Respiratory Medicine (2006) **100**, 972–979

ELSEVIER

respiratoryMEDICINE

Noninvasive proportional assist ventilation and pressure support ventilation during arm elevation in patients with chronic respiratory failure. A preliminary, physiologic study

Roberta Poggi, Lorenzo Appendini, Guido Polese, Roberto Colombo, Claudio F. Donner, Andrea Rossi*

Respiratory Division, Ospedali Riuniti, L.go Barozzi, 1, 24128 Bergamo, Italy

Received 20 October 2004; accepted 7 October 2005

KEYWORDS
Noninvasive positive pressure ventilation;
COPD;
Rehabilitation;
Proportional assist ventilation;
Chronic respiratory failure

Summary
Background: It has been shown that upper limbs activity increases the respiratory workload in patients with chronic respiratory failure (CRF). The object of the present study was to investigate whether, in these patients: (i) noninvasive positive pressure ventilation (NPPV) could sustain the inspiratory muscles to meet the greater ventilatory demand during upper limbs activity with the arm elevation test (AE); (ii) proportional assist ventilation (PAV) might be superior to pressure support ventilation (PSV) during AE, because of its potential more adaptable response to sudden changes in the ventilatory pattern.
Methods: The study was performed in the pulmonary function laboratory of the Pulmonary Division in Verona General Hospital, Verona, Italy. We studied 8 male patients with CRF due to chronic obstructive pulmonary disease (COPD). Each patient received 2 treatment in random order with a crossover design: spontaneous breathing (SB), SB with AE, either PSV or PAV without and with AE, SB without and with AE, either PSV or PAV without and with AE. We measured: lung function tests, lung mechanics, ventilatory pattern and diaphragmatic effort (pressure time product, PTP_{di}).
Results: (i) AE increases minute ventilation (+14%) and PTP_{di} (+64%); (ii) ventilatory support, both with PSV and PAV unloads the diaphragm both at rest (PTP_{di} −77% and −54%, respectively) and during arm elevation (PTP_{di} −54% and −44%, respectively).
Conclusions: PAV and PSV unloads the diaphragm in patients with CRF due to COPD both during SB and AE; PAV can be more efficient than PSV in assisting the diaphragm during AE in producing a greater level of minute ventilation for a similar rise in PTP_{di}

*Corresponding author. Tel.: +390 35 26 97 14.
E-mail address: arossi@ospedaliriuniti.bergamo.it (A. Rossi).

doi:10.1016/j.rmed.2005.10.007

compared to PSV. Noninvasive ventilatory support should be considered in rehabilitation programs for training of upper limbs activity.

Introduction

It has been reported that pulmonary rehabilitation is an effective intervention in the management of patients with chronic obstructive pulmonary disease (COPD).[1–3] However, poor exercise tolerance due to the mechanical abnormalities of the respiratory system in those patients might cause significant limitation to rehabilitation programs.[4–6] Artificial ventilatory assistance could improve exercise tolerance and hence help severe COPD patients to achieve a higher level of training.[7–10] This approach has been applied during lower limbs exercise only, whereas also upper limbs exercise can be important for the daily activities and the quality of life of such patients.[11]

Some years ago, a series of papers by Celli and colleagues[12–15] showed that, in patients with severe COPD, simple arm elevation (AE) for a few minutes determined a sharp and remarkable increase in the patient's inspiratory effort to meet the substantial rise in the metabolic load and ventilatory demand. More recently, Velloso and colleagues[11] showed that many daily activities involving arm exercise determined a substantial rise in ventilatory demand. We wondered whether noninvasive positive pressure ventilation (NPPV) could be helpful during AE as it was shown to be during conventional cycle exercise. If so, NPPV could help in more complete rehabilitation programs, including upper limb exercise.

In a few recent reports, proportional assist ventilation (PAV) was applied[16–19] while either pressure support ventilation (PSV)[7,9,10] or continuous positive airway pressure (CPAP)[8] was the mode of ventilatory assistance in previous studies. Theoretically, PAV should better adapt to a sharp rise in ventilatory demand than PSV.[20] In fact, PAV is a patient-guided ventilatory mode in which the level of assistance is proportional to the patient's ventilatory drive and timing. To our knowledge, PAV and PSV were compared in stable COPD patients,[21,22] and during lower limb exercise,[16,17] but not yet during arm exercise.

Therefore, this study was designed to answer to 2 questions. First we aimed to investigate whether ventilatory assistance could unload the inspiratory muscles and meet the greater ventilatory demand during upper limb exercise in the form of the AE test. Second we compared PAV and PSV to investigate whether PAV was superior to PSV as it might be hypothesized on the basis of theory.

Methods

This protocol was approved by the Institutional Ethics Committee of the Azienda Ospedaliera di Verona, where the experimental procedure was performed and informed consent was given by the patients.

Patients

We studied 8 male patients (64.9 $\pm$ 11.4 years) with chronic respiratory failure (CRF) due to COPD. In 2 of the 8 patients also kyphoscoliosis was present. Diagnosis of COPD was made initially according to the European Respiratory Society Guidelines.[23] The diagnosis of CRF was based on the clinical records showing chronic hypoxia and chronic CO_2 retention, i.e. values of $PaCO_2$ >45 mmHg, consistently in the months, if not years, preceding the study. Values of arterial blood gases at the time of inclusion in the study are shown in Table 1. In all patients with one exception, arterial blood was sampled after a few minutes of breathing room air. In one patient (no. 7) arterial blood was sampled while breathing oxygen (2 L/min)-enriched air, because the patient did not tolerate oxygen withdrawn. Spirometric values from clinical records are also reported in Table 1. In addition to the evidence of CRF and COPD, inclusion criteria were the followings: (i) stable clinical condition, i.e. stability in blood gas values and pH (>7.35), and lack of exacerbations in the preceding 4 weeks; (ii) absence of exclusion criteria. The latter were: (i) presence of other chronic organ failure (e.g. renal, hepatic or cardiac failure documented by certified clinical history); (ii) any kind of neoplastic disorder; (iii) inability to cooperate; (iv) lack of informed consent.

All patients were on long-term oxygen therapy. Seven patients were also on home NPPV, in the PSV mode with bi-level ventilator for 5–6 h in the day or night, depending on the patient's and caring physician's choice. All the patients received regular treatment with inhaled bronchodilators, inhaled

Table 1 Patients' characteristics, arterial blood gases and spirometry.

Patient	Diagnosis	Age (yr)	pH	PaO_2 (mmHg)	$PaCO_2$ (mmHg)	VC (L)	FEV_1 (L)	FEV_1/VC
1	COPD	79	7.39	61	53	2.26	0.72	0.32
2	COPD*	62	7.35	41	67	0.75	0.37	0.39
3	COPD*	71	7.37	51	58	1.09	0.56	0.51
4	COPD	70	7.38	54	48	2.55	0.79	0.31
5	COPD	48	7.40	52	54	2.60	0.80	0.31
6	COPD	76	7.35	52	66	2.08	0.58	0.28
7	COPD	50	7.37	81	63	1.72	0.84	0.49
8	COPD	83	7.44	51	57	2.22	1.13	0.51
Mean		65	7.38	56	59	1.91	0.72	0.40
SD		11	0.03	12	6	0.67	0.23	0.10

*COPD and kyphoscoliosis.

steroids, and other medications, according to the prescriptions of the caring physicians.

Measurements

Routine spirometry was obtained by means of a Collins type 13 L spirometer (Biomedin, Padova, Italy) with the patient in the seated posture according to standard procedure.[24]

Flow ($\dot{V}$) was measured with a heated Lilly pediatric-type pneumotachometer connected to a differential pressure transducer (SM5552-001-D, Silicon Microstructures Inc., Fremont, CA). The pneumotachograph was inserted between the nasal mask and the plateau valve of the ventilator circuit.[21]

Volume (V) was obtained from numerical integration of the flow signal. Changes in pleural (P_{pl}) and abdominal (P_{ab}) pressures were estimated from changes in oesophageal (P_{es}) and gastric (P_{ga}) pressures, respectively. Both P_{es} and P_{ga} were measured using 2 balloon-tipped catheter systems connected to 2 differential pressure transducers (SM5552-030-D, Silicon Microstructures Inc., Fremont, CA). The catheters were 80 cm in length and 1.7 mm in internal diameter; the balloons were 10 cm in length and 2.4 cm in circumference. Another similar catheter and pressure transducer (SM5552-030-D, Silicon Microstructures Inc., Fremont, CA) were used to sample the pressure at the airway opening (P_{ao}) via a side port inserted between the nasal mask and the pneumotachograph. Transpulmonary (P_l) and transdiaphragmatic (P_{di}) pressures were obtained by subtracting P_{es} from P_{ao} and P_{ga}, respectively.[22]

Minute ventilation ($\dot{V}_E$), tidal volume (V_T), inspiratory (T_I) and expiratory time (T_E), total cycle duration (T_T), respiratory frequency (f), mean inspiratory flow (V_T/T_I), and the duty cycle (T_I/T_T) were obtained as average values from 1 min continuous records of flow and volume. Transpulmonary pressure was used to calculate dynamic lung compliance ($C_{dyn,}$L) and pulmonary resistance at mid-inspiratory volume (RL_{insp}) as previously described.[25] Dynamic intrinsic positive end-expiratory pressure ($PEEP_{i,dyn}$) was measured as the decrease in P_{pl} preceding the inspiratory flow and, when necessary, this measurement was corrected for expiratory muscles activity.[25] The magnitude of the diaphragmatic effort was estimated from the pressure-time product (PTP_{di}).[21,22,25]

Experimental procedure and study design

Patients were studied in the morning, in seated and comfortable position. After the application of topical anaesthesia with xylocaine spray 10%, the 2 balloon-tipped catheters were consecutively inserted through the nose into the stomach. The patients were encouraged to swallow during this procedure. The balloons were then inflated with 1 ml of air and a positive pressure swing synchronous with manual pressure of the abdominal wall indicated that they were in the stomach. The oesophageal balloon was then deflated and withdrawn into the middle third of the oesophagus and inflated with 0.5–0.7 ml of air. The "occlusion test" was performed to verify the correct positioning of the oesophageal balloon, and it was satisfactory in every instance. Then a commercial nasal mask

(Respironics, Murrysville, PA, USA) was applied and connected to the pneumotachograph and patients were instructed to keep their mouth closed and breathing normally. PAV and PSV were delivered by means of the Vision ventilator (Respironics Inc., Murrysville, PA). The ventilator delivers PAV according to the equation of motion generating a pressure in proportion to patient's spontaneous effort.[21,22,26] A value of CPAP amounting to 4 cmH_2O was set by the ventilator for both PAV and PSV.

Once the patient was accustomed to the experimental setting and appeared to be relaxed, the procedure to set PAV, namely volume assist (VA) and flow assist (FA) adjustments, as well as PSV were performed as previously described.[21,22] Oxygen administration was continuously delivered throughout the procedure to guarantee a $SpO_2 > 92\%$, as measured with finger pulsoximetry. The patients breathed through the nose mask and the pneumotachograph, having removed the ventilator tubing for about 5 min (spontaneous breathing = SB). Then the patient, still seated, was asked to raise both arms anteriorly at a 90° angle and to maintain the posture for 2 min (unsupported arm elevation (AE) = SB–AE). Thereafter we randomized the administration of PAV or PSV. The patient received ventilatory assistance (PAV or PSV) for 5 min at rest, then a 2 min AE test was repeated and recorded during PAV or PSV (PAV–AE and PSV–AE, respectively). Then the procedure was repeated for the other mode of ventilatory assistance. Each patient followed the entire procedure for a total length of about 40 min, according to the randomized sequence.

Data analysis

Using a Pentium II 266 MHz personal computer equipped with an A/D board (DI 200, DATAQ Instruments, Akron OH), all signals were analogue to digital converted, displayed on line throughout the procedure, and stored on hard disk at a sampling rate of 100 Hz. Data were collected under each experimental condition. The mean value of each physiologic variable during the last minute of recording was used for subsequent analysis.

Results are expressed as mean ± 1standard deviation (SD). One-way analysis of variance for repeated measures (ANOVA) was performed, and, when allowed by the F value, the significance between treatments was computed using Fisher's protected least significant difference test. Probability values less than 0.05 ($P < 0.05$) were considered significant.

Results

A representative record from a patient through different phases of the study is shown in Fig. 1. Table 2 shows mean (±SD) data for the breathing

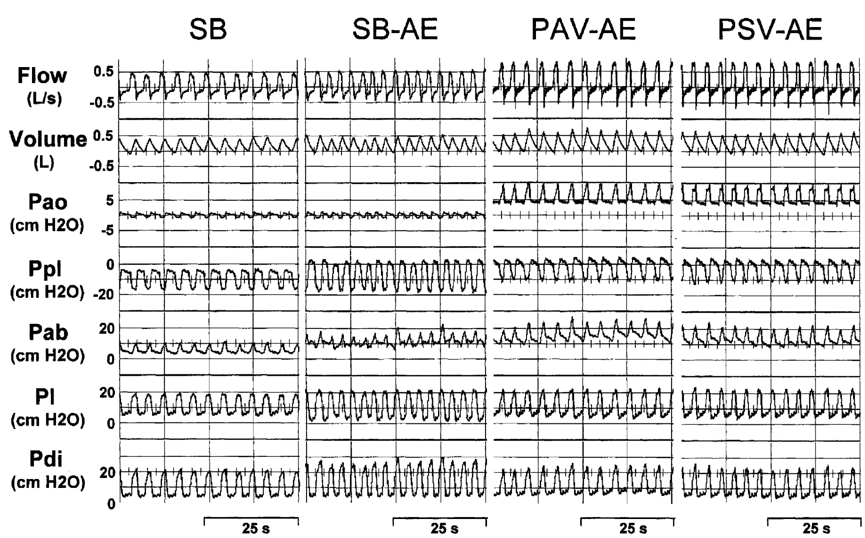

FIGURE 1. Representative record from patient #4 during both spontaneous breathing at rest (SB) and during the arm elevated test performed breathing spontaneously (SB-AE) and under ventilatory assistance with PAV (PAV-AE) and PSV (PSV-AE).

Figure 1 Representative record form patient #4 during both spontaneous breathing at rest (SB) and during the arm elevated test performed breathing spontaneous (SB–AE) and under ventilatory assistance with PAV (PAV–AE) and PSV (PSV–AE).

Table 2 Breathing pattern and respiratory mechanics in the different conditions of the study.

		SB	SB–AE	PAV	PAV–AE	PSV	PSV–AE
V_T	(L)	0.42±0.08	0.46±0.15	0.53±0.11	0.72±0.4*	0.62±0.2*	0.77±0.4*
F	(b/min)	22±5	25±7	21±6	22±8	18±4	20±6
V′E	(L/min)	7.9±1.4	9.0±1.9	9.6±2.2	13.6±1.9*	9.7±1.1*	11.9±3.2*
T_I	(s)	1.2±0.5	1.1±0.6	1.1±0.3	1.2±0.7	1.2±0.4	1.2±0.6
T_E	(s)	1.7±0.4	1.6±0.5	2.03±0.6	1.9±0.8	2.3±0.5	2.1±0.7
T_I/T_{TOT}		0.41±0.05	0.41±0.05	0.35±0.04	0.38±0.03	0.34±0.03	0.36±0.06
C_{dyn},L	(L cmH$_2$O^{-1})	0.08±0.05	0.07±0.05	0.12±0.07*	0.11±0.07*	0.12±0.07*	0.11±0.07*
RL_{insp}	(cmH$_2$O L^{-1} s)	11.8±3.8	13.8±4.6*	9.1±2.9*	10.7±4.0*	10.0±3.2	10.9±4.1
$PEEP_{i,dyn}$	(cmH$_2$O)	2.2±1.4	5.7±4.9*	1.3±0.9	3.6±4.4	0.9±1.0	3.8±4.3
PTP_{di}	(cmH$_2$O min)	292±130	478±277*	134±74*	268±170*	68±27*	219±75*
ΔPTP_{di}	(cmH$_2$O min)	—	186±220	—	133±166	—	151±168
ΔV′E	(L/min)	—	1.11±1.34	—	3.96±1.69*	—	2.32±2.15*,†

Definition of abbreviations: SB, spontaneous breathing; AE, arm elevation; PAV, proportional assist ventilation; PSV, pressure support ventilation; V_T, tidal volume; *f*, frequency of breathing; VE, minute ventilation; T_I, inspiratory time; T_E, expiratory time; T_{TOT}, total breathing duration; C_{dyn},L, dynamic lung compliance; RL, total pulmonary resistance; $PEEP_{i,dyn}$, dynamic intrinsic positive end expiratory pressure; PTP_{di}, pressure time product of diaphragm; ΔPTP_{di}, PTP_{di} difference between each treatment and corresponding AE; ΔV′E, V′E difference between each treatment and corresponding AE.

*$P<0.05$ vs. SB.

†$P<0.05$ vs. PAV–AE.

pattern and respiratory mechanics. We failed to observe any difference in the reaction to ventilatory support between the 2 patients who had COPD and kyphoskoliosis and the 6 patients with only COPD. Since the 2 baseline measurements preceding PAV and PSV were not different, we refer to the first baseline SB and the first AE test. On average, AE caused slight changes in the breathing pattern and minor changes in dynamic compliance (−12% on average) and pulmonary resistance (+17% on average). By contrast, $PEEP_{i,dyn}$ more than doubled (+160% on average) and was associated with a remarkable increase in PTP_{di} (+64%, on average). In 2 of the 8 patients, $\dot{V}_E$ not only did not increase but rather decreased from SB to SB–AE.

In comparison with baseline SB, both PAV and PSV increased minute ventilation (+22% and +23% on average, respectively). In particular, PSV increased V_T (+48% on average) and reduced the frequency of breathing (−18%, on average). $PEEP_i$ substantially decreased during PAV and PSV periods (−41% and −59% on average, respectively), and lung compliance increased (+50% on average). Both PAV and PSV reduced significantly the diaphragmatic effort compared to unsupported breathing (PTP_{di}: −54% and −77%, on average, respectively) (Table 2).

When the AE exercise was performed during ventilatory assistance, $\dot{V}_E$ and V_T were substantially greater (50% on average) and the inspiratory effort lower than during unsupported AE. On average, PTP_{di} decreased to −44% with PAV and to −54%, with PSV. $PEEP_{i,dyn}$ decreased by more than 30% with both modes of ventilatory assistance in comparison with the unsupported AE conditions. In other words, ventilatory assistance during AE allowed a higher ventilation with lower inspiratory effort. During PAV–AE all patients were able to increase $\dot{V}_E$.

To ascertain the efficiency of the patient–ventilator system, we computed the increase in the magnitude of the inspiratory effort (ΔPTP_{di}, required to meet the increase in ventilation ($\Delta\dot{V}_E$) from rest (SB, PAV, and PSV) to unsupported (SB–AE) and supported (PAV–AE and PSV–AE) arm elevation. The increase of the diaphragmatic effort needed to sustain ventilation during AE was not significantly different between the unsupported (SB) and the assisted condition (PAV and PSV). In other words, though starting from very different baseline values, the increase in respiratory effort was very similar when arms were elevated. Clearly, the final diaphragmatic effort remained lower with ventilatory assistance than during unsupported breathing, because of the different starting values. On the other hand, the rise in ventilation was greater with both modes of ventilatory assistance than without any support (SB). In other words, a similar increase in the inspiratory effort generated more ventilation when the patients were connected to the ventilator than when they were breathing on their own. However, the rise in $\dot{V}_E$ with PAV was significantly greater not only compared to SB, but also compared to PSV. This is illustrated in Fig. 2 where the output, i.e. $\dot{V}_E$ is plotted against the input from the diaphragm, i.e. PTP_{di}. It can be observed that the steeper $\dot{V}_E$ vs. PTP_{di} relationship

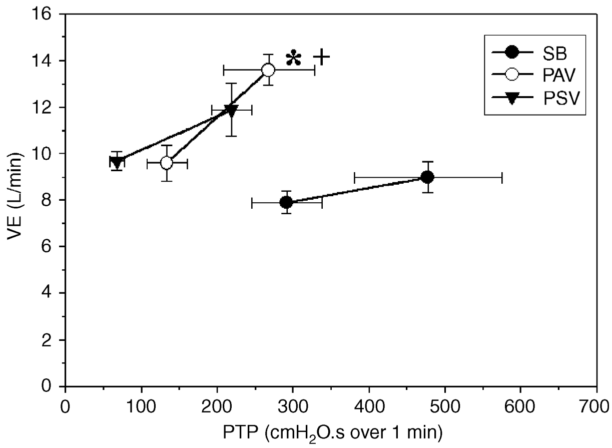

Figure 2 Relationship between changes in diaphragm energy expenditure (PTP_{di}) and minute ventilation (VE) at baseline (B) and in the last minute of arm elevation (AE) in the 3 conditions tested: SB, spontaneous breathing; PAV, proportional assist ventilation; PSV, pressure support ventilation. Data are expressed as mean value $\pm$ standard error; $^{*}P<0.001$ PAV vs. SB.

with PAV than with PSV, indicating that the patient–ventilator system was more efficient with PAV, because a similar increase in PTP generated a greater rise in V′E.

Discussion

The results of this study show that, in patients with stable severe COPD and CRF; (1) respiratory muscle function is impaired during upper limb exercise; (2) ventilatory assistance operated by both PAV and PSV substantially unloads the diaphragm both at rest and during AE; (3) PAV can be more efficient than PSV in assisting the diaphragm to sustain a greater level of V′E.

To our knowledge this is the first study addressing mechanical ventilatory assistance, and comparing PAV and PSV, during upper limb efforts in patients with severe COPD and CRF. Furthermore, this study confirms and extends the results of previous studies, in which it was shown that artificial ventilation can assist the respiratory muscles during lower limb exercise and, hence, it can be useful in rehabilitation and training programs for COPD patients.[15–17] However, our study is on a small group of patients and the data should be considered physiologic, preliminary data, requiring additional confirmation in larger clinical studies.

Leg fatigue is a common limiting factor in exercise in COPD patients.[27,28] To what extent this is due to general deconditioning of the patients or to the systemic effects of COPD remains to be established. Nevertheless, training of leg skeletal muscles can improve patient's mobility and hence his/her general health status and social relationships. However, also the capability to use properly the upper limbs is important in daily life activities, e.g. washing, combing, etc.[11]

Upper limb exercise may impair ventilation. In fact, the use of upper limbs may need the activation of the accessory respiratory muscles for the posture of the trunk.[12] Under those circumstances, the ventilatory workload must be faced by the diaphragm, whose pressure-generating capacity is impaired substantially by pulmonary hyperinflation.[14] This condition can influence not only daily activities but also rehabilitation programs aimed to a more general skeletal muscle training than only to leg exercise.

Our data are in line with the previous results.[11–15] As suggested by Celli and colleagues,[12,13] it was the diaphragm which had to carry over the additional ventilatory burden during AE.

NPPV unloads the inspiratory muscles, reduces breathlessness, and allows a better limb exercise by a redistribution of blood flow from the respiratory to skeletal muscles.[16,18] Similarly to PSV, PAV unloads the inspiratory muscles of patients with moderate to severe COPD at rest[21,22] and improves exercise tolerance and breathlessness during cycle exercise.[17,29] Bianchi and colleagues[17] after their short-term study and Hawkins and colleagues[18] after their 6 weeks randomized, prospective study concluded that ventilatory assistance in general, and PAV in particular, could be useful in pulmonary rehabilitation programs because of the better exercise performance of severe COPD patients when the respiratory muscles are unloaded and ventilation assisted.

In the present study both PAV and PSV were able to unload the respiratory muscles during quiet breathing. During the AE with ventilatory assistance, the additional PTP_{di} needed to perform the test was slightly but not significantly lower than without ventilatory support. However, since the initial PTP_{di} with both PSV and PAV was much lower than during SB, the additional effort was well tolerated by all patients who could perform the AE test without excessive dyspnea and without active coaching.

Assisted breathing with PSV and PAV also induced changes in minute ventilation compared to unsupported breathing. It has to be noted that the rise in $\dot{V}_E$ to match the higher ventilatory demand showed a trend to increase with PSV (+23% on average) and it was significantly greater with PAV (+42% on average) than without ventilatory assistance (SB, +14% on average). In other words, thank to the ventilator, the patients could better meet the increased ventilatory requirements determined by AE. However, this change reached statistical significance only during PAV. The better efficiency obtained with PAV, i.e. a greater rise in ventilation for the same increase in diaphragmatic effort, can be explained by the unique design of PAV based on physiological considerations.[20] However, the number of subjects examined in his protocol is rather small, only 8 patients, and not completely homogeneous, 2 patients had also kyphoskoliosis and not pure COPD. Under these circumstances, a type $\beta 2$ error might be induced. Certainly, this is a significant limitation of our study. In order to be extrapolated to a more general population of patients with CRF due to COPD, the results of this protocol should be validated on a larger group of patients. However, these are delicate patients, in whom the insertion of 2 balloons, in the oesophagus and in the stomach, to keep inside for almost 1 h, is unpleasant and might prevent the possibility to recruit a larger group as it may occur when using noninvasive techniques.[26] This may be considered a preliminary physiologic study, which might be followed by protocol on larger groups using mainly noninvasive techniques.

In this study, 4 cmH_2O of positive expiratory pressure were set by the ventilator during both PAV and PSV. Nava and colleagues[30], and O'Donoghue and colleagues[31] reported that a few cmH_2O of CPAP were helpful to further reduce the inspiratory effort during PSV in stable COPD patients. Furthermore, Petrof and colleagues[8] showed that CPAP improved the exercise capacity of COPD patients by counterbalancing the intrinsic PEEP. Therefore, it is very likely that positive expiratory pressure contributed to the reduction of patients' inspiratory efforts. In fact, Dolmage and Goldstein[16] suggested that the combination of CPAP and PAV increased exercise tolerance in patients with COPD better than either alone. In our study, the level of positive expiratory pressure was the same with both PAV and PSV and was not changed from rest to AE.

As recurrently cited in many experimental procedures with PAV, a major problem is the setting of the ventilator.[16,17,19,21,24,26] According to the theory, the tailoring of PAV would require the measurement of the mechanical properties of the respiratory system to implement patient's elastance and resistance in the equation of motion.[20] We measured lung compliance and flow resistance by means of the oesophageal balloon technique only off-line at the end of the procedure (Table 2). We did not attempt to set the ventilator according to those data because respiratory mechanics computation takes time and can unduly prolong the period during which the patients have to keep the oesophageal balloon on, thus providing an additional source of discomfort that can challenge the patient's cooperation. Hence, we decided to set PAV at patient's comfort,[21,22] in consideration of the cooperation required by the following procedure. Nevertheless, this sort of empirical setting did not disrupt the effectiveness of PAV and, to some extent, made the condition more comparable with PSV.

In conclusion, the results of the present study, although in a small number of patients, confirm that in patients with COPD and CRF, the use of upper limbs poses a substantial burden on the inspiratory muscles and in particular on the diaphragm, the contribution of the extra-diaphragmatic respiratory muscles being limited by their participation to the trunk posture. We show that ventilatory assistance helps to unload the inspiratory muscles, particularly the diaphragm, and to match the increased ventilatory demand. Therefore, ventilatory assistance could be considered not only during leg exercise, but also in complete rehabilitation programs aimed to improve the upper limbs capability to meet the daily activities. Finally, our data suggest that PAV can equally unload the inspiratory muscles but follow better the changes in ventilatory demand compared to PSV. Hence PAV, as suggested by a few authors,[16,17,29] could be considered in general rehabilitation programs for patients with advanced COPD.

References

1. Pauwels RA, Buist S, Calverlay PM, et al. Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2001;**163**:1256–76.
2. Lacasse Y, Womg E, Guyatt GH, King D, Cook DJ, Goldstein RS. Meta analysis of respiratory rehabilitation in chronic obstructive pulmonary disease. *Lancet* 1996;**348**:1115–9.
3. Griffiths TL, Burr ML, Campbell IA, et al. Results at 1 year of outpatient multidisciplinary pulmonary rehabilitation: a randomised controlled trial. *Lancet* 2000;**335**:362–8.
4. O'Donnel DE, D'Arsigny C, Fitzpatrick M, Webb KA. Exercise hypercapnia in advanced chronic obstructive pulmonary disease. The role of lung hyperinflation. *Am J Respir Crit Care Med* 2002;**166**:663–8.
5. Kilian KJ, Leblanc P, Martin DH, et al. Exercise capacity and ventilatory, circulatory and symptom limitation in patients with chronic airflow limitation. *Am Rev Respir Dis* 1992;**146**:935–40.
6. Belman MJ. Factors limiting exercise performance in lung disease ventilatory insufficiency. *Chest* 1992;**101**:253s–4s.
7. Maltais F, Reissmann H, Gottfried SB. Pressure support reduces insipiratory effort and dyspnea during exercice in chronic airflow obstruction. *Am J Respir Crit Care Med* 1995;**151**:1027–33.

8. Petrof BJ, Calderini E, Gottfried SB. Effect of CPAP on respiratory effort and dyspnea during exercise in severe COPD. *J Appl Physiol* 1990;**69**(1):179–88.
9. Polkey MI, Hawkins P, Kyroussis D, et al. Inspiratory pressure support prolonge exercise induced lactataomia in severe COPD. *Thorax* 2000;**55**:547–9.
10. Polkey MI, Kyroussis D, Milis GH, et al. Inspiratory pressure reduces slowing of inspiratory muscles relaxation rate during exhaustive treadmill walking in severe COPD. *Am J Respir Crit Care Med* 1996;**154**:1146–50.
11. Velloso M, Garcia Stella S, Cendon S, Silva AC, Jardin JR. Metabolic and ventilatory parameters of four activities of daily living accomplished with arms in COPD patients. *Chest* 2003;**123**:1047–53.
12. Celli BR, Rassulo J, Make BJ. Dyssincronous breathing during arm but not leg exercise in patients with chronic airflow obstruction. *N Engl J Med* 1986;**314**:1485–90.
13. Celli B, Criner G, Rassulo J. Ventilatory muscle recruitment during unsupported arm exercise in normal subjects. *J Appl Physiol* 1988;**64**:1936–41.
14. Martinez FJ, Couser JI, Celli BR. Respiratory response to arm elevation in patients with chronic airflow obstruction. *Am Rev Respir Dis* 1991;**143**:476–80.
15. Epstein SK, Celli BR, Williams J, Tarpy S, Roa J, Shannon T. Ventilatory response to arm elevation. Its determinants and use in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1995;**152**:211–6.
16. Dolmage TE, Goldstein RS. Proportional assist ventilation and exercise tolerance in subjects with COPD. *Chest* 1997;**111**:948–54.
17. Bianchi L, Foglio K, Pagani M, Vitacca M, Rossi A, Ambrosino N. Effect of nasal proportional assist ventilation (PAV) on exercise performance and breathlessness of COPD patients with chronic hypercapnia. *Eur Respir J* 1998;**11**:422–7.
18. Hawkins P, Johnson LC, Nikoletou D, et al. Proportional assist ventilation as an aid to exercise training in severe chronic obstructive pulmonary disease. *Thorax* 2002;**57**:853–9.
19. Bianchi I, Foglio K, Porta R, Baiardi P, Vitacca M, Ambrosino N. Lack of additional effect of adjunct of assisted ventilation to pulmonary rehabilitation in mild COPD patients. *Respir Med* 2002;**96**:359–67.
20. Younes M. Proportional assist ventilation a new approach to ventilatory support. *Am Rev Respir Dis* 1992;**145**:114–20.
21. Polese G, Vitacca M, Bianchi L, Rossi A, Ambrosiono N. Nasal proportional assist ventilation unloads the inspiratory muscles of stable patients with hypercapnis due to chronic obstructive pulmonary disease. *Eur Respir J* 2000;**16**:491–8.
22. Porta R, Appendini L, Vitacca M, et al. Mask proportional assist vs. pressure support ventilation in patients in clinically stable condition with chronic ventilatory failure. *Chest* 2002;**122**:479–88.
23. Optimal assessment and management of chronic obstructive pulmonary disease. ERS consensus statement. *Eur Respir J* 1995;**8**:1398–420.
24. Standardization of spirometry 1994 update. The official statement of the ATS. *Am J Respir Crit Care Med* 1985;**152**: 1107–36.
25. Appendini L, Patessio A, Zaboni S, Carone M. Physiologic effects of positive end-expiratory pressure and mask pressure support during exacerbations of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1994;**149**: 1069–76.
26. Serra A, Polese G, Braggion C, Rossi A. Non-invasive proportional assist and pressure support ventilation in patients with cystic fibrosis and chronic respiratory failure. *Thorax* 2002;**57**:0–4.
27. Boni E, Corda L, Franchini D, et al. Volume effect and exertional dyspnoea after bronchodilator in patients with COPD with and without expiratory flow limitation at rest. *Thorax* 2002;**57**:528–32.
28. Diaz O, Villafranca C, Ghezzo H, et al. Breathing pattern and gas exchange at peak exercise in COPD patients with and without tidal flow limitation at rest. *Eur Respir J* 2001; **17**:1120–7.
29. Hernandez P, Maltais F, Gursahaney A, et al. Proportional assist ventilation may improve exercise performance in severe chronic obstructive pulmonary disease. *J Cardiopulmonary Rehab* 2001;**21**:135–42.
30. Nava S, Ambrosino N, Rubini F, et al. Effect of nasal pressure support ventilation and external PEEP on diaphragmatic activity in patients with severe stable COPD. *Chest* 1993;**103**:143–50.
31. O'Donoghue FJ, Catcheside PG, Jordan AS, Bersten AD, McEvory RD. Effect of CPAP on intrinsic PEEP, inspiratory effort, and lung volume in severe stable COPD. *Thorax* 2002;**57**:533–9.