J Exp Clin Med 2012;4(3):149–153

Contents lists available at SciVerse ScienceDirect

Journal of Experimental and Clinical Medicine

journal homepage: http://www.jecm-online.com

ORIGINAL ARTICLE

Randomized Crossover Study of Lung Expansion Therapy Using Negative Pressure and Positive Pressure in Bronchiectasis

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ARTICLE INFO

Article history:
Received: Dec 9, 2011
Revised: Feb 20, 2012
Accepted: Feb 20, 2012

KEY WORDS:
bronchiectasis;
intermittent positive pressure breathing;
lung expansion;
negative pressure ventilation;
postural drainage

Background: For patients with bronchiectasis, the mechanical mobilization of secretion constitutes a key therapeutic approach. However, the effectiveness of lung expansion therapy to mobilize secretion in bronchiectasis patients has not been investigated extensively. This study compares patients' exercise tolerance and physical assessment outcomes after secretion clearance using intermittent positive pressure breathing (IPPB) or negative pressure ventilation (NPV) as adjuncts to postural drainage.

Methods: This prospective, randomized crossover study examined the data for 18 stable outpatients with bronchiectasis. The outcomes were compared for four treatment sessions of either IPPB or NPV, used as adjuncts to postural drainage. The short-term outcomes involved pulmonary functions and a six-minute walk test (6MWT). We also assessed pulmonary functions and physical clinical signs as immediate treatment effects.

Results: Patients' forced vital capacity (FVC), forced expiratory volume in the first second (FEV_1), and cough efficacy did not change significantly after individual postural drainage sessions using either IPPB or NPV. However, a reduction in the use of accessory muscles was noted after NPV; patients with low baseline FVC might benefit particularly from this reduction ($r = 0.699$, $p < 0.05$). No significant differences between two techniques were found for the patient's walking distance. However, the pulse rate after 6MWT was significantly ($p < 0.05$) lower in the NPV group.

Conclusion: NPV may provide as an effective adjunct to postural drainage as IPPB in weekly lung expansion therapy for outpatients with bronchiectasis. The benefits of NPV might include a reduction in the use of accessory muscles during lung expansion.

1. Introduction

Bronchiectasis is an abnormal dilatation of the bronchi and bronchioles caused by repeated cycles of airway infection and inflammation.[1] Patients with bronchiectasis display a chronic cough and sputum production and are prone to bacterial infections, which results in a loss of lung function and an impaired mucociliary clearance mechanism.[2] The recurrence or persistence of airway infection and inflammation results in airway damage that leads to further infection, in a spiraling cycle of infection and inflammation and, ultimately, the destruction of airway and lung parenchyma.[3] In addition to medication, the removal of secretion is a major therapy and is strongly recommended.[4]

The anatomic distortion of conducting airways, which is responsible for the association between atelectasis of the lung and bronchiectasis, is recognizable from computed tomography (CT) scanning.[5,6] The resorption atelectasis occurs when mucus plugs are present in the airways and block ventilation of the affected region. Gas distal to the obstruction is absorbed by the passing blood in the pulmonary capillaries, which causes partial collapse of nonventilated alveoli. To mobilize secretion and facilitate expectoration, therapy should focus on expanding the lungs to reopen them before postural drainage is applied, to promote an effective cough.

Intermittent positive pressure breathing (IPPB) may be useful for patients with clinically diagnosed atelectasis that does not respond to incentive spirometer or chest physical therapy.[7] In contrast, negative pressure ventilation (NPV) facilitates increased diaphragmatic breathing, which might aid lower lobe expansion. A recent study has shown that IPPB was unable to achieve additional improvement in postoperative pulmonary function when it was

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1878-3317/$ – see front matter
doi:10.1016/j.jecm.2012.04.004

added to standard physical therapy after a major lung resection.[8] A study on rabbits demonstrated that NPV resulted in superior oxygenation that was unrelated to lung perfusion, which may have been due to an improved inflation of lung volume during both inspiration and expiration.[9] Previous research also discovered that in normal awake human subjects, NPV allowed a significant increase in minute ventilation.[10] Negative pressure differs from nasal intermittent positive pressure ventilation, in which the glottic width interferes with the delivered mechanical ventilation; thus NPV may offer potentially more effective ventilation.

Although previous studies of patients with bronchiectasis have demonstrated the effectiveness of techniques to mobilize secretion and of relevant exercise training,[11,12] the utility of NPV has not been thoroughly investigated. We hypothesized that NPV might be more beneficial than IPPB with regard to pulmonary functions, six-minute walk distances, and efficacy of secretion clearance in patients with bronchiectasis. The primary end point of this clinical trial was the physical assessment of clinical signs directly after postural drainage, to gauge the immediate effect of therapy. The secondary end point was an assessment of pulmonary functions and six-minute walk test (6MWT), representing the short-term effect.

2. Methods

2.1. Design

This study used a prospective, randomized cross-over control design. The principles outlined in the Helsinki Declaration were followed. Informed consent was obtained from all participants.

2.2. Participants

Patients with stable bronchiectasis were recruited from the outpatient clinic at Shuang Ho Hospital of Taipei Medical University from December 2010 to October 2011. The enrollment criteria were patients with: (1) bronchiectasis, diagnosed from high resolution CT scans and assessment of clinical symptoms by a chest physician; (2) productive cough with at least 30 ml sputum per day; (3) medical stability over the preceding two months; (4) high motivation to receive therapy; (5) no previous lung expansion therapy; and (6) the ability to perform forced expiration techniques. The exclusion criteria were: (1) inability to perform pulmonary function tests or a 6MWT; (2) current pneumothorax or rib fracture; (3) hemoptysis; and (4) obstructive sleep-apnea. Patients who experienced an exacerbation during the study were withdrawn. Baseline medication, such as long-acting β-2 agonist or antibiotics, was not altered. Our final study group comprised 18 patients with bronchiectasis.

Study participants were randomly divided into one of two groups, receiving either NPV or IPPB. Each treatment was administered at the outpatient clinic for four weeks in a randomized crossover design, as previous research had found that NPV administered over four weeks could improve patients' respiratory function in hypercapnic chronic obstructive pulmonary disease (COPD).[13] All enrolled participants were numbered using a computer-generated randomized method.

2.3. Interventions

For NPV treatment, the patient rested on the back on a thin foam-rubber mattress inside a Porta-lung, with the head protruding through a porthole at one end. A neck collar surrounding the porthole was tightened, and negative pressure generated by an NEV-100 ventilator (Lifecare Company, Lafayette, CO, USA) at the opposite end. The ventilator settings were as follows: assist-control, with negative pressure between 10 and 15 cmH_2O, and a respiratory rate of 10 breaths/minute. Portholes allowed access to the patient when secretion was coughed out. The treatment duration was 1 hour.

For IPPB, the patient sat comfortably on a chair, and positive pressure was administered through a mouthpiece with a preset Bird Mark 7 ventilator (Bird Corporation, Palm Springs, CA, USA). The initial setting of positive pressure was between 15 and 20 cmH_2O, and was adjusted according to the patient's condition during the therapy period. The total IPPB treatment duration was 1 hour, but the patient could rest intermittently.

All patients were requested to perform postural drainage and active cycle breathing techniques (ACBT), which were supervised by respiratory therapists immediately after lung expansion therapy. For both the NPV and IPPB groups, therapy lasted four weeks with the outpatient sessions being conducted once per week.

2.4. Measurements of pulmonary functions and 6MWT

Patients were asked not to use oxygen for 4 hours or a bronchodilator for 8 hours before the tests. The forced vital capacity (FVC) and forced expiratory volume in the first second (FEV_1) were measured using a portable spirometer (Spiro Analyzer ST 250; Fukuda, Sangyo, Japan) according to the recommendations of the American Thoracic Society.[14]

Patients performed the 6MWT in a 24 m corridor.[15] Each participant was encouraged every minute by vocalizing two statements: "You are doing well" and "Keep up the good work." They were allowed to stop and rest during the test but were instructed to resume walking as soon as they felt able to continue. Supplemental oxygen was provided to maintain SpO_2 at $>$90% after the 6MWT if needed.

A pulse oximeter (3301; BCI International, Waukesha, WI, USA) was used to obtain real data on the patient's pulse rate (PR) and oxygen saturation (SpO_2) measurements every 6 seconds, and the data were continuously printed. The modified Borg scale was used to evaluate the patient at rest and again after the 6MWT (expressed as RBorg and ExBorg).[16] The verbal descriptors in the original 10-point Borg scale had been carefully translated into Chinese.[16] Patients were instructed to quantify the intensity of their breathlessness at rest and immediately after walking. The RPR and $RSpO_2$ represent PR and SpO_2 after 5 min of complete rest, while ExPR and $ExSpO_2$ represent PR and SpO_2 immediately at the end of the 6MWT. Physiological changes after the 6MWT in PR (ΔPR), SpO_2 (ΔSpO_2), and Borg score (ΔBorg) were calculated by subtracting the R values from the Ex values. Patients completed the 6MWT and subsequent tests at baseline and again after each therapy session.

2.5. Cough efficacy and assessment of accessory muscles usage

A subjective assessment of "the degree of cough difficulty" was determined using a scale with the following five fixed points: 1, "very easy"; 2, "easy"; 3, "no change"; 4, "with difficulty"; and, 5, "very difficult". The main muscles observed were the scalene and sternocleidomastoid muscles, and the same therapist assessed all patients. The use of accessory muscles was noted by muscle contraction while the patient remained in a seated posture to rest and breathe. The grades used in this study were allocated using modified manual muscle tests.[17] The scale was as follows: 1, "no accessory muscle contraction" ; 2, "palpable but not visible accessory muscle contraction"; 3, "visible accessory muscle contraction" (muscles display a slightly forced contraction); and 4, "dominant accessory muscle contraction" (a tonic contraction with prominent neck muscles). Measurements were obtained before lung

expansion and again after postural drainage at the fourth session for several variables, namely pulmonary functions, pulse rate, oxygen saturation, Borg score, cough difficulty, and accessory muscle usage.

2.6. Data analysis

Data were analyzed using Statistical Analytic System 9.2 (SAS, Cary, NC, USA). Paired sample *t* tests were used to examine the effects of the interventions on pulmonary functions, 6MWTs, and physical assessment scores. We tested for significant differences between baseline and postintervention data within each group, and also compared the results between the two therapy groups. Spearman correlation coefficients were calculated to examine the association between accessory muscle usage and pulmonary functions. Statistical significance was set at a p-value of <0.05.

3. Results

Eight out of 26 patients initially recruited to the study were withdrawn because of an infective exacerbation. Our final study group thus consisted of 18 patients, of whom 10 were male. Fourteen patients completed the crossover trial. Four patients completed only one therapy (one patient used NPV and three IPPB). Baseline characteristics for the 18 patients are shown in Table 1.

Table 2 compares the results of physical assessment before and after postural drainage as an adjunct to IPPB or NPV. Patients in the IPPB group had a significantly lower pulse rate ($p = 0.034$) and appeared to cough more easily ($p = 0.02$) after postural drainage, compared with baseline. Patients in the NPV group also had a significantly lower pulse rate ($p = 0.006$) after postural drainage, as well as less apparent breathlessness ($p = 0.019$) and a decreased use of accessory muscles ($p = 0.006$). No significant difference was found for accessory muscle usage between the two techniques.

In the 6MWT, no significant differences were found between the IPPB and NPV groups apart from ExPR ($p = 0.049$), which was lower in the NPV group (Table 3). For NPV, a significant improvement in walking distance was noted ($p = 0.004$), with the mean walking distance increasing from 511.6 m at baseline to 535.6 m after the fourth treatment session. The change in pulse rate during walking was greater after four weeks of IPPB compared with baseline ($p = 0.010$), and the change in Borg score during walking was larger after four weeks of NPV compared with baseline ($p = 0.023$).

Table 4 shows the correlation between change in accessory muscle usage and lung volume. The baseline FVC and FEV_1 before NPV and baseline FEV_1 before IPPB were all moderately correlated with change in accessory muscle usage after the interventions ($r = 0.699$, $p = 0.003$; $r = 0.523$, $p = 0.045$; and $r = 0.513$, $p = 0.035$ respectively). Furthermore, one-way analysis of variance found a significant correlation ($p = 0.0008$) between the changes in FVC and accessory muscle usage after NPV.

Table 1 Baseline characteristics of patients with bronchiectasis

Parameters	Mean (SE) ($n = 18$)
Age (y)	58.56 (2.42)
Gender	10M:8F
Weight (kg)	53.78 (2.01)
Height (cm)	159.78 (2.02)
BMI (kg/m^2)	21.05 (0.71)
Pulmonary function tests	
FVC (L)	1.78 (0.14)
FVC (% of predicted)	51.54 (3.45)
FEV_1 (L)	0.98 (0.10)
FEV_1 (% of predicted)	31.54 (3.02)
FEV_1/FVC (%)	54.48 (2.87)
FEV_1/FVC (% predicted)	67.04 (3.70)

Test for normality indicated that all variables appeared to be normally distributed.
BMI = body-mass index (weight/height^2); FEV_1 = forced expiratory volume in the first second; FVC = forced vital capacity.

4. Discussion

This study showed that NPV, used as an adjunct to postural drainage, was as effective as IPPB in aiding sputum clearance in patients with bronchiectasis. Both types of lung expansion maneuvers were associated with significant improvement in patient outcomes such as pulse rate, cough efficacy, Borg score, and use of accessory muscles. As the peripheral lung clearance should be assessed by regional lung image,[18] the patients could only subjectively identify central lung clearance ability, thus they expressed cough more easily after IPPB. Previous studies have reported that NPV provided effective relief of dyspnea and a significant change in breathing patterns, characterized by an increase in tidal volume and a decrease in respiratory frequency.[19] Our findings were congruent with those results. Furthermore, we found that patients with low baseline FVC benefitted more from NPV than from IPPB with regard to reduced use of accessory muscles, even after a single trial. Previous studies of NPV using dynamic CT suggested that the lung distension achieved with negative pressure is characterized by a greater proportion of normally aerated lung (with less atelectasis) during inspiration and at end-expiration, resulting in superior oxygenation.[9] The earlier finding on higher levels of tidal volume associated with NPV could explain the reduction in the use of accessory muscles and the increase in FVC.[10,20]

The excessive airway secretion in patients with bronchiectasis is one indication for therapy with NPV.[21,22] Documented guidelines for treating noncystic fibrosis bronchiectasis include the following point: “Where postural drainage is essential for clearing secretion in a breathless patient, consider offsetting the increased load using noninvasive ventilatory support, such as noninvasive ventilation or intermittent positive pressure breathing.”[4] These guidelines are relevant to clinical practice. Our study found improvement in patients’ walking distances after four weeks of therapy with NPV, although no significant difference was found between the NPV and IPBB groups. We believe that the small sample size may have affected the power of the statistics. For NPV patients, ΔBorg increased significantly during walking and the distance walked was greater compared with baseline. We thought that multiple factors might contribute to a dyspnea sensation during exercise for moderately to severely impaired patients. Our study emphasized forced expiratory techniques and postural drainage for effective secretion clearance, which may explain why earlier studies found no improvement in exercise tolerance in patients with severe COPD after NPV.[23] A significantly lower pulse rate increase during the 6MWT was observed for NPV compared with IPPB ($p = 0.049$). Moreover, our results demonstrated that patients with lower FVC benefitted particularly from NPV; hence, the benefits of lung expansion by NPV might explain the lower change in pulse rate during exercise. Previous studies have demonstrated that NPV may be effective in improving the functional reserve of inspiratory muscles in selected hypercapnic COPD patients who exhibit signs of inspiratory muscle dysfunction.[24] We also suspected that additional factors of muscle relaxation or opening of the small airways may contribute to the beneficial effect of NPV.

Traditionally, IPPB has provided convenient therapy for a spontaneously breathing patient, to aid the clearance of secretion. However, we found that NPV but not IPPB improved patients’ exercise tolerance and reduced their use of accessory muscles. Previous research found that neither NPV nor IPPB was associated

Table 2 Comparisons of physical assessments at the beginning and end of postural drainage as an adjunct to IPPB or NPV

	IPPB		IPPB	NPV		NPV	IPPV-NPV
	baseline	posttreatment	within group	beseline	posttreatment	within group	between groups
			p			*p*	*p*
FVC (L)	1.86 (0.16)	1.83 (0.14)	0.511	1.67 (0.19)	1.70 (0.16)	0.651	0.960
FEV_1 (L)	1.02 (0.10)	0.98 (0.09)	0.085	0.93 (0.12)	0.96 (0.12)	0.098	0.126
SpO_2 (%)	95.35 (0.55)	95.00 (0.54)	0.188	94.67 (0.68)	94.20 (0.73)	0.187	0.836
PR (beat/min)	88.18 (3.50)	83.77 (3.07)	0.034*	89.47 (3.75)	84.40 (3.76)	0.006*	0.887
Borg	1.94 (0.20)	1.75 (0.21)	0.083	1.93 (0.15)	1.60 (0.13)	0.019*	0.336
Cough efficacy	3.00 (0.12)	2.71 (0.11)	0.020*	2.40 (0.13)	2.47 (0.17)	0.670	0.137
Accessory muscles usage	2.53 (0.13)	2.47 (0.13)	0.668	2.53 (0.13)	2.13 (0.09)	0.028*	0.055

Data are expressed as mean (SE); *$p < 0.05$; Borg = dyspnea sensation.
FEV_1 = forced expiratory volume in the first second; FVC = forced vital capacity; PR = pulse rate; SpO_2 = oxygen saturation.

Table 3 Comparisons of changes in respiratory functions during six-minute walk test after four weeks of each type of therapy

	IPPB		IPPB	NPV		NPV	IPPV-NPV
	baseline	posttreatment	within group	baseline	posttreatment	within group	between groups
			p			*p*	*p*
ΔSpO_2 (%)	−8.06 (2.17)	−8.29 (1.75)	0.851	−8.33 (1.91)	−8.00 (1.98)	0.691	0.867
ΔPR (beats/min)	39.29 (4.27)	52.71 (5.76)	0.010*	42.07 (5.62)	46.00 (4.67)	0.189	0.084
ΔBorg	2.97 (0.38)	2.77 (0.29)	0.662	2.33 (0.37)	3.53 (0.44)	0.023*	0.142
$ExSpO_2$ (%)	87.00 (2.70)	86.65 (2.29)	0.784	86.20 (2.56)	85.93 (2.67)	0.772	0.877
ExPR (beats/min)	129.47 (2.82)	139.18 (4.19)	0.016*	133.20 (4.31)	133.33 (3.23)	0.958	0.049*
ExBorg	4.94 (0.40)	4.53 (0.32)	0.386	4.87 (0.38)	5.27 (0.41)	0.305	0.286
WD (m)	540.22 (19.57)	545.02 (18.42)	0.502	511.64 (27.84)	535.59 (29.74)	0.004*	0.078

Data are expressed as mean (SE). Change after exercise is expressed as Δ (parameter measured at end of 6MWT minus measurement at rest); *$p < 0.05$.
Borg score = dyspnea sensation; ExBorg = Borg score at the end of 6MWT; ExPR = heart rate measured at the end of 6MWT; $ExSpO_2$, oxygen saturation measured at the end of 6MWT;PR = pulse rate; SpO_2 = oxygen saturation; WD = walking distance.

Table 4 Correlations between change in accessory muscle usage (after postural drainage) and baseline lung volume

baseline lung volume	Δ accessory muscle usage	
	IPPB ($n = 17$)	NPV ($n = 15$)
FVC (L)	0.365 (0.150)	0.699 (0.003*)
FEV_1 (L)	0.513 (0.035*)	0.523 (0.045*)

Data are expressed as r coefficient (*p*-value); Δaccessory muscle usage = measurement at end of therapy minus baseline; *$p < 0.05$.
FEV_1 = forced expiratory volume in the first second; FVC = forced vital capacity; IPPB = intermittent positive pressure breathing; NPV = negative pressure ventilation.

with any immediate additional improvement in lung volume after postural drainage.[23,25] Our findings confirmed those of Ludwig IPPB did not result in additional improvement in postoperative pulmonary function.[8]

Our results indicate that NPV exerts only a marginal effect on airway clearance in bronchiectasis patients. However, the findings may have been influenced by the short duration of the study period or by the use of a small study sample. Our study was also subject to other limitations. First, we did not have access to data on the causes of acute exacerbation. Second, the assessment of accessory muscle use might have been somewhat unreliable due to its subjective quality and the rating by a single human assessor. Third, patients' individual use of potentially relevant medications was not recorded. Fourth, difficulty in coughing was rated by a subjective scale rather than a regional lung image, possibly resulting in lower validity for the assessment of secretion clearance.

5. Conclusion

The techniques of NPV or IPPB, when used as an adjunct to postural drainage, demonstrate equal effectiveness for lung expansion as measured by lung volume and six-minute walk distances. However, we demonstrated that pulse rate after a six-minute walk was significantly lower after NPV than IPPB. This finding may indicate an advantage of NPV due to a reduction in the use of accessory muscle, which was particularly beneficial for patients with low FVC.

Acknowledgments

This study was funded by the Research Review Committee of the Shuang Ho Hospital. We wish to thank the respiratory nurse specialist Han-Fang Cheng for her tender care of patients.

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