

Pressure support ventilation via face mask in acute respiratory failure in hypercapnic COPD patients

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Abstract. *Objective:* To test whether non-invasive ventilation via facial mask could reduce the need for tracheal intubation when mechanical ventilation must be initiated in COPD patients.

Design: Open prospective interventional study.

Setting: General Intensive Care Service of a County Hospital.

Patients: We have studied 12 COPD patients during 14 episodes of acute exacerbation of chronic respiratory failure who failed to improve with intensive medical therapy and showed impairments in severe respiratory acidosis and/or hypercapnic encephalopathy leading their attending physicians to order mechanical ventilation

Interventions: In these circumstances, a trial of pressure-support (PS) ventilation (Servo Ventilator 900C®) via facial mask Vital Signs Inc.®) was performed. The level of pressure support was adjusted to obtain a tidal volume >400 ml. If the patient deteriorated, tracheal intubation and standard mechanical ventilation were performed.

Measurements and results: Measurements are presented as means ± SEM. A pressure-support level of 14 ± 3 cmH₂O was used during a period of 8 ± 4 h. Low levels of external PEEP were used in 4 patients, while it generated excessive leaks in the others. Significant differences ($p < 0.05$ ANOVA for repeated measures) in data obtained on admission, when patients deteriorated and after pressure support was administered were only observed in PaCO₂ (68 ± 3 versus 92 ± 3 versus 67 ± 3 mmHg), arterial pH (7.27 ± 0.03 versus 7.19 ± 0.02 versus 7.31 ± 0.01), SaO₂ (60 ± 4 versus 86 ± 3 versus 92 ± 1%) and respiratory rate (35 ± 2 versus 32 ± 2 versus 23 ± 1 breaths · min⁻¹). Three patients needed intubation and one of them died in the ICU.

Conclusion: Non-invasive ventilation (pressure-support) via face mask may reduce the need for tracheal intubation in the severe hypercapnic failure of COPD patients.

Key words: Mechanical ventilator – COPD – Hypercapnic failure – Mask ventilator

Patients with chronic obstructive pulmonary disease frequently need mechanical ventilatory support for acute exacerbations of the disease or by concurrent illness other than COPD, i.e. trauma, surgery or intoxications [1]. Increased airway resistance, mucous plugging and respiratory muscle fatigue also play a role in the development of acute respiratory failure. In this setting, mechanical ventilation offers a transient help against all these factors, but significant side effects may occur [2]. When an acute deterioration of COPD occurs, there is no wide consensus about the best moment to start mechanical ventilation. Physicians need to weight up the risks of delaying intubation (respiratory arrest, arrhythmias, damage to other organs) against those of early but unnecessary intubations (tracheal injury, longer ventilatory assistance, nosocomial pneumonia, weaning difficulties) [3].

A new perspective for physicians dealing with COPD patients with severe hypercapnic failure appeared with the advent of noninvasive ventilation. While it can be administered by external negative pressure (iron-tank) or chest wall oscillations [4, 5], only with the use of nasal or face masks has it improved acceptance. It has been proved to be of benefit for long periods in patients with chronic neuromuscular disorders but few clinical reports have shown improvement in COPD patients [6–9].

Additionally, the recent use of pressure support ventilation (PS) as a mode of partial support either during weaning or as a conventional ventilatory strategy offers a more physiological and comfortable method of improving ventilation. The usefulness of PS via face mask to improve the course of acute exacerbations of COPD in a group of patients when compared with historical controls has been proven [10]. In a very recent paper, Meduri et al. [11] showed a beneficial effect of PS via face mask to avoid endotracheal intubation in severe hypercapnic COPD patients.

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The objective of this study was to further test whether noninvasive face mask PS ventilation may provide sufficient and safe ventilatory support in order to avoid intubation in cases of very severe hypercapnic failure in COPD patients, who, in standard conditions outside the protocol, would be immediately intubated.

Patients and methods

Patients with hypercapnic respiratory failure entered the study consecutively after admission to the ICU of the Hospital de Sabadell for impaired clinical condition despite intensive medical care in the Emergency Room. We have studied 12 COPD patients during 14 episodes of acute exacerbation of chronic respiratory failure. Two patients (number 1 and 3) entered the study twice but in different hospitalization periods. The protocol was approved by the Research Committee of our Institution and informed consent was obtained from patients' relatives in each case.

The patients's demographic characteristics are shown in Table 1. We worked out their APACHE II score [12] and the associated mortality risk was calculated. Diagnosis of COPD was based on clinical history and previous spirometric data. Only one case (number 9) entered the study due to a sudden exacerbation during her stay in the ICU. The intensive medical treatment included oxygen supply by means of Venturi masks, bronchodilators (salbutamol and ipatropium bromide in aerosols) and intravenous aminophylline, corticosteroids and antibiotics.

Patients were accepted in the study when their attending physicians, who were not involved in the study, decided that endotracheal intubation and mechanical ventilation could no longer be delayed. The uniform criteria for this decision were: severe worsening in hypercapnia, acidosis or encephalopathy.

Criteria for excluding patients from the study included the following: (1) systolic blood pressure lower than 90 mmHg or the use of a high dose of vasopressors, (2) presence of unstable angina or recent (<3 months) myocardial infarction, (3) need for endotracheal intubation to protect the airways (coma or seizure disorders).

At this moment, the research team started a trial of noninvasive mechanical ventilation via face mask in the pressure support mode. When the trial was well tolerated and the clinical condition improved, we decided to maintain PS without interruptions. On the other hand, when PS was judged to be ineffective, i.e. when the patients' condition which had given rise to supported ventilation did not improve, endotracheal intubation and standard mechanical ventilation were performed.

Pressure support was supplied by a commercial ventilator (Servo Ventilator 900 C, Siemens Elema, Solna, Sweden) and standard circuitry, connected to a pneumatic sealed face mask (Downs CPAP Mask, Vital Signs Inc, Totowa, NJ) fixed with rubber head straps.

Ventilators were used without any additional calibration other than the regular manufacturer's maintenance. The trigger sensitivity was adjusted to 0.5 cmH₂O, and the working pressure to 60 cmH₂O in order to obtain a very high inspiratory flow delivery. Oxygen concentration was adjusted to the previous level supplied to patients, but was progressively reduced while maintaining hemoglobin saturation greater than 90% measured by pulse oximetry (HPM 1020 A, Palo Alto, CA). The level of pressure support was increased in steps of 3 cmH₂O with a minimum target expiratory tidal volume of 400 ml provided that there was no leakage around the mask.

If patients showed an elevated inspiratory effort to trigger the ventilator, we added external end-expiratory positive pressure (PEEP) in steps of 3 cmH₂O, while watching for a reduction in the apparent intercostal or sternocleidomastoid contraction [13]. If high leakage around the mask induced by PEEP, it was not used because leakage reduced the ability of patients to effectively trigger the pressure support system.

When patients were too unco-operative, mostly due to hypercapnic encephalopathy with hypotonic facial and pharyngeal muscles, the mask was manually adjusted by nurses or physicians [14] during the period needed to determine whether PS was effective or not, ordinarily 10 to 20 min.

When the attending physicians decided that the acute phase indicating mechanical ventilation had disappeared, PS was stopped and the mask was removed without any kind of weaning and oxygen at low concentrations was then supplied by Venturi mask.

During the whole protocol, patient surveillance was based on the standard equipment of our ICU (Hewlett Packard M1166A, Palo Alto, CA) composed of ECG (three channels) and heart rate, blood pressure either noninvasive or by means of an indwelling arterial cannula and hemoglobin saturation by pulse oximetry.

After the first 60 min of PS trial, clinical data and arterial blood gases were collected. Blood gas analysis was performed by means of a ABL 500- OSM 3 Blood Gas System (Radiometer Copenhagen, Denmark). We calculated the oxygenation index (arterial PO₂/alveolar PO₂) to explore whether arterial oxygen tension changes were related to improved gas exchange which could not be explained by an increase in alveolar ventilation alone [15]. Alveolar pressure was calculated as PAO₂ = (PB - P_{H₂O}) × FiO₂ - (PaCO₂/0.8), where PB is barometric pressure and we assumed a fixed P_{H₂O} of 40 mmHg.

An additional set of determinations were performed within 24 h of the discontinuation of PS in order to evaluate the maintenance of benefits of PS.

Table 1. Patient demographic data, baseline spirometric values, arterial blood gases at room air on admission, ICU stay and outcome

Case no.	Age (year)	Sex	Diagnostic	FVC (ml)	FEV ₁ (ml)	PaO ₂ (mmHg)	PaCO ₂ (mmHg)	Apache II score	Mortality risk	PS level (cmH ₂ O)	ICU stay (days)	Intubation	Survival
1	75	F	COPD, heart failure	960	580	51	63	18	22	14	12	Yes	Yes
2	74	F	COPD, pulmonary edema	NA	NA	35	60	15	15	12	8	No	Yes
3	74	F	COPD, scoliosis	NA	NA	32	69	20	27	16	4	No	Yes
4	70	F	COPD	1550	680	59	54	17	20	22	8	No	Yes
5	74	M	COPD	NA	NA	41	65	19	25	20	3	No	Yes
6	85	M	COPD, pneumonia	2240	1060	43	56	25	53	15	13	Yes	Yes
7	67	M	COPD	1130	370	22	105	13	12	14	3	No	Yes
8	66	M	COPD, pneumonia	1570	770	40	64	16	23	14	6	No	Yes
9	74	F	COPD, heart failure	960	580	46	80	12	12	14	7	No	Yes
10	74	M	COPD	1730	660	29	74	27	54	15	3	No	Yes
11	69	M	COPD	2130	740	65	64	25	44	12	27	Yes	No
12	74	F	COPD, scoliosis	NA	NA	32	75	20	27	10	4	No	Yes
13	66	M	COPD	1510	410	57	58	16	18	10	3	No	Yes
14	65	M	COPD	2650	720	30	70	15	15	15	6	No	Yes
Mean	72			1643	657	42	68	18.4	26.2	14.5	8		
± SEM	1.4			150	52	3.3	3.3	1.2	3.8	3.3	1.7		

Apache, Acute physiologic and chronic health evaluation; ICU, intensive care unit; COPD, chronic obstructive pulmonary disease

Patients' subsequent clinical course was followed up during a period of six months and the number and reasons for new hospital admissions and the need for mechanical ventilation were recorded. Additionally, their quality of life in terms of number of physical dependencies, Karnofsky index, and subjective perception was evaluated by personal interview 6 months after discharge from the ICU.

Statistical analysis

We evaluated patients on admission to the Emergency Room (ADMISSION), after the deterioration period leading up to PS (PRE-PS), after the first hour on PS (DURING PS) and after 24 h of discontinuation of PS (AFTER 24 h). We compared average responses for all variables at the evaluation times using analysis of variance (ANOVA) for repeated measures and, when significant differences were found, Newman-Keuls multiple comparison tests with significance level at $p < 0.05$ were performed.

Results

All the patients enrolled in the study completed the whole trial without incidence: no mask intolerances were observed and hemodynamic disturbances were not detected. The duration of PS averaged 8 ± 4 hours and the level of PS used was 14.5 ± 3.3 cmH₂O. Three patients (21%) did not clearly improve with PS and finally received endotracheal intubation: two of them by sputum retention due to an inability in achieving a productive cough and the third because of a superimposed crisis of bronchospasm provoking a sudden respiratory crisis with signs of imminent respiratory arrest. One of them (7% of the whole population studied) died after 27 days in the ICU because of a septic shock due to *Pseudomonas aeruginosa* pneumonia.

The mean stay (mean \pm SEM) in ICU was 7.6 ± 1.7 days, differing greatly among patients not needing intubation (5.0 ± 2.0 days) and those needing intubation (17.3 ± 8.4 days) ($p < 0.001$) (Fig. 1).

Hemodynamic and gas exchange data is shown in Table 2. While minimal clinical hemodynamic changes were observed at each step of the protocol, very significant changes were found in respiratory status (PaCO₂, arterial pH and respiratory rate).

These changes between admission and Pre-PS periods were in accordance with the attending physician's opinion

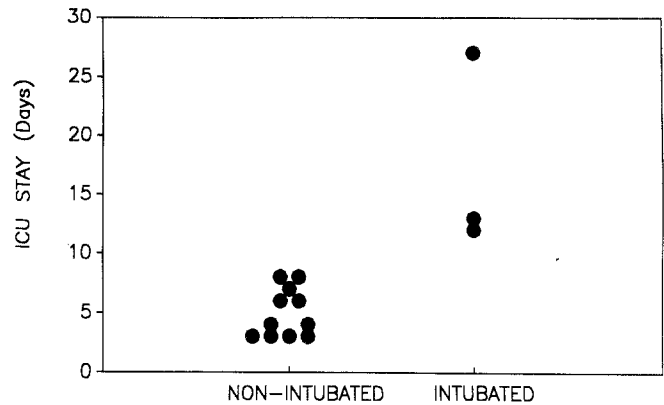


Fig. 1. Days in ICU of nonintubated patients versus patients needing tracheal intubation

that the patients condition was worsening, leading to very high PaCO₂ (68 ± 3.3 vs 92 ± 3.6 mmHg $p < 0.001$) and very low pH (7.27 ± 0.03 vs 7.19 ± 0.02 $p < 0.001$) despite significant increment in SaO₂ (60 ± 4.5 vs $86 \pm 3.3\%$ $p < 0.001$).

The main beneficial effect of PS appeared as a reduction in PaCO₂ (92 ± 3.6 vs 67 ± 3.7 mmHg $p < 0.001$) (Fig. 2) with related improvement in pH (7.19 ± 0.02 versus 7.31 ± 0.02 $p < 0.001$) (Fig. 3) and secondary, but non significant improvement in oxygen saturation (86 ± 3.3 versus $92 \pm 1.1\%$ $p < 0.1$), while respiratory rate reduced from 32 to 23 breaths per minute ($p < 0.001$).

We failed to demonstrate significant differences among patients not needing intubation and those needing intubation in terms of diagnosis, age (71 ± 1 versus 76 ± 5 year), Apache II score (17 ± 4 versus 23 ± 4), gas exchange and hemodynamics, either on admission or previous to PS and after PS.

Subjective tolerance of the mask was very good and no patients need to be excluded from the study due to mask intolerance. No cases of facial skin necrosis nor clinically important aerophagia were observed, probably due to the short duration of PS. Pain in the nasal skin area was frequent but easily alleviated when pressure over the mask was slightly reduced.

In 4 cases, we were able to add external PEEP (5.7 ± 0.8 cmH₂O) to counterbalance suspected auto-

Table 2. Results expressed as mean \pm SEM during each step of the study

	Admission	Pre-PS	During PS	After 24 h
Heart rate (min ⁻¹)	105 \pm 5.5	112 \pm 6.5	100 \pm 5.6	92 \pm 4.1
Systolic arterial pressure (mmHg)	142 \pm 6.2	137 \pm 5.9	123 \pm 3.6	124 \pm 4.4
Diastolic arterial pressure (mmHg)	76 \pm 2.3	83 \pm 4.4	71 \pm 3.4	68 \pm 2.7
Respiratory rate (min ⁻¹)	35 \pm 2.5	32 \pm 2.1	23 \pm 0.9*	24 \pm 1.5
FIO ₂	0.21 \pm 0.00*	0.40 \pm 0.05	0.36 \pm 0.02	0.31 \pm 0.02
pH	7.27 \pm 0.03	7.19 \pm 0.02*	7.31 \pm 0.02	7.36 \pm 0.01
PaO ₂ (mmHg)	42 \pm 3.3	98 \pm 25.3	76 \pm 4.7	74 \pm 7.9
PaCO ₂ (mmHg)	68 \pm 3.3	92 \pm 3.6*	67 \pm 3.7	63 \pm 4.0
Bicarbonate (mmol/l)	34 \pm 2.0	37 \pm 2.4	34 \pm 2.2	35 \pm 1.9
Base excess (mmol/l)	6 \pm 1.9	6 \pm 2.5	7 \pm 2.2	9 \pm 1.8
SaO ₂ (%)	60 \pm 4.5*	86 \pm 3.3	92 \pm 1.1	91 \pm 1.5
Oxygenation index (PaO ₂ /PAO ₂)	0.47 \pm 0.02	0.54 \pm 0.05	0.43 \pm 0.03	0.49 \pm 0.03

* $p < 0.001$ compared with the other steps of the study

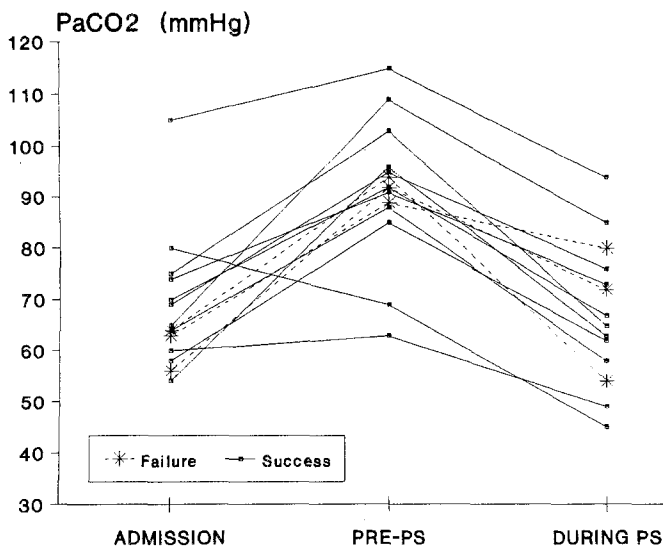


Fig. 2. Changes in PaCO₂ in each patient at each step of the protocol

positive end-expiratory pressure (autoPEEP) without increasing the leakage around the mask. In these patients, the use of PEEP only diminished the apparent inspiratory effort. In some cases, patients spontaneously referred to an alleviation of dyspnea when PEEP was added.

Within the first 24 s of discontinuation of PS, the 11 cases that maintained spontaneous ventilation showed no significant changes in hemodynamics and respiratory parameters during this period (Table 2).

None of the 11 patients that benefited from PS needed a secondary admission to ICU during the same hospitalization period. Two patients (number 1 and 3) entered in the protocol twice. This happened during different hospitalization periods, three and four months later respectively.

During the six months follow-up period after ICU discharge, 8 (73%) of the 11 patients who improved and

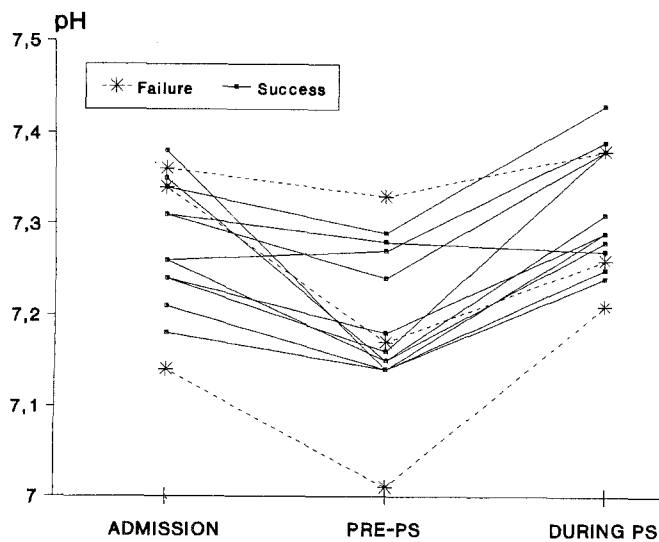


Fig. 3. Changes in pH in each patient at each step of the protocol

Table 3. Arterial blood gases, intubation rate and mortality index in COPD patients developing acute respiratory failure in different studies from the literature and in the present study

	Patients (n)	PaO ₂ (mmHg)	PaCO ₂ (mmHg)	Intubation (%)	Death (%)
Gilbert (1977) [32]	36	37	59	30	11
Bone (1978) [33]	123	54	50	23	7
Warren (1980) [20]	49	33	68	16	10
Brochard (1990) [10]	13	53	65	85	15
Present study	14	42	68	21	7

avoided intubation during the first trial of PS needed to be admitted to hospital again. All of them because of exacerbations of COPD. Two of them re-entered the study as stated in methods section. During the follow-up period none of the patients died and quality of life was judged no worse than previous by the majority of patients.

Discussion

The results of the present study demonstrate that noninvasive face mask PS ventilation may reduce the need for tracheal intubation in as much as 79% of severe hypercapnic COPD patients.

Pressure support ventilation offers the possibility to increase spontaneous tidal volume. Patients may maintain their own breathing pattern (respiratory rate and inspiratory-expiratory partitioning) while the increased inspiratory pressure, i.e. an increased pressure available for flow, delivers a higher inspiratory flow and a higher tidal volume for the same inspiratory time and inspiratory effort [16, 17]. Patients normally adapt their breathing pattern to this improved alveolar ventilation with a reduction in respiratory rate which increases expiratory time, reducing the burden to the respiratory muscles. It has been shown that PS reduces the work of breathing and the oxygen consumption of the respiratory muscles in proportion to the level of PS used [18, 19].

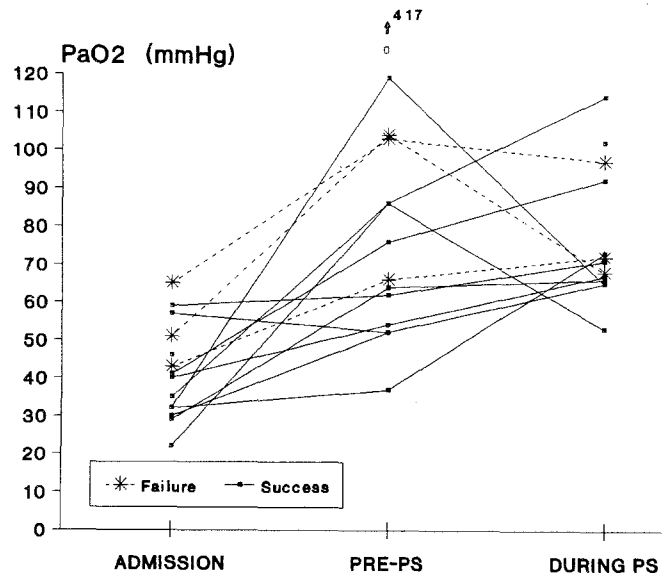


Fig. 4. Changes in PaO₂ in each patient at each step of the protocol

Some investigators have developed original devices to more effectively supply PS by reducing the work needed to activate both inspiratory demand valves or expiratory triggering systems [10]. These sophisticated devices can be of value in highly tachypneic patients or those severely affected by respiratory muscle weakness, but reduce the availability of this type of support for the majority of ICUs. For this reason, in the present study, we preferred to use a commercially available ventilator that allows us to widely extrapolate our results to the majority of ICUs.

Despite some differences regarding patients population, diagnosis, mechanical devices to supply PS and endpoints, our results are in accordance with these previous studies on the use of non-invasive ventilation (Table 3). Brochard et al. [10] found a lower ratio of intubation and duration of ICU stay in COPD patients in hypercapnic failure treated earlier with noninvasive PS, but a mortality ratio similar to the present study was observed. They compared the study population with a historically matched control group. In our protocol we decided to study more advanced patients when their attendant physicians indicated the need for non-delayed intubation. Our approach is very similar to that of Meduri et al. [11], and in this way, with such a high expected incidence of intubation, any reduction in intubation rate may be strongly attributable to PS treatment. Thus, the observed 21% intubation rate is clinically impressive and reinforces the results of Meduri et al. [11].

In our study, the time needed to improve patients' clinical status was shorter than in previous studies [10, 11]. The fact that we used PS in a continuous fashion may account for differences with studies done in an intermittent manner. The concomitant presence of heart failure in 3 cases (1, 2 and 9) could explain the fact that some of the patients responded quickly to the mask pressure support, but the fact that one of them needed intubation probably goes against this possibility.

The effect of treatment on mortality is more difficult to establish with the design of the study. Nevertheless, a mortality rate of 7% in COPD patients ventilated non-invasively for hypercapnic failure is similar to that of Meduri et al. [11] and is lower than the ordinary mortality rate in these patients in our ICU and in the majority of ICUs [1, 20].

While not directly dealing with the impact of PS treatment on the number of complications during the stay in the ICU, our study suggests that it was favorable. No cases of nosocomial pneumonia were detected in the nonintubated population while one intubated patient (33%) developed pneumonia. Moreover, sedation and curarization were avoided in patients that improved with PS and eluded intubation.

The fact that the wide majority of patients successfully treated with PS showed no clinically significant changes within 24 h after discontinuation of PS and that they did not require mechanical ventilation during the whole hospitalization period, allows us to reject contentions about a merely transient effect of PS on the clinical evolution of patients.

Patients' evolution was good, bearing in mind that they were severe COPD patients. There was a 73% hospi-

talization rate at six months and it is difficult to evaluate whether PS treatment may have modified the spontaneous evolution of the disease, but at least it was not any worse than that indicated in their previous medical history. Moreover, the fact that no patients died during the 6 month follow-up period seems an evolution no worse than expected for such severely ill patients [1]. Warren et al. [20] found a survival rate of only 65% one year after admission for severe acute on chronic respiratory failure. In the study of Gillespie et al. [21] addressed to patients requiring prolonged mechanical ventilation, 26% of COPD patients died in the ICU, while mortality at 1 year was 44%.

In patients with severe stupor, the facial mask needed to be manually adapted for a variable period, between 10 and 20 min. After that, consciousness returned to a sufficient level in order for the patients to be able to closely cooperate with the medical team and maintain the mask in place without leakage. It was related to a clear reduction in hypercapnia attributable to the increased alveolar ventilation induced by PS.

The possible role of external PEEP as a factor that reduces the inspiratory work of breathing in patients with autoPEEP [22, 23] remains to be elucidated in our study. The fact that in only four cases we can add PEEP without great leakage around the masks diminishes the impact of PEEP on the whole population.

The effect of oxygen supply on our patients deserves mention (Fig. 4). The oxygen-induced hypercapnia in COPD patients is a widely known physiopathologic feature [1]. However, its exact mode of action is not quite clearly understood. Some investigators suggested that the major mechanism of oxygen-induced hypercapnia should be the worsening in V/Q mismatching induced by the suppression of the hypoxic pulmonary vasoconstriction while the effect on the reduction of the discharge of the respiratory centers should act to a lesser extent [25]. Conversely, Dunn et al. [26], after measuring the CO₂ recruitment threshold in mechanically ventilated COPD patients argued that suppression of hypoxic drive plays an important role in the pathogenesis of oxygen-induced hypercapnia. Our patients received FIO₂ at Pre-PS (0.40 ± 0.05) higher than the recommended strategies in stable COPD patients. Such oxygen supplementations probably worsened hypercapnia, but were not the major determinant, as suggested by the fact that a very similar FIO₂ during PS (0.36 ± 0.02) did not preclude the clear-cut improvement in PaCO₂.

Tolerance of the apparatus was excellent in the wide majority of the cases. We can separate two components that may affect the comfort of the patients: the ventilator [27–29] and the mask. The ventilator used in this study can supply a very high starting inspiratory flow. At the pressure levels achieved during our protocol, the Siemens Servo 900 C offers an inspiratory flow close to 100 l/min when working pressure is preset at 60 cmH₂O and this high airflow overcompensates for the added inspiratory work needed to trigger the demand valve of the ventilator [20].

In order to improve comfort, the characteristics of the mask seem more important than those of the ventilator.

Different models of masks dedicated to noninvasive ventilation have been proposed by several investigators. Some of these methods, silicone customized nasal mask [31] and silicone filled masks [10] are less useful in the emergency setting because they need a time-consuming procedure to be made. This was the rationale for using a commercial mask and to compensate for the added dead space with a slightly higher PS level. Leakage around the mask was mainly eliminated by the pneumatic sealing device of the mask.

We conclude that noninvasive pressure support ventilation via face mask is an easy and safe method in order to improve alveolar ventilation in the hypercapnic failure of COPD patients. We found no major side effects and this method allows patients to maintain spontaneous ventilation while the medical treatment achieves its optimal effectiveness.

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