

Haemodynamic effects of pressure support and PEEP ventilation by nasal route in patients with stable chronic obstructive pulmonary disease

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Abstract

Background—Intermittent positive pressure ventilation applied through a nasal mask has been shown to be useful in the treatment of chronic respiratory insufficiency. Pressure support ventilation is an assisted mode of ventilation which is being increasingly used. Invasive ventilation with intermittent positive pressure, with or without positive end expiratory pressure (PEEP), has been found to affect venous return and cardiac output. This study evaluated the acute haemodynamic effects of short sessions of pressure support ventilation by nasal mask, with and without the application of PEEP, in patients with severe stable chronic obstructive pulmonary disease and hypercapnia.

Methods—Nine patients with severe stable chronic obstructive pulmonary disease performed sessions lasting 10 minutes each of pressure support ventilation by nasal mask while undergoing right heart catheterisation for clinical evaluation. In random order, four sessions of nasal pressure support ventilation were applied consisting of: (1) peak inspiratory pressure (PIP) 10 cm H₂O, PEEP 0 cm H₂O; (2) PIP 10 cm H₂O, PEEP 5 cm H₂O; (3) PIP 20 cm H₂O, PEEP 0 cm H₂O; (4) PIP 20 cm H₂O, PEEP 5 cm H₂O.

Results—Significant increases in arterial oxygen tension (Pao₂) and saturation (SaO₂) and significant reductions in arterial carbon dioxide tension (Paco₂) and changes in pH were observed with a PIP of 20 cm H₂O. Statistical analysis showed that the addition of 5 cm H₂O PEEP did not further improve arterial blood gas tensions. Comparison of baseline values with measurements performed after 10 minutes of each session of ventilation showed that all modes of ventilation except PIP 10 cm H₂O without PEEP induced a small but significant increase in pulmonary capillary wedge pressure. In comparison with baseline values, a significant decrease in cardiac output and oxygen delivery was induced only by the addition of PEEP to both levels of PIP.

Conclusions—In patients with severe stable chronic obstructive pulmonary

disease and hypercapnia, pressure support ventilation with the addition of PEEP delivered by nasal mask may have short term acute haemodynamic effects in reducing oxygen delivery in spite of adequate levels of SaO₂.

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Intermittent positive pressure ventilation (IPPV) applied through a nasal mask has been shown to be useful in the treatment of chronic respiratory failure. It is usually delivered by standard volume cycled ventilators in assisted or control modes.¹ Continuous positive airway pressure (CPAP) administered by the nasal route has been suggested to facilitate respiratory muscle function during sleep in patients with severe chronic obstructive pulmonary disease (COPD).² Pressure support ventilation (PSV) supplies a constant level of positive airway pressure during spontaneous inspiratory efforts, allowing the patient to maintain control of inspiratory and expiratory time and to interact with the set pressure to determine the ultimate flow and tidal volume delivered.³⁻⁵ PSV has been used in different clinical situations⁶⁻⁹ and is being increasingly applied in acute respiratory failure with a facial mask.¹⁰ In patients with severe stable COPD, pressure support ventilation by nasal mask (NPSV) improves diaphragmatic function and alveolar ventilation^{11,12}; this effect may be enhanced by the application of external positive end expiratory pressure (PEEP).¹²

Mechanical ventilation may adversely affect haemodynamics. Invasive IPPV, with or without the application of PEEP, has been found to affect venous return and cardiac output.¹³⁻¹⁵ Other investigators have treated patients with chronic respiratory insufficiency with intermittent ventilation provided by negative pressure ventilators and different results on haemodynamics have been found with the iron lung, Cuirass or Ponchowrap ventilators.¹⁶⁻²¹

To our knowledge no information is available on the haemodynamic effects of non-invasive positive pressure ventilation apart from CPAP in patients with congestive heart failure.²² The aim of this study was therefore to test the acute haemodynamic effects of a short period of NPSV, with and without

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PEEP, in severe stable patients with COPD with hypercapnic respiratory insufficiency.

Methods

SUBJECTS

Studies were carried out on nine patients (eight men, age range 47–67 years), all of whom were smokers or ex-smokers with COPD (mean (SD) FEV₁/FVC, 39% (6%) and respiratory insufficiency (PaO₂, 49 (7) mm Hg; PaCO₂, 56 (7) mm Hg) undergoing right cardiac catheterisation for clinical purposes. The demographic characteristics of the study population are shown in table 1.

At the time of the study the patients had not suffered an exacerbation of respiratory symptoms for several months. No patient showed clinical signs of left ventricular disease or systemic arterial hypertension. One patient had undergone coronary artery bypass surgery 10 years earlier. All but one of the patients were receiving long term oxygen treatment; all but one was taking oral sustained theophylline, three patients were taking inhaled steroids and β agonists, and one was receiving oral β agonists. Two were taking digoxin, two nifedipine, and one transdermal release nitrate. No changes in medical or oxygen treatment were made during the two weeks preceding the study. All patients were familiarised with the technique of NPSV without PEEP for at least two weeks. All patients gave their informed consent for participation in the study which was approved by the ethical committee of Clinica del Lavoro Foundation.

PULMONARY TESTS

Dynamic lung volumes were evaluated with a water spirometer (Biomedin, Padova, Italy) in the seated posture, and static lung volumes were assessed by the helium dilution method. The predicted values used were those of Quanjer.²³ An automated analyser (Radiometer ABL 500, Copenhagen, Denmark) was used to measure gas tensions in blood samples drawn from the radial artery.

VENTILATORY TESTS

After baseline tests, the patients were taught to perform NPSV administered by a bilevel airway pressure ventilator (BIPAP, Respironics, Monroeville, Pennsylvania,

USA) while seated. BIPAP is a nasal CPAP blower modified with a solenoid system that allows timed cyclical delivery of positive airway pressure at two different levels, both in "spontaneous" (assisted) and controlled mode; the details have been extensively described elsewhere.^{11,24} In the "spontaneous" mode inspiratory positive peak inflation pressure (PIP) up to a maximum of 22 cm H₂O, and external PEEP can be set, but the patient triggers inspiration and expiration. In other words, pressure support ventilation can be delivered with the ability to add PEEP if required. NPSV was applied through a comfortable, tightly fitting nasal mask (Respironics, Monroeville, Pennsylvania USA).

On the two days preceding the haemodynamic studies patients underwent several learning sessions with different levels of PIP, with and without PEEP, by BIPAP in "spontaneous mode": (1) PIP set at 10 cm H₂O at the mask with no PEEP (nine patients); (2) PIP set at 10 cm H₂O with PEEP at 5 cm H₂O at the mask (seven patients); (3) PIP set at 20 cm H₂O with no PEEP (nine patients); (4) PIP set at 20 cm H₂O with PEEP at 5 cm H₂O (seven patients).

HAEMODYNAMIC STUDIES

On the third day patients underwent pulmonary artery catheterisation. After baseline measurements were made in the supine position, they again performed the four different sessions of NPSV, each of 10 minutes' duration. NPSV sessions were delivered randomly with no interval between each session. By the percutaneous approach of Seldinger, a 7 Fr balloon tipped thermodilution pulmonary artery catheter (Edwards Laboratory, Santa Ana, California, USA) was positioned under fluoroscopy in one of the main pulmonary arteries. Filling pressures were measured in the standard manner and were zero referred to the level of the right atrium. The pulmonary artery pressure (PAP), right atrial pressure (RAP), pulmonary capillary wedge pressure (PWP), systemic blood pressure directly measured via a catheter inserted in the radial artery (Hewlett-Packard pressure conditioner HP 8805 D and transducer HP 1290 A), and the air pressure delivered at the mask (Honeywell transducer \pm 300 cm H₂O, Freeport, Illinois, USA) were continuously monitored and recorded on a polygraph (Gould ES 1000) together with the ECG. Radial artery pressure tracings were available in seven of nine patients because of the difficulty of inserting an arterial catheter in two patients. Cardiac output was estimated by the standard thermodilution technique with a cardiac output computer (Edwards 9520A, Edwards Laboratory, Santa Ana, California, USA) and the average of three measurements was recorded.

All haemodynamic and blood gas measurements were made at baseline and during the final minute of each NPSV session. Continuous monitoring of blood pressure, PAP, RAP, and ECG helped to ensure that,

Table 1 Mean (SD) demographic and physiological characteristics.

Sex (M:F)	8:1
Age (y)	57 (7)
Weight (kg)	64 (17)
Height (cm)	162 (5)
Body surface area (m ²)	1.66 (0.20)
Vital capacity (% predicted)	44 (11)
FEV ₁ /FVC (%)	39 (6)
Residual volume (% predicted)	211 (66)
PaO ₂ (mm Hg)	49 (7)
PaCO ₂ (mm Hg)	56 (7)
pH	7.37 (0.02)

FEV₁—forced expiratory volume in one second; FVC—forced vital capacity; PaO₂—arterial oxygen tension; PaCO₂—arterial carbon dioxide tension.

Table 2 Mean (SD) changes in blood gases during different sessions of nasal pressure support ventilation (NPSV)

	PaO ₂ (mm Hg)	SaO ₂ (%)	PaCO ₂ (mm Hg)	pH
Baseline	49 (7)	85 (8)	56 (7)	7.37 (0.02)
PIP 10 PEEP 0	55 (8)	89 (7)	54 (6)	7.37 (0.03)
PIP 10 PEEP 5	53 (8)	89 (8)	55 (9)	7.38 (0.04)
PIP 20 PEEP 0	59 (8)*	91 (5)*	50 (7)*	7.39 (0.03)*
PIP 20 PEEP 5	58 (6)	92 (5)	49 (9)*	7.41 (0.03)*

PaO₂—arterial oxygen tension; SaO₂—arterial oxygen saturation; PaCO₂—arterial carbon dioxide tension; PIP—peak inspiratory pressure; PEEP—positive end expiratory pressure.
*p < 0.01, each level of NPSV v baseline

at the time measurements were made, a steady state had been reached. Haemodynamic monitoring continued after the ventilator was stopped until values returned to baseline which usually took about five minutes.

NPSV was performed using a fractional inspired oxygen (FIO₂) value of 0.21 except for two patients who performed the study (baseline and ventilation measurements) on oxygen at an FIO₂ sufficient to maintain a SaO₂ above 90%.

The results are expressed as mean (SD) values. A *t* test for paired data with Bonferroni's adjustment was used to compare each mode of NPSV with baseline and to test the effect of adding PEEP to both levels of PIP. Statistical significance was defined as p < 0.01.

Results

All patients tolerated both levels of PIP. Two patients did not tolerate the application of PEEP because of a sense of discomfort during exhalation.

BLOOD GASES

The results of blood gas analysis before and after 10 minutes of each session of NPSV are shown in table 2. During NPSV PaO₂ increased significantly and PaCO₂ decreased significantly at a PIP of 20 cm H₂O. The addition of PEEP did not further improve blood gas tensions.

HAEMODYNAMICS

Figures 1 and 2 show a typical polygraphic recording of the different levels of ventilation. Haemodynamic parameters before and after 10 minutes of each session of ventilation are shown in table 3. All patients had moderate to severe pulmonary arterial hypertension. No significant change in heart rate, systolic blood pressure, PAP, RAP, and pulmonary vascular resistance was observed with all four levels of ventilation. Compared with baseline values, all levels of ventilatory support except PIP at 10 cm H₂O with no PEEP induced a significant increase in PWP. Only the application of PEEP to both levels of PIP induced small but significant reductions in cardiac output and in oxygen delivery (DO₂). Compared with measurements made under PIP alone, the addition of PEEP to both levels of PIP resulted in a reduction in cardiac output and DO₂ in six out of seven patients. Reductions in cardiac output and DO₂ in comparison with PIP alone did not reach statistical significance even when statistics included only these six patients. The one patient whose cardiac output and DO₂ did increase with the addition of PEEP compared with PIP alone had undergone previous coronary artery bypass surgery. The observed changes did not induce any subjective complaint.

Discussion

Although the results of our study do not differ substantially from what would be expected with the standard use of PSV and PEEP, this

Figure 1 Polygraphic recordings in the basal state and during nasal pressure support ventilation with peak inspiratory pressure (PIP) of 10 cm H₂O without and with addition of positive end expiratory pressure (PEEP) of 5 cm H₂O in a representative patient. Chart speed 5 mm/s. BP—blood pressure; PAP—pulmonary artery pressure; P airway—pressure at the mask; RAP—right atrial pressure.

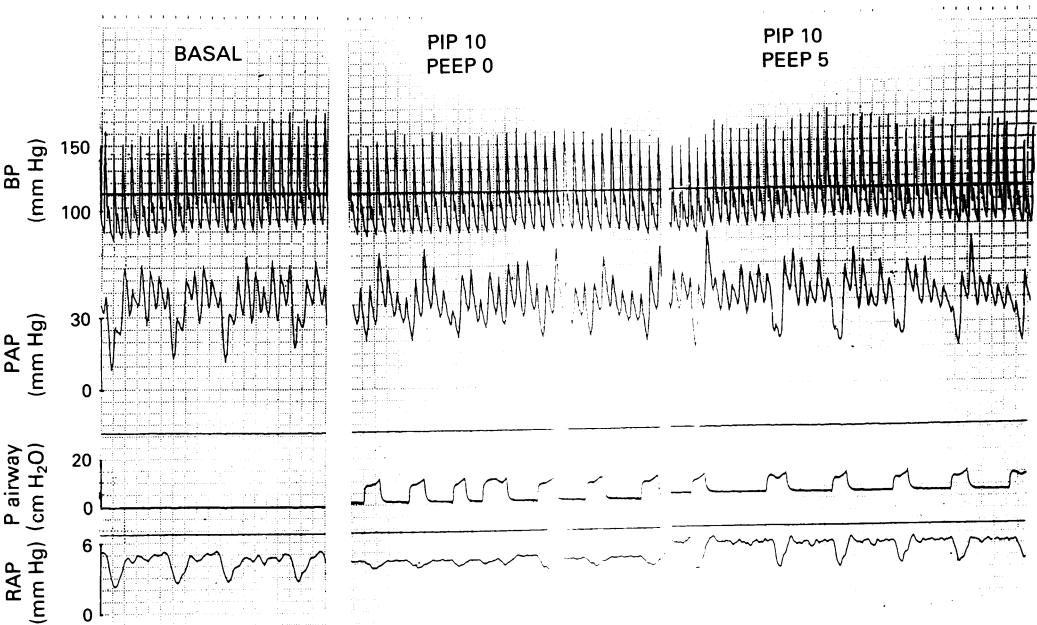
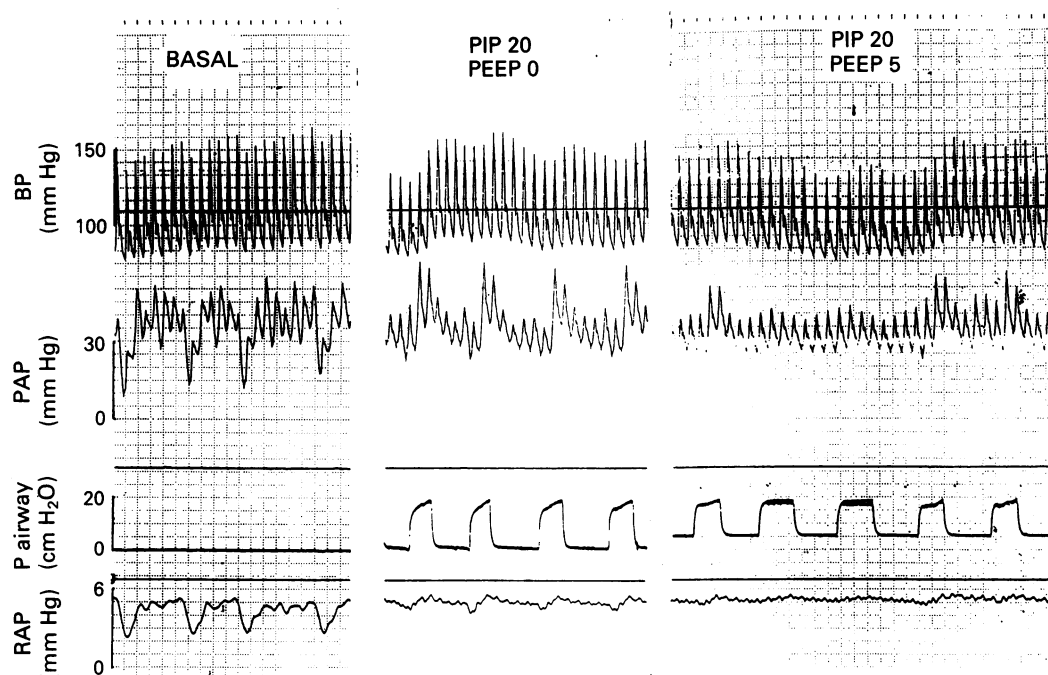


Figure 2 Polygraphic recordings in the basal state and during nasal pressure support ventilation with peak inspiratory pressure (PIP) of 20 cm H₂O without and with addition of positive end expiratory pressure (PEEP) of 5 cm H₂O. Chart speed 5 mm/s. BP—blood pressure; PAP—pulmonary artery pressure; P airway—pressure at the mask; RAP—right atrial pressure.



is the first study of the acute haemodynamic effects on these variables of non-invasive ventilation delivered to patients with COPD. As previously demonstrated,^{11,12} the short time (10 minutes) of application of NPSV with a PIP of 20 cm H₂O improved the arterial blood gas tensions, an effect not further increased by the addition of 5 cm H₂O of PEEP. Only when PEEP was added to both levels of PIP was a reduction in cardiac output observed compared with baseline levels. No improvement in Do_2 was seen with any level of ventilation, and the application of PEEP resulted in a small but significant reduction in Do_2 compared with baseline values.

Mechanical ventilation affecting transpulmonary gradients may greatly affect haemodynamics. In intubated patients, continuous positive pressure ventilation (CPPV) has been shown to depress cardiac output and systemic blood pressure to a degree related to the amplitude of applied PEEP.^{13,14} This effect was attributed initially to the fall in venous return resulting from the rise in pleural pres-

sure. This concept was challenged after the finding that right atrial transmural pressure was unchanged or was even elevated during ventilation with PEEP.²⁵ Diastolic constriction of the ventricles by the inflated lungs occurs both during spontaneous and positive pressure ventilation.²⁶⁻²⁹ The right ventricle may therefore suffer from a relative increase in afterload due to the rise in pulmonary vascular resistance resulting from compression of intra-alveolar vessels,³⁰ but these changes are considered small when compared with the haemodynamic effects of PEEP. Preload seems the main factor limiting cardiac output, especially in view of unchanged myocardial contractility.³¹ The fall in cardiac output and blood pressure is not usually followed either by reflex tachycardia or vasoconstriction, which is what was observed in our patients, suggesting that abnormal neurohormonal responses may contribute to the haemodynamic response to CPPV.³²

Haemodynamics during IPPV without PEEP have received less attention by previous investigators. The fall in pulmonary arterial flow with each inspiration may be attributed to the same preload limiting mechanisms as operate during CPPV.³³ Nocturnal nasal CPAP has become the most important treatment for obstructive sleep apnoea and it has been used in selected patients with combined Cheyne-Stokes respiration and congestive heart failure.²² Leech *et al*³⁴ found no significant effects on heart rate, PAP, ventricular size, or cardiac index assessed non-invasively with increasing positive intrathoracic pressures and consequent lung hyperinflation in 19 normal volunteers and six patients with sleep apnoea. The data on the haemodynamic effects of PSV are few. Prakash and Meij⁷ observed that PSV with PIP levels comparable to those in our study (20–22 cm H₂O) did not induce haemodynamic changes in intu-

Table 3 Mean (SD) changes in haemodynamics during different sessions of nasal pressure support ventilation (NPSV)

	Baseline	PIP 10 PEEP 0	PIP 10 PEEP 5	PIP 20 PEEP 0	PIP 20 PEEP 5
Heart rate (beats/min)	78 (10)	79 (12)	80 (9)	82 (11)	83 (9)
Systolic BP (mm Hg)	131 (16)	135 (14)	137 (14)	134 (16)	126 (18)
Diastolic BP (mm Hg)	78 (22)	75 (11)	76 (12)	76 (11)	74 (14)
Cardiac output (l/min)	5.1 (0.6)	4.9 (0.9)	4.5 (0.6)*	4.7 (0.9)	4.2 (0.8)*
PAP (mm Hg)	27 (6)	28 (6)	27 (6)	28 (6)	28 (6)
PWP (mm Hg)	7 (2)	9 (2)	9 (2)*	11 (2)*	11 (2)*
RAP (mm Hg)	3 (2)	4 (2)	4 (1)	4 (2)	6 (3)
PVR (dynes/s/cm ²)	298 (70)	306 (79)	309 (83)	301 (106)	336 (129)
Do_2 (ml/min/m ²)	422 (45)	417 (73)	382 (46)*	408 (79)	367 (70)*

BP—blood pressure; PAP—pulmonary artery pressure; PWP—pulmonary capillary wedge pressure; RAP—right atrial pressure; PVR—pulmonary vascular resistance; Do_2 —rate of oxygen delivery; PIP—peak inspiratory pressure; PEEP—positive end expiratory pressure.

*p < 0.01 each level of NPSV v baseline.

bated patients undergoing coronary artery bypass surgery. Our results in patients with stable COPD with hypercapnic respiratory insufficiency differ. As positive pressure acts as a ventricular assist device by reducing left ventricular afterload and direct ventricular compression,²⁹ the deleterious effects of positive pressure upon venous return are minimal in patients with poor left ventricular function since they have flat atrial pressure-volume curves. The net effect is therefore unchanged or improved haemodynamics. Left ventricular function in our patients may be indirectly inferred to be satisfactory by their relatively normal levels of PWP and cardiac output. In patients with normal left ventricular function the ventricular assist will be relatively small, but the effect on atrial filling will predominate thereby explaining the fall in cardiac output. In our study NPSV, with and without PEEP, induced haemodynamic changes and, in the short term, reduced DO_2 in spite of the ability of NPSV to improve levels of blood gases. In a previous study¹¹ we observed that NPSV, at a PIP level of 20 cm H_2O without PEEP, was able to increase significantly alveolar ventilation and PaO_2 . As found in an earlier study in patients with COPD,³⁵ a reduced abdomino-thoracic gradient across the diaphragm could explain the reduction in cardiac output with the application of NPSV. NPSV induced haemodynamic changes comparable to those observed in intubated patients undergoing CPPV. In fact, cardiac output decreased significantly and a significant increase in PWP was observed, PVR remaining unchanged. In our study, however, the maximal decrease in cardiac output observed was 30% (in a patient ventilated with PIP of 20 cm H_2O and PEEP of 5 cm H_2O), and overall the reductions in cardiac output seemed not to have clinical relevance, although they induced a consequent reduction in DO_2 . Biondi *et al*³⁶ found a non-significant 11% decrease in cardiac index at levels of PEEP above 10 cm H_2O .

We observed reductions in the respiratory oscillations of diastolic PAP with different levels of PIP and with the addition of PEEP (figs 1 and 2) which may be the result of a reduction in pleural pressure.³⁷ This was found in a separate study in the same patients who, under NPSV, showed a progressive reduction in diaphragmatic electromyographic activity and in pleural (oesophageal) pressure with increasing levels of PIP. This reduction was enhanced by the addition of 5 cm H_2O of PEEP.¹²

This study has some limitations. Firstly, although the duration (10 minutes) of measurement of the haemodynamic effects of PIP/PEEP was short, a period of 10 minutes is considered sufficient to obtain stable and reproducible results,^{12 22 38} and the four ventilatory modes were applied in succession and randomised to avoid any carry over effect. Furthermore, blood pressure, PAP, RAP, and ECG were recorded in real time during the study and at the moment of measurement these parameters were stable. An observation

limited to 10 minutes of each mode of NPSV, however, may not be representative of a genuine therapeutic effect. This makes it difficult to draw conclusions about the addition of PEEP, as most patients with stable COPD would use NPSV for many hours overnight. All patients showed a rapid drop in PaCO_2 on the institution of 20 cm H_2O of PIP which may play a part in the haemodynamic changes seen. With longer use of ventilation, however, homeostatic mechanisms are likely to come into play.³⁹ These include salt and water retention due to activation of the renin angiotensin system as a consequence of the reduced cardiac output, or a reduction in atrial natriuretic factor as a direct effect of PEEP on right atrial size. These mechanisms tend to increase cardiac filling pressures and restore cardiac output. Once a new stable level is reached, cardiac output and DO_2 may improve. The important clinical implication of this study, however, is that FiO_2 should be increased initially to improve DO_2 , even if arterial blood gas tensions are adequate, in an attempt to offset the fall in cardiac output. Lastly, two of the nine patients who performed the study were receiving oxygen. Increasing the FiO_2 would influence PVR; nevertheless, oxygen was administered during both basal measurements and ventilation in order to maintain a SaO_2 above 90%, so the relative changes in haemodynamic parameters should not have been greatly affected.

In conclusion, although the observed changes in haemodynamics had no effect on blood pressure and were not related to clinical signs, this study may suggest that the addition of PEEP to NPSV adds nothing to NPSV alone in improving oxygen delivery in stable patients with COPD.

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