$; †$p < 0.01$.

suggesting that PEP + FET can enhance the control of COPD by improving the efficiency of aerosolized medications. Therefore, PEP + FET may recruit additional collapsed alveoli thereby augmenting the match ratio of ventilation-perfusion and leading to increased DLCO,[27] as demonstrated in this study.

Previous studies have described the effects of PEP mask physiotherapy on lung function in cystic fibrosis, but not in COPD.[27–29] Christensen et al[28] showed that 9-month PEP physiotherapy enhances FEV_1 in cystic fibrosis. Oberwaldner et al[15] proposed that PEP therapy for 6 months improved FVC, FEV_1, $FEF_{25-75\%}$, FEF, and RV/TLC in patients with cystic fibrosis. McIlwaine et al[12] also provided evidence that FVC and FEV_1 improved after 1-year PEP mask treatment in patients with cystic fibrosis compared with that obtained using conventional physiotherapy. Steen et al[29] and Kaminska et al[30] suggested that 4-week PEP mask treatment combined with FET is an effective treatment that increased independence in daily activities. As the same combination therapy was used in this study, it is reasonable to select 4 weeks as the treatment period. This study further confirmed the effect of a 4-week regimen of combination therapy with modified PEP and FET on increasing DLCO and exercise distance in the two study groups. A longer follow-up period than that in this study is required.

High-pressure PEP masks may mechanically irritate intrathoracic airways, thereby resulting in bronchospasms in patients with airway hyperreactivity.[4,31] Furthermore, the discomfort from wearing a fitted mask results in poor treatment compliance. The PEP system utilized in this study generates an expiratory airway pressure of 10–20 cmH_2O[19] in the airways via a mouthpiece and one-way valve. Therefore, PEP reduces discomfort and increases expectoration. This PEP system was well accepted and resulted in complete compliance by patients.

The study sample size was small, with only 16 subjects in each group for 32 data sets. Furthermore, nonsignificant differences for most PFs and Borg's scale, and O_2SAT between groups during exercise may be associated with type II errors due to the small sample size. Therefore, this study should be regarded as a pilot study.

The study design was another limitation. The 4-week intervention in this study is shorter than the 1-year studies by McIlwaine et al[12,13] and Christensen et al.[28] Despite some positive observations, results from this study must be replicated for a longer period. The method had another limitation. Measurements of RV, TLC and FRC in the body plethysmography by painting maneuvers were technically difficult for most of the COPD patients with mucus hypersecretion.

This study demonstrated that PEP as an adjunct to FET is more effective than FET only in improving DLCO, 6MWD, and reducing sputum expectoration difficulty in COPD patients with mucus hypersecretion. Therefore, PEP + FET therapy is a noninvasive, inexpensive, and non-time-consuming domiciliary intervention.

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