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# Respiratory response and inspiratory effort during pressure support ventilation in COPD patients

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**Abstract** *Objective:* Pressure Support Ventilation (PSV) is now widely used in the process of weaning patients from mechanical ventilation. The aim of this study was to evaluate the effects of various levels of PS on respiratory pattern and diaphragmatic efforts in patients affected by chronic obstructive pulmonary disease (COPD).
*Setting:* Intermediate intensive care unit.
*Patients:* We studied ten patients undergoing PSV and recovering from an episode of acute respiratory failure due to exacerbation of COPD.
*Methods:* Three levels of PSV were studied, starting from the lowest (PSb) one at which it was possible to obtain an adequate Vt with a $pH \geq 7.32$ and an $SaO_2 > 93\%$. Then, PS was set at 5 $cmH_2O$ above (PSb+5) and below (PSb−5) this starting level. Ventilatory pattern, transdiaphragmatic pressure (Pdi), the pressure-time product of the diaphragm (PTPdi), the integrated EMG of the diaphragm, static PEEP (PEEPi, stat), dynamic PEEP (PEEPi, dyn), and the static compliance and resistance of the total respiratory system were recorded.
*Results:* Minute ventilation did not significantly change with variations in the level of PS, while Vt significantly increased with PS ($PS-5 = 6.3 \pm 0.5$ ml/kg vs. $PSb = 10.1 \pm 0.9$ [$p < 0.01$] and vs. $PS+5 = 11.7 \pm 0.6$ [$p < 0.01$]), producing a reduction in respiratory frequency with longer expiratory time. The best values of blood gases were obtained at PSb, while at PSb−5, $PaCO_2$ markedly increased. During PSb and PSb+5 and to a lesser extent during PSb−5, most of the patients made several inspiratory efforts that were not efficient enough to trigger the ventilator to inspire; thus, the PTPdi "wasted" during these inefficient efforts was increased, especially during PS+5. The application of an external PEEP (PEEPe) of 75% of the static intrinsic PEEP during PSb caused a significant reduction in the occurrence of these inefficient efforts ($p < 0.05$). Minute ventilation remained constant, but Vt decreased, together with Te, leaving the blood gases unaltered. The PTPdi per breath and the dynamic PEEPi were also significantly reduced (by 59% and 31% of control, respectively, $p < 0.001$) with the application of PEEPe.
*Conclusion:* We conclude that in COPD patients, different levels of PSV may induce different respiratory patterns and gas exchange. PS levels capable of obtaining a satisfactory equilibrium in blood gases may result in ineffective respiratory efforts if external PEEP is not applied. The addition of PEEPe, not exceeding dynamic intrinsic PEEP, may also reduce the metabolic work of the diaphragm without altering gas exchange.

**Key words** PSV · Inefficient efforts · COPD · Edi · PTPdi

## Introduction

Pressure support ventilation (PSV) is an assisted mode of ventilation classically used during the weaning process because it is able to decrease the inspiratory work of breathing and inspiratory muscle effort [1, 2]. Inspiratory muscle effort can be reduced or almost totally eliminated, depending on the level of inspiratory support [3]; prolonged complete unloading may lead to respiratory muscle atrophy and subsequent weaning difficulties [4, 5]. Because of this, various parameters have been proposed to determine the "best" level of pressure support (PS), that which is able to reduce respiratory muscle effort without giving excess support and, at the same time, obtains satisfactory blood gas values [1, 2, 6, 7].

All the studies were performed in nonhomogeneously selected patients with acute respiratory failure, some of whom had "acute" pathologies (ARDS, postoperative complications, pulmonary embolism, congestive heart failure), while others had an acute exacerbation of chronic obstructive pulmonary disease (COPD). These diseases are characterized by totally different respiratory mechanics and respiratory muscle function. In particular, COPD patients may have a prolonged lung-emptying time due to static and/or dynamic hyperinflation, and thereby develop so-called auto or intrinsic end-expiratory positive pressure (PEEP) [8], which has a different physiological mechanism from that observed in ARDS patients, for example [9].

We therefore studied the ventilatory response and the tension-time product of the diaphragm (PTPdi) [10] and its electromyogram (Edi) in a group of COPD patients at different levels of PSV and recovering from an episode of acute respiratory failure. While in some pathologies, such as ARDS, the use of external PEEP (PEEPe) to improve gas exchange is widely accepted [11, 12], its application in COPD patients with static and/or dynamic hyperinflation is controversial and has not been fully explored in the spontaneous breathing modes. We therefore also investigated the effects of PEEPe during PSV on ventilatory pattern and diaphragmatic effort in these patients.

## Materials and methods

Ten COPD patients requiring mechanical ventilation for acute respiratory failure were included in this study. The patient characteristics pertinent to the study are listed in Table 1. The patients were studied at least 48 h after the beginning of PSV, clinical conditions permitting, even if they were not yet ready to be weaned.

The criteria for initiating of PSV were as follows: (a) hemodynamic stability (regular cardiac rhythm and systolic blood pressure > 90 mmHg); (b) a spontaneous respiratory rate > 8 breaths/min when mechanical ventilatory support was briefly discontinued; (c) neuromuscular drive, as assessed by $P0.1 < 6\ cmH_2O$; and (d) good patient compliance to this mode of ventilation, with no need for sedation.

Three levels of PS were studied, starting from the one (PSb = basal PS) defined as the lowest at which a good expiratory Vt (8–10 ml/kg), a satisfactory blood gas equilibrium ($SAO_2 > 93\%$ with a $PaCO_2$ value resulting in a pH above or equal to 7.32), and a good compliance of the patients to the ventilation mode could be maintained. In addition, achieved respiratory rate had to be less than 30 breaths/min [7]. The two other levels of PS studied were $5\ cmH_2O$ above (PSb+5) and below (PSb−5) this starting level. All measurements were performed at a constant $FIO_2$.

Patients were studied in a semirecumbent position. No sedatives or narcotics were administered during the study, except for those used in the measurement of respiratory mechanics. The study was approved by the local Ethics Committee, and informed consent was obtained.

### Measurements

Airflow was measured with a pneumotachograph (Screenmate box 0586, Jaeger, Hochberg, Germany) positioned between the endotracheal tube or the tracheal cannula and the Y of the ventilatory tubings. Tidal volume (Vt) was obtained by integration of the flow signal. The inspiratory (Ti), expiratory (Te) and total breathing (Ttot) cycle durations were calculated from the flow. However, since in most COPD patients, the Pdi swings during inspiration were not synchronous with the inspiratory flow given by the ventilator, we

**Table 1** Clinical and respiratory characteristics of the patients (*ET tube ID* internal diameter of the endotracheal or tracheotomy tube, *Crs* static compliance of respiratory system, *Rrs UNCORR* total inspiratory resistance of respiratory system not corrected for ET, *Rrs CORR* total inspiratory resistance of the respiratory system corrected for ET, *P0.1* mouth occlusion pressure after 100 ms, *PEEPi st* static positive end-expiratory pressure)

| Patient no. | Sex | ET tube or cannula ID (mm) | Crs (ml/cm$H_2O$) | Rrs UNCORR (cm$H_2O$/l/s) | Rrs CORR. (cm$H_2O$/l/s) | PEEPi st (cm$H_2O$) | P0.1 (cm$H_2O$) |
|---|---|---|---|---|---|---|---|
| 1 | F | 8 | 140 | 31.7 | 29.0 | 19.8 | 4.8 |
| 2 | M | 8 | 124 | 15.8 | 18.5 | 5.0 | 4.0 |
| 3 | F | 7.5 | NA | NA | NA | 7.1 | 3.0 |
| 4 | M | 8 | 46 | 12.1 | 14.9 | 4.0 | 2.1 |
| 5 | M | 8 | 109 | 27.1 | 30.6 | 7.7 | 3.3 |
| 6 | M | 7.5 | NA | NA | NA | 2.9 | 2.0 |
| 7 | F | 7 | NA | NA | NA | 4.2 | 2.7 |
| 8 | M | 8 | 109 | 12.8 | 14.9 | 4.0 | 1.9 |
| 9 | M | 8 | 59 | 15.2 | 17.4 | 4.4 | 3.8 |
| 10 | M | 8 | 88 | 35.7 | 39.6 | 10.5 | 3.6 |
| $\bar{x}$ | | 7.8 | 96.4 | 21.4 | 23.6 | 7.2 | 3.1 |
| SD | | 0.3 | 34.2 | 9.8 | 9.5 | 5.1 | 1.0 |

also analyzed the EMG and pressure traces (Pes and Pdi) to obtain respiratory muscle and diaphragm inspiratory times.

Pressure at the airway (Paw) was recorded at the distal end of the endotracheal tube or cannula with a differential pressure transducer (Honeywell ± 300 $cmH_2O$, Freeport, Ill., USA).

Transdiaphragmatic pressure (Pdi) was calculated as the difference between gastric (Pga) and esophageal (Pes) pressures. Pga and Pes were measured using balloon-catheter systems, each of which was connected to a differential pressure transducer (Honeywell ± 300 $cmH_2O$, Freeport, Ill., USA). One balloon was positioned in the middle third of the esophagus according to the classical technique [13] and was filled with 0.5 ml of air; the second balloon was placed in the stomach and inflated with 1 ml of air. The occlusion test was used to check the position of the esophageal balloon [14].

The value of dynamic intrinsic positive end-expiratory pressure (PEEPi dyn) was calculated in COPD patients as the negative deflection in Pes from the onset of inspiratory effort to the point of zero flow during unoccluded breathing, assuming that the change in pleural pressure required to initiate airflow approximated the opposing level of elastic recoil pressure at end-expiration [15].

The pressure-time integral of the diaphragm (PTPdi) was calculated on a breath-by-breath basis. It was measured as the area subtended by Pdi and the chest wall static recoil pressure-time curve over Ti, taking into account the PEEPi. The static recoil pressure-time curve was extrapolated from the static recoil pressure-volume curve of normal subjects, considering this relationship to be linear within the tidal volume range [10, 16].

The integrated electromyography of the diaphragm (Edi) was monitored in seven COPD patients with an esophageal electrode. A Swan-Ganz pacing catheter with a balloon mounted at the tip was used; it was inserted into the stomach, where it was inflated and subsequently anchored to the gastroesophageal junction when a good signal-to-noise ratio was obtained. The EMG was filtered (20 – 1000 Hz band-pass), full-wave rectified, and then integrated using a filter (Pynter) with a time constant of 0.03 s.

PO.1 was measured as the airway pressure developed in the first 100 ms after the first inspiratory effort made after end-expiratory occlusion [17]; it was obtained by pressing the end-expiratory button on the ventilator. The pressure signal was recorded and analyzed with a computerized program (see data analysis section). The value of PO.1 was calculated as the mean of three measurements.

In five patients, the end-expiratory lung volume changes (EELV) were obtained by inductive plethysmography (RIP; Ambulatory Monitoring, Model 150, Ardsley, N.Y., USA) in the DC mode. Two recording bands were placed at the level of the axilla of the rib cage (RC), while the adbominal one (ABD) was positioned just above the umbilicus. The sum of RC and ABD was calibrated using the Vt from the pneumotachograph [18]. One potential problem in using this method is that the calibration obtained during spontaneous breathing may not be very accurate, especially when marked differences in the ABD-RC coordination pattern are present. This was, however, the case in only one patient. The reliability of our measurements was confirmed by the fact that the sum calibration obtained by RIP was repeated at the end of the study, without significant change (< 30 ml over a Vt of 1 l).

Measurements of respiratory mechanics (compliance and resistance) were obtained in all but three patients using the following method, with the patients paralyzed in CMV mode at zero PEEPe. Static positive end-expiratory pressure (PEEPi), was measured in all ten patients with the end-expiratory occlusion technique [19]. Briefly, after several breaths under controlled mechanical ventilation, the airway opening was occluded at the end of a tidal expiration, using the end-expiratory hold button. All the patients studied showed a positive Paw during the occlusion and exhibited a plateau, which represents the elastic recoil pressure. This value provides direct measurement of static PEEPi. The static compliance of the total respiratory system (Cst, rs) was calculated during an occlusion of 3 s at end-inspiration as the ratio between the expiratory Vt and the difference between the end-inspiratory and the end-expiratory (PEEPi) plateau pressures [20]. The end-inspiratory occlusion also makes determination of the resistive properties of the respiratory system possible, as described in detail elsewhere [20]. In calculating the resistance of the respiratory system, we subtracted the resistance of the endotracheal tube, calculated in our laboratories, as previously described [21] (see Table 1), and corrected the errors due to the closing time of the ventilator valve [22].

Arterial blood gases were withdrawn from the radial artery and analyzed with a blood gas analyzer (ABL 500 Radiometer, Copenhagen, Denmark).

## Protocol

Mechanical ventilation was provided by a Cesar (Taema, France) ventilator. In the PSV mode, the pressure trigger was set throughout the study at minimum pressure to avoid auto-triggering ($-1$ $cmH_2O$).

The patients were ventilated with a constant $FiO_2$ able to maintain a $SaO_2 > 93\%$. All the COPD patients were studied for 30 min, starting from PSb at zero PEEP. The other two levels of PS were applied in random order for 30 min each; before the application of a new level, the patients were always returned to PSb for 10 min.

Since in most COPD patients, inspiratory efforts were sometimes not efficient enough to trigger a new ventilator cycle (ineffective efforts), despite a negative deflection in Pdi [23] (Fig. 1) we also recorded the effect of the addition of an external PEEP to the lowest PS level at which a good gas exchange and the lowest number of ineffective efforts could be achieved. The applied PEEP was about 75% of static PEEPi, as already described in the literature [24], except in the case of patient 1 (PEEPi stat = 19.8 $cmH_2O$), in whom we applied a positive pressure of 10 $cmH_2O$, since we did not want to overpass this "critical level". This value was chosen for extrinsic PEEP because PEEPi dyn has been shown to be slightly lower than PEEPi stat [15]; therefore, the application of a PEEPe of 75% PEEPi stat is likely not to exceed the PEEPi dyn, avoiding the risk of hyperinflation [25]. The reliability of this assumption was checked at the beginning of the study when PEEPi dyn was determined. The recording of static PEEPi is much easier to perform in a clinical setting than that of PEEPi dyn, which requires the positioning of gastroesophageal balloons. The level of PS above PEEP, when this was applied, was equal to PSb minus PEEPe.

Between 24 and 48 h before the study, the subjects were sedated with diazepam and then paralyzed with pancuronium bromide to enable us to study their respiratory mechanics.

## Data analysis

Mean Pdi, Pes, Pga, PTPdi, Edi and the Edi/Pdi ratio (index of diaphragm electromechanical coupling) were calculated by averaging the values for seven regular breaths, while minute ventilation and the timing of breathing (Ti, Te, Ttot, Ti/Ttot) were measured over 50 breaths. We also measured the number of ineffective efforts among a total of 50 negative deflections of Pdi. The total PTPdi of the 50 negative Pdi deflections was also calculated and divided into "ineffective PTPdi" and "effective PTPdi", the latter representing the PTPdi needed to trigger a mechanical breath. All the variables except RIP, which was recorded on a separate, two-channel chart recorder, were recorded on a paper recorder (Gould TA 4000, Valley View, Ohio, USA) and on a personal computer by and A/D board at the sampling frequency of 60 Hz. Data analysis was performed

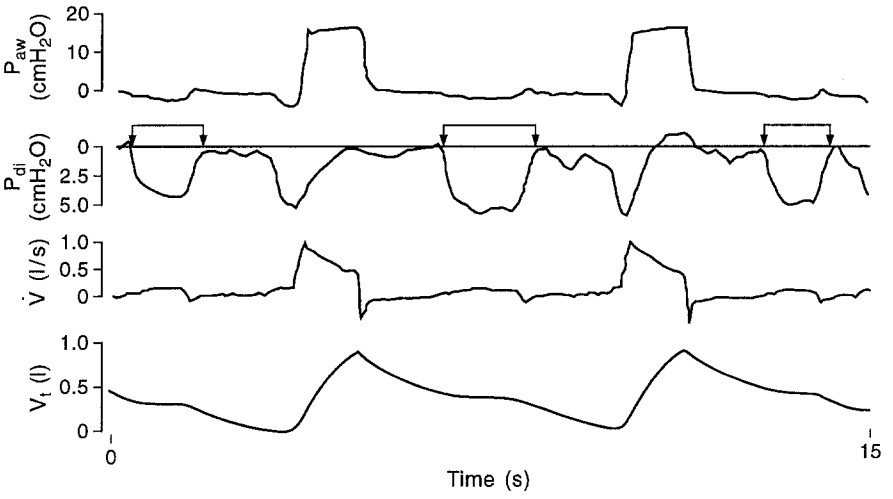


**Fig. 1** Polygraphic recording during PSV in a representative COPD patient. *Top* to *bottom*: airway pressure (Paw) transdiaphragmatic pressure (Pdi), airflow ($\dot{V}$) and tidal volume (Vt). Note the presence of several ineffective efforts (between the *arrows*). See text for further details

with a computerized program (Labdat and Anadat, J. Bates Meakins-Christie, McGill University, Montreal, Quebec, Canada).

Results are expressed as mean values ± SD. A Student's *t*-test for paired data with Bonferroni adjustment was used to check the effects of the different levels of PS and of the addition of PEEP to the PSb [26]. Correlations between various parameters were analyzed using Pearson's correlation coefficient. Statistical significance was defined as a two-tailed $p$-value $< 0.05$.

## Results

### Effects of different levels of PS

As illustrated in Table 2, the patients ventilated with PSb and PSb+5 achieved good blood gas values, while a marked, but not significant, increase in $PaCO_2$ was observed during PSb−5. Mean PSb was 17.6±2 $cmH_2O$. PSb+5 was characterized in 60% of patients by a marked positive deflection of Pes at the end of inspiration, suggesting an excess of PS. Minute ventilation did not significantly differ among the three levels, even if it was slightly higher during PSb. In particular, as shown in Fig. 2, Vt increased significantly with the level of PS [6.3±0.5 ml/kg (PSb−5) vs. 10.1±0.9 (PSb) ($p<0.01$) and vs. 11.7±0.6 (PSb+5) ($p<0.01$)] with a significant reduction in respiratory rate [17.4±3.5 breaths/min) (PSb−5) vs. 12.5±3.7 (PSb) ($p<0.05$) and vs. 8.8±6.8 (PSb+5) ($p<0.01$)]. Te was markedly prolonged at the highest level.

The PTPdi, expressed per breath, was significantly higher ($p<0.05$) during the PSb−5 trial (7.87±3.1 $cmH_2O\ s^{-1}$), while no significant difference was observed at the two highest levels (5.05±2.2 $cmH_2O\ s^{-1}$ for PSb and 4.91+3.1 for PSb+5). The PTPdi depends on the amplitude of Pdi swings and the time for which the contraction is maintained. In normal subjects, the Pdi swing is usually approximately synchronous with the inspiratory flow; in our COPD patients, however, the Pdi swing during PSV always crossed the zero baseline long before the end of inspiratory flow (Fig. 1). The timing of respiratory muscle contraction, expressed as a percentage of Ti (Pes, insp), varied among the COPD pa-

**Table 2** Arterial blood gases during different levels of PS

| PSb (17.6±2.4 $cmH_2O$) | | | | PS+5 | | | PS−5 | | |
|---|---|---|---|---|---|---|---|---|---|
| Patient no. | pH | $PaCO_2$ (mmHg) | $PaO_2/FiO_2$ | pH | $PaCO_2$ (mmHg) | $PaO_2/FiO_2$ | pH | $PaCO_2$ (mmHg) | $PaO_2/FiO_2$ |
| 1 | 7.34 | 63.2 | 280 | 7.33 | 65.9 | 280 | 7.29 | 72.9 | 250 |
| 2 | 7.41 | 39.0 | 310 | 7.40 | 45.1 | 300 | 7.35 | 48.3 | 300 |
| 3 | 7.38 | 43.5 | 250 | 7.38 | 41.5 | 260 | 7.39 | 43 | 260 |
| 4 | 7.35 | 45.0 | 260 | 7.35 | 43.1 | 260 | 7.35 | 45 | 260 |
| 5 | 7.37 | 55.6 | 250 | NA | NA | NA | NA | NA | NA |
| 6 | 7.39 | 49.1 | 280 | 7.38 | 47.3 | 280 | 7.35 | 56.8 | 280 |
| 7 | 7.40 | 48.4 | 170 | 7.40 | 46.5 | 160 | 7.40 | 49.5 | 170 |
| 8 | 7.42 | 43.7 | 190 | 7.42 | 45.9 | 190 | 7.38 | 52.5 | 160 |
| 9 | 7.32 | 50.5 | 230 | 7.32 | 52.5 | 240 | 7.30 | 54.5 | 220 |
| 10 | 7.32 | 59.6 | 200 | 7.32 | 58.1 | 200 | 7.29 | 68.1 | 160 |
| $\bar{x}$ | 7.37 | 49.8 | 242 | 7.37 | 49.5 | 241 | 7.34 | 54.5 | 228 |
| SD | 0.04 | 7.7 | 44 | 0.04 | 7.9 | 47 | 0.04 | 10.1 | 53 |

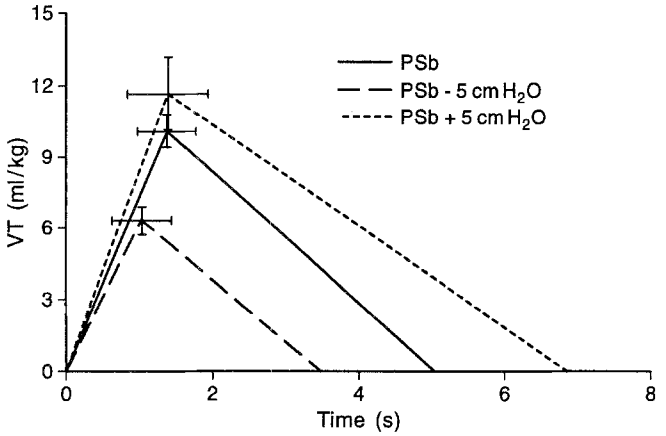


**Fig. 2** Ventilatory pattern (mean±SD) observed during various levels of PS. PSb (*solid line*), PSb-5 (*dashed line*), PSb+5 (*dotted line*). Ti (inspiratory time) begins at 0 and ends at the peak VT. Te (expiratory time) begins at peak VT and ends when crossing the *x*-axis

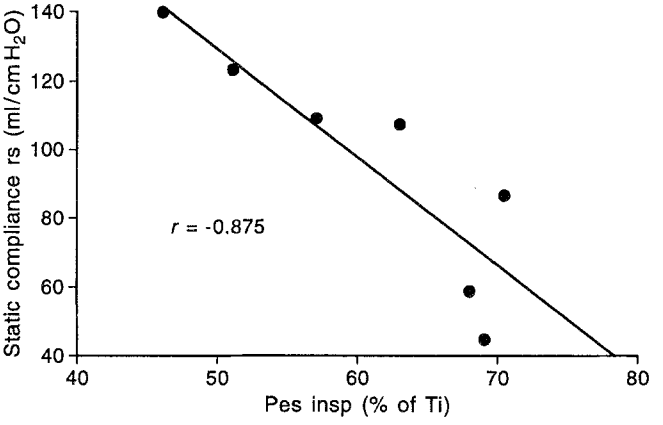


**Fig. 3** Correlation between the static compliance of the respiratory system and the duration of respiratory muscle contraction, expressed as percentage of Ti, at PSb

tients, being significantly correlated ($r = -0.87$ $p < 0.001$) to the static compliance of the respiratory system (Fig. 3). The pressure-time product of the esophageal pressure (PTPes) mainly accounted for changes in PTPdi, since Pga swings during inspiration, as well as during expiration, were small.

Most of the COPD patients (Fig. 1) made ineffective efforts (see Methods section). Table 3 illustrates the number of ineffective Pdi swings (i.e. efforts unable to trigger the ventilator) among a total of 50 efforts, and the total PTPdi in the same time interval, quantified as "ineffective", representing the metabolic work of the diaphragm without triggering a mechanical breath, and "effective" (done during mechanical breath). This phenomenon was almost eliminated during PSb−5, while at PSb+5, ineffective efforts were more frequent than during PSb, with a consequential increase in ineffective PTPdi.

## Effect of the application of PEEPe during PSV

Static PEEPi averaged 7.2±5.1 $cmH_2O$ (range 2.9−19.8 $cmH_2O$). Figure 4 demonstrates that PEEPi, stat was slightly (not significantly) greater than PEEPi, dyn under similar conditions, since the ventilatory parameters in CMV mode were close to the PSB ones (the respective values were: Vt 10.9±1.0 and 10.1±0.9 ml/kg; RR 13.2±2.2 and 12.5±3.7 breaths/min; and I/E 1:3.3 and 1:3.9).

**Table 3** Effect of various levels of PSV on PTPi and the number of ineffective efforts (*i/50* no. of ineffective efforts over a total of 50 inspiratory efforts, *iPTPdi* ineffective PTPdi, *ePTPdi* effective PTPdi)

| PSb | | | | PS+5 | | | PS−5 | | |
|---|---|---|---|---|---|---|---|---|---|
| Patient no. | i/50 | iPTPdi ($cmH_2O/s^{-1}$) | ePTPdi ($cmH_2O/s^{-1}$) | i/50 | iPTPdi ($cmH_2O/s^{-1}$) | ePTPdi ($cmH_2O/s^{-1}$) | i/50 | iPTPdi ($cmH_2O/s^{-1}$) | ePTPdi ($cmH_2O/s^{-1}$) |
| 1 | 17 | 79 | 152 | 22 | 101 | 109 | 5 | 31 | 288 |
| 2 | 23 | 333 | 169 | 31 | 387 | 121 | 8 | 131 | 777 |
| 3 | 21 | 38 | 101 | 29 | 52 | 74 | 2 | 5 | 125 |
| 4 | 2 | 6 | 292 | 10 | 22 | 235 | 0 | 0 | 343 |
| 5 | 6 | 10 | 390 | 6 | 7 | 332 | 0 | 0 | 431 |
| 6 | 0 | 0 | 105 | 0 | 0 | 89 | 0 | 0 | 123 |
| 7 | 0 | 0 | 185 | 8 | 59 | 144 | 1 | 3 | 289 |
| 8 | 13 | 96 | 274 | 22 | 177 | 208 | 4 | 43 | 388 |
| 9 | 0 | 0 | 240 | 9 | 35 | 219 | 0 | 0 | 266 |
| 10 | 11 | 41 | 144 | 19 | 66 | 138 | 10 | 49 | 262 |
| $\bar{x}$ | 9.3 | 60 | 205 | 16 | 91 | 167 | 3* | 26 | 288 |
| SD | 8.9 | 102 | 92 | 10.4 | 116 | 80 | 3.6 | 41 | 185 |

*$P < 0.01$ (difference between PS+5 and PS−5)

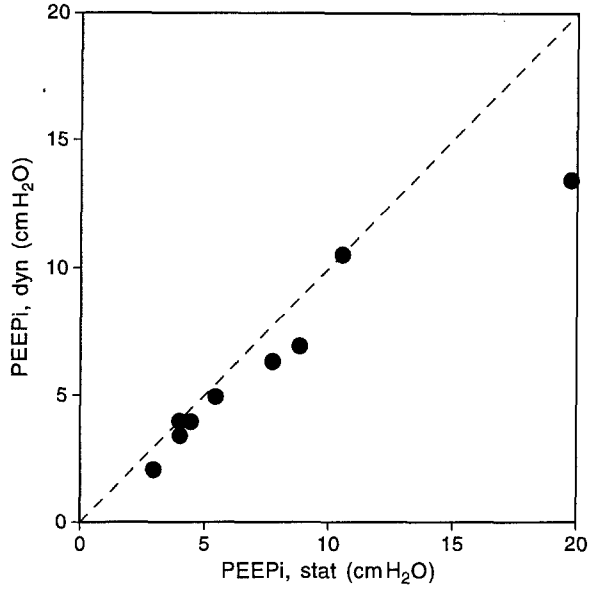


**Fig. 4** Identity plot for values of intrinsic PEEP determined with the occlusion method (PEEPi, stat) in CMV mode and during spontaneous breathing (PEEPi, dyn) at PSb

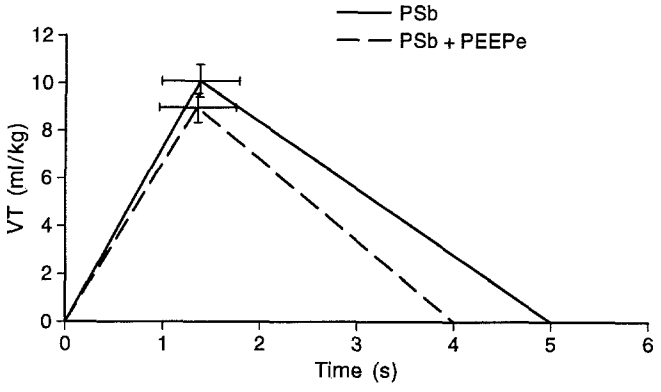


**Fig. 5** Ventilatory pattern (mean±SD) during PSb at zero PEEPe (*solid line*) and with the addition of an external PEEP (*dashed line*). Ti (inspiratory time) begins at 0 and ends at peak VT. Te (expiratory time) begins at peak VT and ends when crossing the *x*-axis

Since PSb was found to be the lowest PS level able to maintain adequate ventilation with good blood gas values and the lowest number of inefficient efforts, we applied a PEEPe equal to about 75% of static PEEPi only when this level was employed. As shown in Fig. 5, the respiratory pattern changed with the addition of PEEPe; tidal volume significantly decreased ($p<0.05$) from 10.1±0.9 ml/kg to 8.2±0.6 while breathing frequency increased, so that minute ventilation did not vary. Ttot significantly decreased ($p<0.05$) from 5.0±1.9 s to 3.9±1.7 s, due mainly to a reduction in Te.

The addition of PEEPe also influenced end-expiratory lung volume, as assessed by RIP. However, only small, insignificant increments were observed (89.1±47.5 ml).

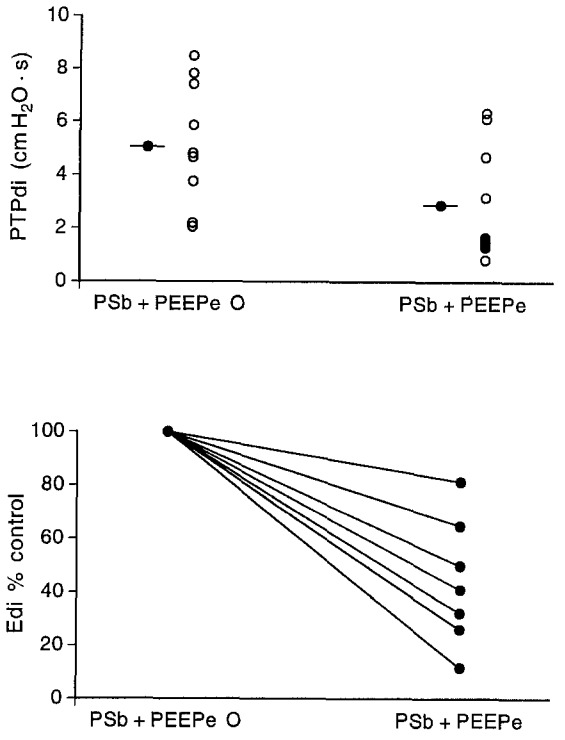


**Fig. 6** Individual and mean changes, after the application of an external PEEP on PSb, of two diaphragmatic indices of energy expenditure: the pressure-time product per breath (PTPdi) (*top*) and the integrated electromyogram (Edi) (*bottom*)

Figure 6 illustrates the significant decrease ($p<0.001$) in PTPdi per breath and Edi, with the application of PEEPe to PSb. Changes in PTPdi were mainly reflected by variations in PTPes. As shown in Table 4, the addition of PEEPe in those patients who made ineffective efforts reduced both the number of such efforts ($P<0.05$) and the "ineffective PTPdi". The dynamic intrinsic PEEP (PEEPi dyn) was also significantly ($P<0.01$) reduced when PEEPe was applied in addition to PSb (6.0±3.4 $cmH_2O$ vs. 1.8±1.7). A decrease in Edi/Pdi (−14.5%±8.5), even though not statistically significant, was observed after the application of PEEPe.

## Discussion

Pressure support ventilation (PSV) has classically been used during weaning from mechanical ventilation in patients affected by acute respiratory failure due to different pathologies [1, 2, 27] and immediately following cardiac surgery [28], since it has the ability to minimize the patient's work of breathing. PSV is an assisted mode of ventilation that supplies a constant level of positive airway pressure during spontaneous inspiratory efforts. It is generally accepted that this mode may allow the patient to maintain control of inspiratory and expiratory time and

**Table 4** Effect of PEEPe during PSb on PTPdi, no. of ineffective efforts, and PEEPi, dyn

| PSb | | | | | PSb + PEEPe | | | |
|---|---|---|---|---|---|---|---|---|
| Patient no. | i/50 | iPTPdi ($cmH_2O/s^{-1}$) | ePTPdi ($cmH_2O/s^{-1}$) | PEEPi dyn ($cmH_2O$) | i/50 | iPTPdi ($cmH_2O/s^{-1}$) | ePTPdi ($cmH_2O/s^{-1}$) | PEEPi dyn ($cmH_2O$) |
| 1 | 17 | 79 | 152 | 13.4 | 0 | 0 | 101 | 6.1 |
| 2 | 23 | 333 | 169 | 5.0 | 12 | 46 | 175 | 1.8 |
| 3 | 21 | 38 | 101 | 6.9 | 7 | 9 | 55 | 2.0 |
| 4 | 2 | 6 | 292 | 3.5 | 0 | 0 | 61 | 0.9 |
| 5 | 6 | 10 | 390 | 6.3 | 0 | 0 | 298 | 1.1 |
| 6 | 0 | 0 | 105 | 2.1 | 0 | 0 | 76 | 0 |
| 7 | 0 | 0 | 185 | 3.8 | 0 | 0 | 75 | 1.4 |
| 8 | 13 | 96 | 274 | 4.0 | 1 | 6 | 204 | 0.3 |
| 9 | 0 | 0 | 240 | 4.4 | 0 | 0 | 153 | 1.5 |
| 10 | 11 | 41 | 144 | 10.5 | 2 | 14 | 62 | 3.5 |
| $\bar{x}$ | 9.3 | 60 | 205 | 6.0 | 2.2* | 7.5 | 126 | 1.8** |
| SD | 8.9 | 102 | 92 | 3.4 | 4.2 | 14 | 80 | 1.7 |

*$P<0.05$; **$P<0.01$

to interact with a set pressure to determine the ultimate flow and tidal volume.

Our results demonstrate that this is not necessarily true in severe COPD patients with abnormally increased static compliance of the respiratory system and who are not yet ready to be weaned. In the present study, the application of various levels of PS in some patients led to a respiratory pattern characterized by a reduced ventilatory rate and increased expiratory time with several "ineffective efforts"; this happened despite satisfactory gas exchange.

The effort of the diaphragm depends not only on the amplitude of the pressure generated but also on the length of time the contraction is maintained (Ti, i.e. inspiratory time). This is easily assessed by the diaphragm pressure-time product (PTPdi), which may provide an estimate of muscle oxygen consumption [10]. In some COPD patients, i.e. patient 2, the PTPdi due to ineffective contractions exceeded that generating inspiratory flow. This is probably due to the greater number of ineffective than of effective inspiratory efforts, and to the prolonged time of contraction during the ineffective efforts for the same tidal Pdi (see Fig. 1). The Pdi values remain positive during the effective efforts for a markedly shorter period than the inspiratory time (Fig. 1). The same time course is also observed in the analysis of diaphragmatic activity from the EMG tracing, in contrast to other pathologies, where the time of muscular contraction is synchronous with inspiratory time. In our COPD patients, the time during which the respiratory muscles actively contract has a good inverse correlation with the static compliance of the respiratory system. The machine Ti is conditioned by the degree of distensibility of the respiratory system (compliance) and by the machine setting, including such factors as the level of PS and the flow threshold that has to be reached for the ventilator to cycle from inspiration to expiration. Because the ventilator continues to inflate the respiratory system long after the inspiratory muscles have ceased to contract, the next inspiratory attempt is likely to occur at a high lung volume, when airway pressure is still markedly positive; thus, the inspiratory effort will not always be sufficient to create a pressure gradient capable of being sensed by the ventilator.

Lowering the PS level ($-5$ $cmH_2O$ from PSb) brings a marked increase in PTPdi with an accompanying deterioration in blood gases. Conversely, the increasing of PS ($+5$ $cmH_2O$) leads to a further increase in the number of ineffective efforts and consequently of PTPdi.

Application of an external PEEP during mechanical ventilation in patients with airflow limitation is controversial [9]. After the enthusiastic reports of the early 1980s, in which it was shown that pursed lip breathing or PEEP may help ventilation by increasing lung volume and dilating the airway while reducing resistance and work of breathing, a paper by Tuxen et al. [29] demonstrated the "detrimental" effect of PEEPe during mechanical ventilation in severe airflow obstruction. This was recently questioned by Ranieri et al. [24] in COPD patients ventilated in the controlled mode. The addition of PEEPe in patients with airflow limitation and hyperinflation may, however, lead to the danger of a further increase in functional residual capacity (FRC). A recent paper by Fernandez Mondejar and coworkers [25] showed that the application of a PEEPe smaller than the PEEPi could avert this problem. In the present study, it was found that the addition of this level of PEEPe to the inspiratory pressure support could almost completely eliminate the ineffective efforts. As shown in Fig. 4, the PEEPi, dyn does not differ significantly from PEEPi, stat, recorded at a different mode of ventilation [CMV]; thus, PEEPe setting for PSV may be easily titrated using 75% of the static PEEPi, avoiding the use of the

gastroesophageal balloons. This is applicable in practice only if the ventilatory pattern during PS is similar to that during CMV, since, if they differ greatly, this method of titration could over- or underestimate the applied PEEP level needed.

Indeed, the reduction in Edi/Pdi after application of PEEP may be due to a more marked decrease in phrenic firing with respect to Pdi, which might suggest a reduction in diaphragmatic energy consumption. The blood gases remained basically unchanged both with and without application of PEEP. This was achieved with a respiratory pattern more closely resembling that usually observed in such patients when breathing spontaneously, with a reduction in Vt and an increase in respiratory rate. The addition of PEEPe also determined a reduction in tidal Pdi without altering Ti, so that TTdi, together with the Edi, was significantly reduced. This was probably due to a reduction in the gradient needed to initiate inspiration, caused by the observed decrease in dynamic PEEPi.

A reduction in diaphragmatic inspiratory activity may also be explained by changes in total lung resistance or compliance, which nevertheless did not vary in our study. Indeed, important changes in airway resistances during an assisted mode like CPAP were found only during induced asthma [30], probably due to reflex bronchodilation through stimulation of the extrathoracic tracheal stretch receptors and glottis reflex [31], mechanisms unlikely to be present in COPD patients. Another study [32] has suggested that a reduction in inspiratory muscle activity may be due to abdominal expiratory muscle recruitment, as, for example, during CPAP. This is not likely to be the case in the present study, since Pga remains basically flat during PSV both with and without PEEPe, even though active expiration may not be completely ruled out, even in presence of flat Pga.

In conclusion, we have shown that different levels of PS in COPD patients may lead to different breathing patterns and diaphragmatic energy expenditure. Particularly at PS levels able to maintain satisfactory arterial blood gases, the majority of the patients showed a prolonged expiratory time; this can result in a very high number of ineffective efforts and therefore in augmented diaphragmatic energy expenditure. Similar observations may be made during volume preset mechanical ventilation with big tidal volumes and long inspiratory times. The application of an adequate external PEEP on PSb eliminates this wasted metabolic work, and at the same time reduces the inspiratory effort needed to trigger ventilation without worsening blood gases.

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