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Noninvasive Positive Pressure Ventilation Using a Helmet in Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease

A Feasibility Study

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Background: **Noninvasive positive pressure ventilation (NPPV) with a facemask (FM) is effective in patients with acute exacerbation of their chronic obstructive pulmonary disease. Whether it is feasible to treat these patients with NPPV delivered by a helmet is not known.**

Methods: **Over a 4-month period, the authors studied 33 chronic obstructive pulmonary disease patients with acute exacerbation who were admitted to four intensive care units and treated with helmet NPPV. The patients were compared with 33 historical controls treated with FM NPPV, matched for simplified acute physiologic score (SAPS II), age, $Paco_2$, pH, and Pao_2: fractional inspired oxygen tension. The primary endpoints were the feasibility of the technique, improvement of gas exchange, and need for intubation.**

Results: **The baseline characteristics of the two groups were similar. Ten patients in the helmet group and 14 in the FM group ($P = 0.22$) were intubated. In the helmet group, no patients were unable to tolerate NPPV, whereas five patients required intubation in the FM group ($P = 0.047$). After 1 h of treatment, both groups had a significant reduction of $Paco_2$ with improvement of pH; $Paco_2$ decreased less in the helmet group ($P = 0.01$). On discontinuing support, $Paco_2$ was higher ($P = 0.002$) and pH lower ($P = 0.02$) in the helmet group than in the control group. One patient in the helmet group, and 12 in the FM group, developed complications related to NPPV ($P < 0.001$). Length of intensive care unit stay, intensive care unit, and hospital mortality were similar in both groups.**

Conclusions: **Helmet NPPV is feasible and can be used to treat chronic obstructive pulmonary disease patients with acute exacerbation, but it does not improve carbon dioxide elimination as efficiently as does FM NPPV.**

SEVERAL randomized studies have found that in patients with acute exacerbation of chronic obstructive pulmonary disease (COPD), noninvasive positive pressure ventilation (NPPV) added to standard therapy reduces the need for tracheal intubation, rate of complications, intensive care unit (ICU) length of stay,[1–3] and mortality.[2] Two recent meta-analyses[4,5] concluded that NPPV should be considered a first-line intervention in patients with acute exacerbation of COPD. A recent American-European Consensus Conference recommended that in patients hospitalized for exacerbation of COPD with rapid clinical deterioration, NPPV should be considered to prevent further impairment in gas exchange, respiratory workload, and need for tracheal intubation.[6]

Noninvasive ventilation is usually delivered through a nasal mask or facemask (FM). The nasal mask is better tolerated, but the FM seems more appropriate in patients with severe decompensation, who are often mouth breathers and cooperate poorly with treatment.[2,6–8] In some patients, pain, discomfort, or claustrophobia may result in intolerance of the mask and require discontinuation of noninvasive ventilation and intubation. Despite continuous improvements in mask design and materials, skin necrosis is frequent in patients receiving NPPV for long periods.[6,7]

In an attempt to improve tolerance, we recently developed a transparent helmet that allows patients to see, read, and speak during NPPV.[9] In that study, we showed the efficacy of NPPV delivered by the helmet in critically ill patients without COPD but with acute hypoxemic respiratory failure.

The helmet has important advantages: (1) It is well tolerated and allows a satisfactory environmental interaction for patients. (2) Its fixation system should minimize the risk of cutaneous lesions. (3) Unlike the FM, it can be applied to any patient regardless of differences in facial contour.[9]

The helmet was initially proposed to deliver continuous positive airway pressure as an out-of-hospital treatment for patients with pulmonary edema. To our knowledge, the helmet with positive pressure ventilation has never been used to treat ICU patients with acute exacerbation of COPD.

The aim of this case-control study was to investigate the feasibility and efficacy of NPPV delivered by the helmet in adults with acute exacerbation of COPD, in comparison to NPPV delivered by a standard FM.

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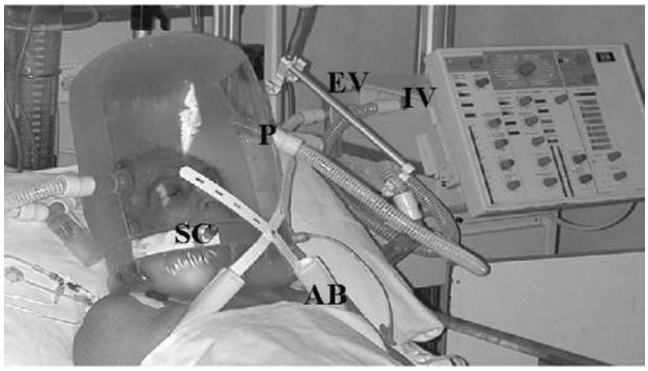

Fig. 1. A patient with the helmet connected to the ventilator. AB = armpit braces; EV= expiratory valve; IV = inspiratory valve; P = port of the helmet connected to the conventional respiratory circuit; SC = seal connection, which allows the passage of a nasogastric tube or permits the patient to drink through a straw or to be fed a liquid diet. Photograph printed with the permission of the patient.

Methods

Equipment

The helmet (CaStar; Starmed, Mirandola, Italy) (fig. 1) is made of transparent latex-free polyvinyl chloride and is secured by two armpit braces to a pair of hooks on the plastic ring that joins the helmet to a soft collar. The collar adheres to the neck and allows a sealed connection; the pressure increase during ventilation increases adherence of the collar to the neck and shoulders while avoiding air leakage.[9] The whole apparatus is connected to an ICU ventilator by a standard respiratory circuit. The two ports of the helmet act as inlet and outlet for inspiratory and expiratory gas flows. The inspiratory and expiratory valves are those of the mechanical ventilator.

A specific connector placed in the plastic ring can be used to allow the passage of a nasogastric tube while avoiding air leak. This connection also permits patients to drink through a straw or to be fed a liquid diet.

In contrast to FM NPPV, with helmet-delivered NPPV patients receive only part of the large volumes delivered by the ventilator after inspiratory trigger activation; the rest of the volume is compressed around the head, pressurizing the helmet. It is therefore impossible to measure patient tidal volumes and flows with conventional bedside monitoring. Occasionally, patient–machine dyssynchrony may occur during helmet NPPV, in which case the patient can breathe unassisted into the pressurized helmet, as with free-flow continuous positive airway pressure.

The internal volume surrounding the head varies between 6 and 8 l, but this usually does not represent a problem for rebreathing, provided that sufficient levels of pressure support are delivered.[9] When measuring partial pressure of inspired carbon dioxide and end-tidal carbon dioxide in healthy volunteers at 10 cmH_2O pressure support (Appendix), we showed that carbon dioxide rebreathing with the helmet is always less than 1.5% and is similar to that detected with the FM. A new version of this helmet, recently developed, has antiasphyxia mechanisms and two inner inflatable cushions to increase comfort and reduce the internal volume.

Study Design and Patient Selection

We conducted a case control study involving all consecutive adult patients with acute decompensation of COPD, eligible for treatment with NPPV between November 2000 and February 2001, who were admitted to four ICUs in Italy (Università Cattolica del Sacro Cuore; Servizio di Anestesia CTO; Università dell'Insubria; and Unità di Terapia Intensiva Respiratoria, Ospedale Forlanini).

On the basis of clinical history, physical examination, and chest radiograph, the patients were determined to have COPD with respiratory acidosis and an elevated bicarbonate level. Additional criteria for enrollment were similar to those proposed by Brochard *et al.*[2] and included an exacerbation of dyspnea lasting less than 2 weeks and at least two of the following: respiratory rate above 30 breaths per minute, Pa_{O_2} below 45 mmHg, and arterial pH below 7.35 after breathing at fractional inspired oxygen tension (F_{IO_2}) below 0.35 for at least 10 min.

Patients with any of the following were excluded: requirement for emergency intubation or cardiopulmonary resuscitation, respiratory arrest, severe hemodynamic instability, encephalopathy; respiratory failure caused by neurologic disease or status asthmaticus; more than two new organ failures[10] (*e.g.*, simultaneous presence of renal and cardiovascular failures), tracheostomy, or facial deformities. No patients received active humidification.

An ad hoc ethics committee approved the protocol, and all patients gave informed consent. For each patient treated with helmet NPPV, one matched historical control was selected according to predetermined criteria. The patients and controls all received similar medical treatment as clinically appropriate, including inhaled β-2 agonists, steroids, and antibiotics. The SAPS II was calculated 24 h after admission to the ICU.[11] Each team that enrolled patients had ample experience with noninvasive ventilation.

Helmet Positive Pressure Ventilation

During NPPV, the ventilator was connected to the helmet with conventional tubing. The head of the bed was kept at a 45-degree angle. Once the helmet was positioned, a baseline pressure support level was set at 10 cmH_2O and was raised in increments of 2–3 cmH_2O to obtain patient comfort, respiratory rate lower than 25 breaths/min, and disappearance of accessory muscle activity, evaluated by palpating the sternocleidomastoid muscle.[12] Positive end expiratory pressure (PEEP) was set at 5–7 cmH_2O to counterbalance the possible pres-

ence of PEEPi. We used both flow and pressure triggers; the pressure trigger was set at -1 cmH_2O and the flow trigger at 5 l/s. If tracheal intubation was required, the helmet was easily removed and the patient intubated within few seconds.

FM Group

The control patients were selected from a group of 198 patients admitted to the ICU in the 12 months preceding the study with a diagnosis of respiratory failure due to acute exacerbation of COPD and treated with FM NPPV. The control group had the same enrollment criteria as the helmet group. The physician who selected the controls did not know the results of the study and was not informed about the course of treatment.

For each patient treated with helmet NPPV, one matching control was selected according to the following criteria: severity of illness on admission within four points as assessed by SAPS II[11] and age within 10 yr of the treated patients; $Paco_2$ within 8 mmHg of the values of the treated patients; arterial pH on admission within 0.04 points of the treated patients; and Pao_2:Fio_2 ratio (while receiving Fio_2 below 0.35 by a Venturi mask (Deaflux Line; DEAS, Castelbolognese, RA, Italy) within 10 points of the treated patients. When matching each patient we gave priority to $Paco_2$, pH, age, and SAPS II score.

FM Positive Pressure Ventilation

During NPPV, the ventilator was connected with conventional tubing to a clear FM with an inflatable soft cushion seal (Gibeck, Upplands, Sweden, or Vitalsigns Inc, Towota, NJ and Benefit, Puritan Bennett Co., Overland Park, KS). The mask was secured by head straps while avoiding a tight fit, and the head of the bed was kept elevated at 45-degree angle. In most patients, a protective hydrocolloid sheet was applied over the nasal bridge. For patients with a nasogastric tube, a seal connector in the dome of the mask was used to minimize air leakage. After the mask was secured, the initial level of 10 cmH_2O pressure support was gradually increased in increments of 2–3 cmH_2O to obtain a respiratory rate of less than 25 breaths/min, disappearance of accessory muscle activity (evaluated by palpating the sternocleidomastoid muscle),[12] and patient comfort. PEEP was set at 5–7 cmH_2O to counterbalance the intrinsic PEEP level. The pressure trigger was set at -1 cmH_2O or the flow trigger at 5 l/s.

Monitoring and Weaning

All patients had continuous electrocardiography and arterial oxygen saturation monitoring. We used two types of mechanical ventilators: the Servo 300 Siemens (Siemens Elema, Uppsala, Sweden) or the Evita 4 (Dräger Medical AG, Lübeck, Germany). In both groups, ventilator settings were adjusted on the basis of continuous pulse-oxymetry and repeated measurements of arterial blood gases. No patient received sedatives.

Duration of NPPV was standardized in both groups according to a standard protocol[13]: NPPV was delivered almost continuously in the first 24 h, with short intervals of spontaneous breathing with oxygen supplementation; in the subsequent days the length of NPPV was gradually decreased, according to the clinical response (but never < 6 h/day). NPPV was discontinued if the patient had a normal mental status; was hemodynamically stable; maintained a respiratory rate lower than 30 breaths/min; had an arterial pH 7.35 or greater; and had a Pao_2 greater than 55 mmHg, with Fio_2 ≥ 0.35 or peripheral oxygen saturation 90% or higher, *without* ventilatory support and in the absence of dyspnea, activation of accessory muscles of respiration, and paradoxical abdominal motion.

Criteria for Endotracheal Intubation

Patients who were not treated successfully with NPPV were intubated with cuffed endotracheal tubes (ID, 7.5–8.5 mm) and mechanically ventilated. The predetermined major criteria for tracheal intubation were similar to those used by Brochard *et al.*[2] and included respiratory arrest, respiratory pauses with loss of consciousness, psychomotor agitation making nursing care impossible and requiring sedation, heart rate below 50 beats per minute with loss of alertness, and hemodynamic instability with systolic arterial blood pressure below 70 mmHg; development of conditions requiring intubation either to protect the airways (coma or seizure disorders) or to manage copious tracheal secretions; and inability of the patient to tolerate the FM or helmet, including discomfort, claustrophobia, or pain.[2] Patients with unsuccessful treatment because of intolerance of noninvasive ventilation included those who refused to continue noninvasive ventilation despite improved gas exchanges, no difficulty managing their secretions, improvement of dyspnea, and disappearance of accessory muscle activity. Minor criteria were respiratory rate above 35 breaths/min and above the value on admission; arterial pH below 7.30 and below the value on admission; and Pao_2 below 45 mmHg despite NPPV. The presence of two minor criteria after the first hour of NPPV was considered an indication for intubation. Major and minor criteria were identical for both groups.

Endpoints and Definitions

The primary endpoints were the need for tracheal intubation and the improvement of gas exchanges at any time during the study and the incidence of complications related to NPPV (facial skin necrosis, gastric distension, and intolerance). Secondary endpoints included complications not present on admission (such as ventilator-associated pneumonia or extrapulmonary sepsis),

duration of ventilatory assistance, length of hospital stay, and ICU mortality.

Arterial blood gas levels were determined at baseline, while breathing through a Venturi mask with F_{IO_2} below 0.35, at 1 h during NPPV, when clinically needed, and at discontinuation of support that corresponded to (1) the moment of tracheal intubation for those not successfully treated with NPPV, or (2) definitive weaning from noninvasive ventilation for those successfully treated. Improvement in gas exchange was defined as an increase in pH over 7.34 and decreases in $Paco_2$ to at least 10 points below baseline. Improvement in gas exchange was evaluated within 1 h after study entry (initial improvement) and over time (sustained improvement). Sustained improvement in gas exchange was defined as the ability to maintain the improvement in gas exchanges without intubation until NPPV was discontinued.

Sepsis, severe sepsis, and septic shock were defined according to consensus guidelines.[14] Patients who developed clinical manifestations of pneumonia[15] underwent bronchoscopy with bronchoalveolar lavage.[16] The methods and laboratory procedures followed consensus guidelines.[17] Bacterial pneumonia was diagnosed when at least 10,000 colony-forming units of bacteria/ml were measured in bronchoalveolar lavage fluid.[17] Multiple organ failure was defined according to previously described criteria.[10]

Data Analysis

Results are given as mean ± SD. Demographic and physiologic characteristics of the two groups were compared using the Student *t* test for continuous data (separate variance estimates were used when variances were significantly different) and the Mantel-Haenszel extended chi-square test for categorical data. The Fisher exact test (two-tailed) was used when appropriate (expected number of cases per cell < 5).[18] The SPSS package (SPSS Inc., Chicago, IL) was used for all analyses.

A precise calculation of sample size was not possible in this study. Calculation of sample size was therefore based on preexisting data to estimate the baseline rate of the primary outcome, but no data on the intubation rate of COPD patients with acute exacerbation treated with the helmet were available before the present study.

Results

Characteristics of the Patients and Etiology of Acute Respiratory Failure

From November 2000 to February 2001, 108 patients with acute respiratory failure caused by exacerbation of COPD were admitted to the participating ICUs. Twenty-three patients were already tracheostomized, 15 were treated with nasal or FM in the emergency department or ICU, 35 were already intubated, and two refused to participate. The other 33 met the enrollment criteria and were treated with helmet NPPV. These patients were compared with 33 matched controls treated with the FM. The baseline characteristics, comorbid conditions, and causes of acute respiratory failure of the two groups were similar except that the heart rate was higher in the helmet group (table 1).

Table 1. Baseline Characteristics of the Two Groups

	Helmet (n = 33)	Mask (n = 33)	*P*
Patient characteristics			
Male, No. (%)	24 (69)	25 (72)	0.50
SAPS II, m (SD)	36 (8)	36 (6)	0.99
Age (yr), m (SD)	74 (8)	73 (6)	0.64
GCS, m (SD)	14 (1)	14 (1)	0.11
FEV_1, (% of predicted), m (SD)	33 (4)	31 (4)	0.32
BMI, m (SD)*	25 (4)	27 (5)	0.10
Comorbid conditions, No. (%)			
Fibrothorax	2 (6)	2 (6)	0.69
Heart ischemic disease	7 (21)	5 (15)	0.37
Hypertension	8 (24)	8 (24)	0.61
Diabetes	7 (21)	6 (18)	0.50
Solid tumors	2 (6)	2 (6)	0.69
None	7 (21)	10 (30)	0.31
Condition exacerbating COPD, No. (%)			
Community pneumonia	10 (30)	9 (27)	0.50
Extrapulmonary sepsis	6 (18)	5 (15)	0.50
Cardiac decompensation	7 (21)	4 (12)	0.25
Bronchospasm	6 (18)	9 (27)	0.28
Viral infection	4 (12)	6 (18)	0.36
Basal values			
WBC count (cells × 10,000), m (SD)	11,6 (5)	10,6 (4)	0.40
$Paco_2$ (mmHg), m (SD)	86 (17)	82 (15)	0.22
Pao_2:Fio_2, m (SD)	142 (36)	155 (32)	0.14
pH, m (SD)	7.25 (0.07)	7.25 (0.04)	0.70
Respiratory rate (breaths/min), m (SD)	37 (12)	34 (3)	0.27
Body temperature (C°), m (SD)	37 (0.7)	37 (0.7)	0.96
Systolic blood pressure (mmHg), m (SD)	133 (18)	141 (20)	0.11
Heart rate (bpm), m (SD)	111 (24)	100 (15)	0.03

* Body mass index (BMI) is calculated with the following formula: body weight (kg)/height^2 (m). Nine BMI values were missing (four in the helmet group and five in the mask group).

bpm = beats per minute; COPD = chronic obstructive pulmonary disease; FEV_1 = forced expiratory volume in one second; Fio_2 = fractional inspired oxygen tension; GCS = Glasgow Coma Score; m = mean; $Paco_2$ = arterial carbon dioxide tension; Pao_2 = arterial oxygen tension; SAPS II = Simplified Acute Physiologic Score II; SD = standard deviation; WBC = white blood cell.

Outcome Variables

After 1 h of treatment, both groups had significant reductions of $Paco_2$ (12% in the helmet group; 20% in the FM group) with an improvement of pH compared to baseline. However, the decrease in $Paco_2$ was less in the helmet group (75 ± 15 *vs.* 66 ± 15 mmHg, $P = 0.01$) (table 2). Moreover, at discontinuation of support, $Paco_2$ values for patients receiving helmet NPPV were higher

Table 2. Outcome Variables

	Helmet (n = 33)	Mask (n = 33)	*P*
Baseline			
Level of pressure support (cmH_2O), m (SD)	20 (5)	15 (7)	<0.0001
PEEP (cmH_2O), m (SD)	6 (2)	5 (1)	0.11
Duration of NPPV (h), m (SD)	39 (42)	30 (21)	0.25
No. of endotracheal intubations, No. (%)	10 (30)	14 (42)	0.22
Initial improvement in gas exchanges, No. (%)	16 (48)	19 (57)	0.62
Sustained improvement in gas exchanges without intubation, No. (%)	20 (60)	19 (57)	0.50
Length of stay in ICU (days), m (SD)	15 (15)	18 (22)	0.40
ICU mortality, No. (%)	3 (9)	4 (12)	0.49
Hospital mortality, No. (%)*	7 (21)	10 (30)	0.28
After 1 h of treatment			
$Paco_2$ (mmHg), m (SD)	75 (15)	66 (15)	0.01
Pao_2:Fio_2, m (SD)	193 (43)	204 (64)	0.30
pH, m (SD)	7.32 (0.07)	7.34 (0.06)	0.12
Respiratory rate (breaths/min), m (SD)	29 (6)	28 (3)	0.72
Body temperature (C°), m (SD)	ND	ND	—
Systolic blood pressure (mmHg), m (SD)	127 (23)	131 (23)	0.26
Heart rate (bpm), m (SD)	109 (18)	91 (13)	<0.001
At end of treatment†			
$Paco_2$ (mmHg), m (SD)	68 (18)	57 (9)	0.002
Pao_2:Fio_2, m (SD)	211 (56)	204 (37)	0.60
pH, m (SD)	7.35 (0.09)	7.39 (0.05)	0.02
Respiratory rate (breaths/min), m (SD)	27 (9)	26 (4)	0.62
Body temperature (C°), m (SD)	36.9 (0.6)	37 (0.6)	0.90
Systolic blood pressure (mmHg), m (SD)	142 (20)	130 (21)	0.01
Heart rate (bpm), m (SD)	102 (22)	86 (11)	0.001

* Hospital deaths include the intensive care unit (ICU) deaths. † End of treatment values correspond to discontinuation of support for successful patients and to the time of endotracheal intubation for patients not responding to noninvasive positive pressure ventilation (NPPV).

bpm = beats per minute; Fio_2 = fractional inspired oxygen tension; m = mean; ND = not done; $Paco_2$ = arterial carbon dioxide tension; Pao_2 = arterial oxygen tension; PEEP = positive end expiratory pressure; SD = standard deviation.

than those treated with FM NPPV (68 ± 18 *vs.* 57 ± 9 mmHg, $P = 0.002$) and pH was significantly lower (7.35 ± 0.09 *vs.* 7.39 ± 0.05, $P = 0.02$) (table 2). One patient in the helmet group who had 106 mmHg $Paco_2$ with pH 7.25 on admission refused to continue NPPV or any other medical therapy after 3 h of treatment. He left the hospital alive after 36 h.

Both groups had similar improvement of Pao_2:Fio_2. Within the first hour of NPPV, 16 patients (48%) in the helmet group and 19 (57%) in the FM group had an improvement in gas exchange ($P = 0.62$). Pao_2:Fio_2 improved over time in 20 (60%) of the 33 patients in the helmet group and in 19 (57%) of the 33 treated with FM ($P = 0.50$). Respiratory rates were not different in the two groups over time.

The levels of PEEP applied were similar in the two groups. The levels of pressure support in the helmet group were higher than in the FM group ($P < 0.001$) and without major air leaks. Duration of NPPV was similar ($P = 0.25$) (table 2).

Ten patients (30%) in the helmet group and 14 (42%) in the FM group ($P = 0.22$) were not successfully treated with NPPV and were intubated. All of the intubations (10 patients) in the helmet group and half of those (seven patients) in the FM group occurred during the first 24 h of treatment. The reasons for NPPV treatment failure and tracheal intubation of the two groups are reported in figure 2. Six patients (18%) in the helmet group and seven patients (21%) in the FM group failed to respond to noninvasive ventilation within the first 12 h of treatment ($P = 0.49$). In the helmet group, no patients were unable to tolerate NPPV, whereas 5 of the 14 FM patients (36%) required intubation ($P = 0.047$). Length of stay in the ICU and mortality in the ICU and hospital were not different between the groups.

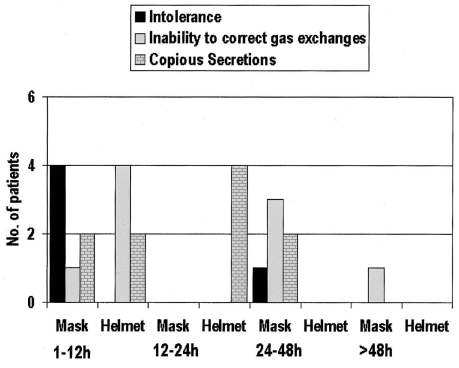

Fig. 2. Timing and reasons for tracheal intubation. No patients failed to respond to NPPV because of helmet intolerance, whereas 5 of the 14 patients (36%) in the FM group required intubation ($P = 0.047$).

Table 3. Outcome Variables in Patients Treated Successfully and Unsuccessfully

	Treatment Success			Treatment Failure		
	Helmet (n = 23)	Mask (n = 19)	*P*	Helmet (n = 10)	Mask (n = 14)	*P*
Baseline						
SAPS II, m (SD)	38 (8)	34 (3)	0.07	33 (8)	38 (7)	0.06
Age (y), m (SD)	76 (8)	72 (5)	0.08	70 (6)	74 (3)	0.02
GCS, m (SD)	14 (1)	14 (1)	0.47	14 (1)	13 (1)	0.47
BMI, m (SD)*	26 (3)	28 (6)	0.12	23 (4)	25 (4)	0.10
Level of pressure support (cmH_2O), m (SD)	21 (5)	12 (3)	<0.0001	22 (4)	11 (2)	<0.001
PEEP (cmH_2O), m (SD)	6 (2)	5 (1)	0.20	6 (1)	5 (1)	0.17
$Paco_2$ (mmHg), m (SD)	88 (14)	81 (14)	0.12	84 (21)	84 (17)	0.90
Pao_2:Fio_2, m (SD)	139 (39)	169 (50)	0.05	143 (41)	154 (41)	0.55
pH, m (SD)	7.26 (0.07)	7.24 (0.04)	0.14	7.25 (0.06)	7.26 (0.04)	0.44
Respiratory rate (breaths/min), m (SD)	36 (12)	34 (3)	0.64	39 (11)	34 (4)	0.17
Heart rate (bpm), m (SD)	108 (22)	99 (15)	0.14	119 (26)	99 (15)	0.04
Systolic blood pressure (mmHg), m (SD)	149 (31)	129 (12)	0.008	140 (20)	136 (20)	0.60
After 1 h of treatment						
$Paco_2$ (mmHg), m (SD)	72 (12)	62 (10)	0.004	81 (18)	71 (18)	0.22
Pao_2:Fio_2, m (SD)	193 (43)	222 (61)	0.10	186 (39)	181 (65)	0.82
pH, m (SD)	7.34 (0.06)	7.35 (0.06)	0.74	7.26 (0.05)	7.33 (0.08)	0.02
Respiratory rate (breaths/min), m (SD)	28 (6)	28 (2)	0.87	32 (7)	28 (5)	0.15
Heart rate (bpm), m (SD)	103 (16)	89 (13)	0.002	122 (15)	94 (13)	<0.001
Systolic blood pressure (mmHg), m (SD)	135 (24)	124 (17)	0.12	140 (18)	136 (27)	0.61
At end of treatment†						
$Paco_2$ (mmHg), m (SD)	63 (11)	57 (10)	0.08	79 (20)	58 (9)	0.009
Pao_2:Fio_2, m (SD)	220 (57)	214 (35)	0.66	189 (48)	194 (40)	0.78
pH, m (SD)	7.40 (0.05)	7.40 (0.05)	0.97	7.26 (0.07)	7.39 (0.06)	<0.001
Respiratory rate (breaths/min), m (SD)	24 (6)	26 (2)	0.12	33 (10)	27 (5)	0.08
Heart rate (bpm), m (SD)	93 (16)	86 (14)	0.15	121 (21)	86 (7)	<0.001
Systolic blood pressure (mmHg), m (SD)	142 (23)	126 (18)	0.02	141 (16)	131 (22)	0.22
Outcome						
Duration of NPPV (h), m (SD)	39 (41)	33 (17)	0.07	12 (8)	29 (23)	0.02
Length of stay in ICU (days), m (SD)	14 (14)	10 (16)	0.82	25 (23)	24 (21)	0.90
ICU mortality, No. (%)	1 (4)	1 (5)	0.70	2 (20)	3 (21)	0.66
Hospital mortality, No. (%)‡	4 (17)	4 (21)	0.53	3 (30)	6 (42)	0.41

* Calculated with the following formula: body weight (kg)/height^2 (m). Nine body mass index (BMI) values were missing (four in the helmet group and five in the mask group). † End of treatment values correspond to when support was discontinued for successful patients and to the time of intubation for those not responding to noninvasive positive pressure ventilation (NPPV). These values do not include the patient who refused therapy and was discharged alive and conscious from the hospital (see text). ‡ Hospital deaths include patients who died in the intensive care unit (ICU).

bpm = beats per minute; Fio_2 = fractional inspired oxygen tension; GCS = Glasgow Coma Score; m = mean; $Paco_2$ = arterial carbon dioxide tension; Pao_2 = arterial oxygen tension; PEEP = positive end expiratory pressure; SAPS II = Simplified Acute Physiologic Score II; SD = standard deviation; WBC = white blood cell.

Outcome of Patients Treated Successfully and Unsuccessfully

After stratification by treatment failure or success, the 23 successfully treated patients in the helmet group and the 19 in the FM group had similar characteristics at baseline, except that Pao_2:Fio_2 was higher in the FM group. After 1 h of NPPV, $Paco_2$ decreased by 19% in the helmet group and by 24% from baseline in the FM group ($P = 0.004$) (table 3). At discontinuation of support, there was a 30% decrease of $Paco_2$ from baseline in both groups and the pH was similar. In comparison to the 31% decrease in $Paco_2$ in the 14 FM patients who were not successfully treated, the 10 helmet NPPV patients who were not successfully treated had only a 6% decrease in $Paco_2$ at the time of intubation ($P = 0.009$), their pH was significantly lower ($P < 0.001$), and their treatment was deemed unsuccessful earlier (after 12 ± 8 h of noninvasive ventilation compared to 29 ± 23 h, $P = 0.02$) (table 3).

Complications and Lethal Events

The number of patients who developed complications after the study entry was similar in each group. Five (15%) in the helmet group and four (12%) in the FM group developed nosocomial pneumonia after study entry ($P = 0.50$) (table 4). All incidents occurred after the failure of NPPV treatment and tracheal intubation. The causative agents were *Pseudomonas aeruginosa* (three patients), *Klebsiella pneumoniae* (one patient), and *Acinetobacter* (one patient) in the helmet group, and *P. aeruginosa* (three patients) in the FM group; in the other patient the causal agent was not identified.

No patient developed skin necrosis, gastric distension, conjunctivitis, or intolerance during NPPV in the helmet group in comparison with 12 patients (36%) who did in the FM group ($P < 0.001$) (table 4). One patient with severe malnutrition who was ventilated with the helmet for 48 h developed a deep venous thrombosis of the left

Table 4. Complications

Complications	Helmet (n = 33)	Mask (n = 33)	*P*
Severe, No. (%)			
VAP	5 (25)	4 (12)	0.50
Septic shock, severe sepsis	2 (6)	4 (12)	0.33
Acute renal failure	1 (3)	4 (12)	0.17
Sinusitis	0 (0)	2 (6)	0.24
Related to NPPV, No. (%)			
Skin breakdown	0 (0)	4 (12)	0.06
Conjunctivitis	0 (0)	2 (6)	0.24
Gastric distension	0 (0)	0 (0)	0.99
Intolerance	0 (0)	6 (18)	0.02
DVT*	1 (3)	0 (0)	0.51
Total	0 (0)	12 (36)	<0.001

All ventilator associated pneumonia (VAP) occurred after intubation in patients who failed to respond to noninvasive positive pressure ventilation (NPPV). Four cases of community pneumonia (two in each group) progressed to severe sepsis and septic shock after study entry. In the mask group, the other two cases of septic shock and severe sepsis were due to urinary tract infection and central venous catheter–related sepsis.

* Deep venous thrombosis (DVT) occurred in the left axillary vein in one patient with cancer, who was also cachectic. DVT was due to the prolonged compression of the armpit brace and was documented by echo-color-Doppler.

axillary vein, probably related to the compression of the armpit braces that held the helmet in place.

Discussion

This study evaluated the application of NPPV by means of a helmet to treat patients with acute exacerbation of COPD who required ICU admission for respiratory failure. During NPPV the helmet was as effective as a conventional FM in reducing the need for tracheal intubation, with similar results with regard to ICU and hospital mortality, length of ICU stay, and rate of infectious complications. Helmet NPPV was better tolerated.

Both techniques achieved improvement in Pa_{O_2}:F_{IO_2} and a significant decrease in Pa_{CO_2}. However, the reduction in Pa_{CO_2} was less in the group of patients treated with the helmet than those treated with the FM. The helmet and the FM were equally effective in improving Pa_{O_2}:F_{IO_2}.

A wide consensus exists about the use of NPPV as first-line treatment for hypercapnic respiratory failure in patients with acute exacerbation of COPD.[4–6] Four randomized, controlled trials, including more than 200 ICU patients, have evaluated the application of NPPV by FM in these cases[1–3,19]. These studies have found that early application of NPPV significantly improved gas exchange, respiratory rate, dyspnea score, and intubation rates. NPPV also reduced morbidity and mortality in the ICU and hospital.[2]

Despite these striking results, approximately 30% of patients receiving FM NPPV do not respond to treatment and require intubation.[1–5,20] Treatment failure is generally caused by mask intolerance, uncontrolled leaks, or lack of improvement in gas exchange.[2,13] The helmet is better tolerated and allows NPPV for prolonged periods, with minimal air leaks, so it may be a possible alternative to the FM.

The only existing study on the use of the helmet as an alternative to the FM for delivering NPPV focused on patients with acute hypoxemic acute respiratory failure (not related to COPD).[9] We found a similar effect on gas exchange, intubation rates, ICU, and hospital mortality, but a significant improvement in patients' tolerance: no patients failed to respond to NPPV in the helmet group because of claustrophobia, discomfort, or pain related to the technique, compared to 38% of FM patients.[9] Patients in the helmet group tolerated longer periods of NPPV, despite levels of PEEP higher than those applied with the FM.[9] Those results and those of the present study suggest a worthwhile advantage of helmet use in patients with severe hypoxia and hypercapnia, in whom the continuous, prolonged application of NPPV with better tolerance and avoidance of skin breakdown can be crucial.[13]

In the present study, the treatment failure rate with noninvasive ventilation was higher than reported elsewhere.[1–5] This was probably because our patients had higher severity scores, a large number had pneumonia, and all met the criteria for mechanical ventilation.

In our study, helmet NPPV reduced hypercapnia less efficiently than did FM NPPV. Two possible factors might have influenced this: (1) carbon dioxode rebreathing, and (2) less reduction of inspiratory effort. The partial pressure of inspired carbon dioxide and end-tidal carbon dioxide values measured in three healthy volunteers (Appendix) showed that carbon dioxide rebreathing with the helmet and the mask is similar and always less than 1.5%. A less efficient reduction of the inspiratory effort may be due to partial dissipation of the inspiratory pressure. Part of this pressure is used to expand the soft collar of the helmet, so the pressurization rate might be lower than with the FM and sometimes may affect the trigger and cycling: under this condition, patient–machine dyssynchrony may occur. In this case, the patient breathes unassisted into the pressurized helmet, similar to breathing in free-flow continuous positive airway pressure. Currently, the helmet should be avoided in patients with more severe conditions who require a rapid increase of alveolar ventilation.

This study adds further evidence that NPPV reduces the probability of pneumonia.[2,20–22] Patients successfully treated with NPPV (by helmet or FM) did not develop pneumonia. All cases of pneumonia in both groups occurred only after NPPV treatment failure and intubation. The only helmet-related complication was a case of deep venous thrombosis in the left axillary vein in a patient with severe malnutrition, and cachexia, probably due to prolonged compression from the armpit brace. Deep venous thrombosis diagnosed after the end

of NPPV was successfully managed with anticoagulants. This suggests that fixation of the braces in severely malnourished patients needs close attention.

A major criticism to the present study may be directed toward its design. A case-control study, as opposed to a randomized trial, is biased toward an overestimation of the positive effects in the treatment group.[23] The limited value of case-control studies compared to randomized trials has been partially reappraised in recent systematic reviews of the literature,[24,25] which have concluded that well-designed observational studies that avoid or consistently reduce the confounding factors are likely to provide valid results.

The lack of a power analysis is a weakness of the current study design; however, calculation of a sample size is based on preexisting data to estimate the baseline rate of the primary outcome. In fact, to give *a priori* hypothesis on expected intubation, the usual intubation rate of COPD patients treated by helmet should be known, but no previous data existed on helmet application in these patients.

In conclusion, the helmet can be effective in providing NPPV for COPD patients with acute exacerbation, but it is less efficient than the FM in carbon dioxide elimination. Currently, its use should be limited to COPD patients who do not tolerate the FM in the ICU setting under strict monitoring.

Appendix

With the helmet, because of the presence of a large volume (6–8 l), interposed between the inspiratory and expiratory limbs of the ventilator circuit, some rebreathing may occur. A substantial amount of the air delivered by the ventilator at each inflation distends the soft wall of the helmet and does not actually reach the patient's airway. To quantify the actual amount of rebreathing occurring while delivering NPPV with the helmet, compared to the FM, we conducted an experiment in three healthy volunteers: after a period of 15 min, *using a small, dedicated mouthpiece at the mouth of the subjects*, we measured the end-tidal carbon dioxide and the partial pressure of inspired carbon dioxide by mainstream capnometry (CO_2SMO plus model 8100; Novametrix Medical System Inc., Wallingford, CT) with the same helmet and FM used in the clinical study. In addition, by means of a 3-way connector a 2-l reservoir bag was placed at the end of the expiratory limb of the respiratory circuit, proximally to the expiratory port of a Servo 300 ventilator (Siemens Elema, Uppsala, Sweden). At the distal end of the reservoir bag, a stopcock was mounted to collect the exhaled gas in a syringe and determine the carbon dioxide partial pressure (NovoBiomedical, Statprofile Ultra, Waltham, MA). This value represented the actual mean carbon dioxide partial pressure within the two interfaces, with the ventilator set in pressure supported ventilation mode with an inspiratory pressure of 10 cmH_2O and a positive end expiratory pressure of 5.

The respiratory rates, inspiratory tidal volumes, end-tidal carbon dioxide, partial pressure of inspired carbon dioxide, and percent carbon dioxide were the same in both the helmet and FM groups (table 5). The carbon dioxide partial pressure values corresponding to the average carbon dioxide pressure were higher in the FM group, which was not surprising considering that the air exhaled was diluted in a much larger volume with the helmet as opposed to the mask. The partial pressure of inspired carbon dioxide values corresponded to a carbon dioxide concentration of 0.55% in the FM group and 0.95% in the helmet group.

Table 5. Carbon Dioxide Measurement with Helmet and Mask in Three Healthy Subjects

	Mask PSV	Helmet PSV
TV, ml	933 ± 251	1,166 ± 58
RR, breaths/min	12 ± 3	11 ± 4
$Etco_2$, mmHg	36 ± 1	33 ± 12
$Pico_2$, mmHg	4.48 ± 1	5.22 ± 3
CO_2 concentration, %	0.55 ± 0.1	0.95 ± 0.55
$CO_{2_{bag}}$, mmHg	16 ± 3	7 ± 3

CO_2 = carbon dioxide; $CO_{2_{bag}}$ = carbon dioxide partial pressure; $Etco_2$ = end-tidal carbon dioxide; $Pico_2$ = partial pressure of intramuscular carbon dioxide; PSV = pressure supported ventilation; RR = respiratory rate; TV = tidal volume.

These data show that a small amount of rebreathing is present with both the helmet and the mask but that it is clinically not relevant and is always below 1.5%.

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