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The use of noninvasive pressure support ventilation for severe respiratory insufficiency due to pulmonary oedema

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Abstract *Objective:* Experimental use of noninvasive pressure support ventilation (NIPSV) in patients with severe pulmonary oedema who would have been intubated if noninvasive ventilation were not available.
Design: Open, prospective, within patients non comparative study.
Setting: Internal intensive care unit (11 beds) at a university hospital.
Patients: 29 patients with severe respiratory distress and confirmed pulmonary oedema.
Interventions: NIPSV was applied via a tight fitting face mask delivering between 13 and 24 cmH_2O inspiratory airway pressure and 2 to 8 cmH_2O expiratory airway pressure.
Measurements and results: One patient required endotracheal intubation. Mean plethysmographic oxygen saturation rose significantly within 30 min from 73.8 ± 11 to 90.3 ± 5 %, while the oxygen supply was reduced from 7.3 ± 3.7 to 5.1 ± 3 l/min. Mean pH increased significantly ($p < 0.01$) from 7.22 ± 0.1 before NIPSV to 7.31 ± 0.07 after 60 min of NIPSV. Partial pressure of carbon dioxide was 62 ± 18.5 mmHg but decreased significantly within 60 min to 48.4 ± 11.5 mmHg. Heart rate and blood pressure stabilised continuously during the observation time. Mean duration of NIPSV was 6 h 9 min (range 60 min to 24 h). There were no serious side effects. Four patients died from underlying diseases between 1 and 28 days after NIPSV.
Conclusion: NIPSV is a highly effective technique with which to treat patients with severe cardiogenic pulmonary oedema.

Key words Pulmonary oedema · Noninvasive ventilation · Face mask

Introduction

Treatment of severe pulmonary oedema requires mechanical positive pressure ventilation with positive end-expiratory pressure (PEEP) to reduce venous return and to improve alveolar ventilation and the ventilation-perfusion relationship [1]. Although orotracheal intubation and mechanical ventilation secure continuous oxygen and volume supply, this intervention has considerable side effects. Sedation is necessary and may cause circulatory depression, prolonged constipation and encephalopathy. The risk of nosocomial pneumonia increases significantly after the first day [2]. Advanced age is a further risk for developing complications of prolonged mechanical ventilation [3].

Noninvasive ventilation techniques have been developed to avoid these side effects. They are used for acute [4] and chronic respiratory failure due to chronic obstructive lung disease, post-tuberculosis syndrome and neuromuscular diseases [5]. In 1991, Bersten and coworkers [6] reported results showing that continuous positive airway pressure (CPAP) by face mask in patients with cardiogenic pulmonary oedema leads to a reduction in morbidity compared to conventional therapy.

Mehta et al. [7] performed a randomised, controlled study using noninvasive pressure support ventilation (NIPSV) versus CPAP in patients with mild pulmonary oedema and found a significant improvement in arterial carbondioxide tension, pH, heart rate, breathing frequency and dyspnea score among those patients receiving NIPSV, whereas the CPAP group only showed significant improvement in breathing frequency.

We studied the effect of NIPSV with PEEP on severe respiratory insufficiency due to pulmonary oedema. The aim of the study was to investigate whether NIPSV is able to avert endotracheal intubation in patients who were likely to need it. The study was performed in agreement with the Helsinki Declaration.

Materials and methods

Patient selection

Between March 1995 and June 1997 29 patients (17 male and 12 female) were enrolled in this prospective, non comparative trial. All patients were admitted to our intensive care unit with severe pulmonary oedema. On arrival conservative treatment was carried out including oxygen 5 l/min or more via nose/mouth, intravenous furosemide, continuous infusion of nitroglycerine if the systolic blood pressure was above 120 mmHg or continuous infusion of catecholamines (adrenaline, dopamine, dobutamine) if mean blood pressure was below 60 mmHg.

All of the following three criteria were necessary for enrolment: (1) pulmonary oedema confirmed by bilateral rales over both lungs and pulmonary congestion found on the chest X-ray taken within the first hour after admission, (2) severe respiratory distress with dyspnea, respiratory rate greater than 25 breaths per min, use of accessory respiratory muscles and (3) peripheral oxygen saturation (SpO_2) below 85 % with $\geq$ 5 l/min oxygen via nose or mouth or an observed decline in saturation of more than 10 % during a 10 min period. Patients with neurologic disorders were not enrolled.

Ventilation

NIPSV was delivered using a BiPAP-S/T machine (Respironics, Murraysville, PA, USA) for 22 patients and a RespiCare machine (Dräger, Lübeck, Germany) for 7 patients. The mode of both ventilators was pressure support ventilation in equivalent settings. The BiPAP system was used with a whisper swivel (Respironics) for expiration, the RespiCare system has an exhalation device similar to the whisper swivel. Both ventilators have a leakage compensation and can supply up to 30 cmH_2O inspiratory pressure. The use of two different ventilators was necessary because the same respirator was not always available when needed. Oxygen was insufflated into the system between exhalation device and the face mask.

Mask

We used tight fitting masks covering mouth and nose. There was the choice between two equivalent products: full face mask (Respironics, Murraysville, PA, USA) and a mouth-nose mask (face mask with adjustable air cushion, Vital Signs, Totowa, NJ, USA). The selection was made according to the need for minimum air leakage and good compliance.

Protocol

Ventilation was started with 16 cmH_2O inspiratory pressure (IPAP) and 5 cmH_2O expiratory pressure (EPAP). Both pressure levels were adjusted with the aim to reach a high inspiratory pressure level without relevant leakage and to create a situation which is relatively convenient for the patient and can be tolerated for several hours.

During ventilation heart rate and SpO_2 were measured continuously, blood pressure every 5 min using a Hewlett Packard monitoring system and SpO_2 documented with pulse curve registration. The above parameters were noted before NIPSV and every 30 min during the first 2 h and every hour thereafter. Arterial oxygen tension (PaO_2) (Blood Gas Analysator, AVL Medical Systems, Schaffhausen, Switzerland) was obtained from the radial or femoral artery within the same time interval if not contraindicated or technically impossible. Samples for arterial blood gases were not taken if the patient was receiving oral anticoagulation or if a myocardial infarction with possible thrombolysis could not be excluded. Arterial puncture was not repeated more than twice if the first attempt was not successful. The partial pressure of carbon dioxide (PCO_2) and pH were measured in venous blood samples.

Oxygen was reduced every 15 min by 1 l/min until 2 l/min was reached. Then IPAP was lowered in steps of 2 cmH_2O every 15 min as soon as arterial oxygen saturation SaO_2 reached 90 %. After an IPAP level of 10 mbar was reached, NIPSV was interrupted. It was continued if SpO_2 fell below 90 %.

Criteria for the change from noninvasive to invasive ventilation were one of the following: no increase of SpO_2 during the first 15 min of NIPSV, any worsening of respiratory function not related to technical equipment (i.e. poor fitting of mask) during NIPSV and persistent pathological respiratory parameters without signs of improvement in the last 2 h of NIPSV.

All results are reported as mean standard deviations. Physiological changes were compared with the use of paired, two sample Student $\times$ s *t*-test on the basis of a priori ordered hypothesis. The SPSS package was used for analysis.

Results

A total of 29 patients were enrolled and received NIPSV. The mean age of the patients was 71.4 $\pm$ 11.6 years (range 51 to 91 years) Mean IPAP was 16.6 cmH_2O (range 12.4–24 cmH_2O). Mean EPAP was 5.5 cmH_2O (range 2–8 cmH_2O). Underlying diseases were arterial hypertension ($n = 8$), myocardial infarction ($n = 5$), mitral valve insufficiency ($n = 1$), renal failure ($n = 2$), pneumonia ($n = 1$) and left ventricular failure ($n = 13$) without specification. In these last 13 cases invasive diagnostic procedures, especially coronary angiography, was not possible during follow-up either because the patient gave no consent or contraindications existed. All patients were treated intravenously with furosemide, 5 patients required catechalomines, and 17 received continuous intravenous nitroglycerine.

Altogether we treated 151 patients with NIPSV for suspected pulmonary oedema during the study period;

Table 1 Patient characteristics (*Sat* saturation, *PCO_2/PO_2* partial pressure of carbon dioxide/oxygen, *O_2* oxygen supply via nose/mouth in l/min, *HR* heart rate, *BP* blood pressure before NIPSV and parameters of ventilatory and medical therapy, *IPAP/EPAP* inspiratory/expiratory positive airway pressure, *a* adrenaline, *dp* dopamine, *db* dobutamine, *n* nitrogen, *f* furosemide, *Time* duration of NIPSV, *LVF* left ventricular failure, *Renal* renal failure, *HYPT* arterial hypertension, *MI* myocardial infarction, *MVI* mitral valve insufficiency, *Suc* successful use of NIPSV, *D* died during hospital stay, *Fail* failure and intubation)

Patients	Sex	Age (years)	Sat (%)	PCO_2 (mm Hg)	pH	O_2 (l/min)	HR (beats/min)	BP (mm Hg)	IPAP (mbar)	EPAP (mbar)	Therapy	Time (min)	Diagnosis	Outcome
1	M	85	69			6	106	83/47	16.4	5.4	a, dp, db, f	320	LVF	Suc
2	M	61	60			10	97	229/113	16.2	6.7	n, f	120	Renal, HYPT	Suc
3	F	72	55	52	7.24	15	145	199/117	16	5	n, f	170	HYPT	Suc, D
4	F	91	82			5	121	153/94	15	5	n, f	100	LVF	Suc
5	M	86	65	36	7.21	12	90	140/95	19.7	7.8	n, f	540	LVF	Suc, D
6	F	51	73	59	7.31	5	96	148/86	11.4	5.4	n, f	1020	LVF, MVI	Suc
7	M	74	50			5	139	160/65	15	5	n, f	300	HYPT	Suc
8	F	75	75			10	184	68/34	16.1	6.1	dp	1080	MI	Suc, D
9	F	71	85	64	7.16	10	95	151/83	15	5.8	n, f	110	LVF	Suc
10	M	75	81	70	7.18	7	120	150/90	15	6	n, f	120	LVF, MVI	Suc
11	F	71	93	70	7.25	8	105	120/68	15	5	n, f	180	LVF	Suc
12	M	58	82	45	7.4	2	128	110/97	13	5	db, f	1020	MI	Suc, D
13	F	60	88	55	7.22	10	100	187/102	12.4	5.1	n, f	125	HYPT	Suc
14	M	64	70	60	7.25	0	100	135/70	16	6	db, f	540	LVF	Suc
15	F	76	85	55	7.35	3	140	132/70	20	2	n, f	120	MI	Suc
16	M	51	89	43	7.33	3	112	114/76	15	6	n, f	135	MI	Suc
17	F	79	80	42	7.36	5	72	159/46	14	2	n, f	240	LVF	Suc
18	F	83	82			10	148	114/57	24	8	dp, f	480	LVF	Suc
19	F	76	70	103	7.22	15	139	147/67	20	6	n, f	840	LVF	Suc
20	M	91	69	42	7.1	5	150	176/74	22	6	n, f	480	LVF, HYPT	Suc
21	M	76	72	78	7.1	6	163	160/95	18	3	n, f	180	MI	Suc
22	F	63	83	51	7.33	7	139	100/68	15	5	f	540	LVF	Suc
23	M	76	75	75	7.14	5	77	139/70	15	5	f	185	LVF, MVI	Suc
24	M	52	67			10	118	177/95	20	7	f	190	LVF, HYPT	Suc
25	M	65	72	80	7.1	10	127	177/85	22	8	f	240	LVF, HYPT	Suc
26	M	71	76	69	7.23	5	122	121/73	14	5	f	160	LVF	Suc
27	M	60	69			5	140	120/78	15	5	f	360	LVF	Suc
28	M	86	50	88	7.0	6	157	206/107	17	5	f	360	HYPT	Suc
29	M	70	80			5	80	130/64	15	5	n, f	120	LVF, pneumia, renal	Fail

11 received NIPSV and were later excluded because the chest X-ray did not confirm pulmonary oedema; 35 fulfilled the inclusion criteria and were treated successfully with NIPSV, although the documentation during the first hour was incomplete due to logistic reasons; 76 patients were treated successfully but were included in the study because the first recorded SpO_2 was above 85 %.

Within the first 30 min of NIPSV, SpO_2 improved significantly in all patients treated successfully (Table 1). Before NIPSV, mean SpO_2 was 73.8 ± 11 % while the oxygen flow rate was 7.3 ± 3.7 l/min. After 30 min of ventilation, SpO_2 increased significantly to 90.3 ± 4.83 % (Fig. 1) and supplemental oxygen was reduced to 5.1 ± 3 l/min. Within 1 h pH increased significantly from 7.22 ± 0.1 to 7.31 ± 0.07. PCO_2, which was elevated when NIPSV was started (mean 62 ± 18.5 mmHg), decreased significantly to 48.3 ± 11.5 mmHg after 60 min ($p < 0.01$). Heart rate and blood pressure normalised (Table 2).

Mean duration of NIPSV was 6 h 9 min with a wide range of between 120 min to 16 h. Eleven patients completed NIPSV within 3 h; the remaining patients recovered more slowly. None of the patients experienced a recurrence of pulmonary oedema within 24 h after the end of NIPSV.

We observed two specific subgroups among the study population, patients with myocardial infarction ($n = 5$) and severely hypercapnic patients ($n = 7$). No differences were found between these groups. There is a tendency for hypercapnic patients to tolerate higher respiratory pressure levels and improve faster. In one case intubation could not be avoided. The patient presented clinical signs of pulmonary oedema. SpO_2 increased from 65 to 80 % within the first 30 min of NIPSV. However, saturation did not improve to above 80 %. He was intubated after 2 h, received mechanical ventilation and was extubated after 16 h. Leukocytosis, purulent bronchial secretions and a high temperature developed during the first 12 h in hospital. Bronchoalveolar lavage confirmed

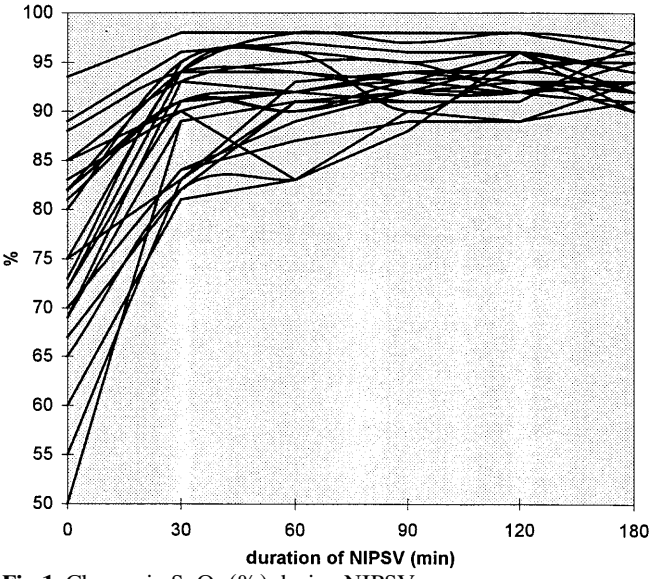

Fig. 1 Change in SpO_2 (%) during NIPSV

bacterial pneumonia. The patient was not excluded because analysis showed that the patient suffered from two overlapping conditions, pulmonary oedema and pneumonia.

Four patients experienced vomiting during NIPSV. No signs of aspiration were found on the follow-up chest X-ray. The face mask caused growing discomfort with the increasing duration of NIPSV. Three patients developed skin lesions on the nose caused by the pressure of the mask which healed within days.

Four patients died from underlying diseases between 1 and 28 days after NIPSV. Three patients had recurrent myocardial infarction. A "Do not Resuscitate" order was decided before the lethal situation occurred.

Discussion

This study was initiated to evaluate the outcome of patients with severe pulmonary oedema being treated with NIPSV. The reason for strict exclusion guidelines was that we wanted to focus on those patients who were at a high risk for orotracheal intubation within the next 30 to 60 min according to clinical signs. Our results revealed that orotracheal intubation was avoided even in patients with a poor prognosis because of greater age, multiple morbidity and recurrent pulmonary oedema.

Mehta et al. [7] solved the problem by comparing Bi-PAP versus CPAP in acute pulmonary oedema. The study evaluates patients with mild pulmonary oedema presenting a PaO_2 of 80 mmHg in the NIPSV group and $aPaO_2$ of 112 mmHg in the CPAP group. After 30 min of NIPSV a significant improvement ($p < 0.05$) of heart rate, blood pressure and blood gas values occurred. There was no significant difference in blood gases. We used higher IPAP levels than Mehta, which might contribute to a shorter duration – 7.1 h versus 6 h 9 min – of NIPSV. The efficacy of CPAP has been shown in a randomised, controlled trial presented by Bersten et al. [6]. They compared 19 patients with CPAP to 20 patients receiving oxygen insufflation and were able to show that the latter required endotracheal intubation significantly more often. All patients in the CPAP group improved, whereas 7 of the 20 patients in the oxygen group needed intubation. Similar to our results, a significant improvement of blood gases was observed within the first 30 min in the CPAP group.

The comparison of SaO_2, amount of hypoxaemia and oxygen supply between the different studies is difficult, because if ventilators (i.e. BIPAP-S/T) are used which do not produce a fixed oxygen mixture and oxygen is added behind the respirator, the determination of PaO_2:FiO_2 (fractional inspired oxygen) ratio is highly inaccurate. Varying flow rates and small amounts of leakage have a great influence on this ratio. We faced the same problem and were not able present confirmed values of PaO_2:FiO_2 ratio. We chose SpO_2 as a mean parameter because it is one of the key technical devices in continuous monitoring of patients with respiratory insufficiency in an emergency situation. Arterial blood gases only characterise single moments and are not available continuously. Suspected pulmonary embolism or myocardial infarction prevent arterial puncture. Non-invasive monitoring can detect physiological techniques much faster than invasive techniques because they provide continuous supervision of the patient [8]. Venous

Table 2 Mean values (± standard deviation) of respiratory and circulatory parameters during NIPSV

	Before NIPSV	After 30 min	After 60 min	After 120 min	After 180 min
Saturation (%)	73.8 ± 11	90.3 ± 4.83*	91.7 ± 4.0*	93.5 ± 2.4*	93.7 ± 2.4*
pH	7.22 ± 0.1	7.29 ± 0.08**	7.31 ± 0.07*	7.35 ± 0.06*	7.39 ± 0.05*
PCO_2 (mm Hg)	62 ± 18.5	48.1 ± 13.1**	48.4 ± 11.5*	46.3 ± 8.0**	40.1 ± 8.3*
PO_2 (mm Hg)	57.6 ± 13.1	70.3 ± 17.1	72.5 ± 15.3	87.6 ± 16.1	76.6 ± 14.1
Oxygen (l/min)	7.3 ± 3.7	5.1 ± 3.0*	4.9 ± 3.0*	3.4 ± 1.6*	2.7 ± 1.4*
Heart rate (b/min)	123.7 ± 26.1	110.2 ± 21.3*	104.9 ± 23.2*	103.9 ± 24.2*	99.1 ± 23.9*
Systolic blood pressure (mm Hg)	145.7 ± 36.7	126 ± 22.1*	120 ± 27.7*	123.3 ± 26.4*	132.8 ± 22.2*

* $p < 0.01$, ** $p < 0.05$ compared to value before NIPSV

blood gas samples are as appropiate as arterial samples to measure pH and CO_2 tension, as shown in patients undergoing bypass surgery [9] or in patients with diabetic ketoacidosis [10].

Meduri et al. [11] ventilated six patients noninvasively with hypercapnic and four with hypoxaemic respiratory failure and thereby showed that noninvasive ventilation is a potential method for reversing acute respiratory failure. Later, increasing numbers of patients with chronic obstructive lung disease (COPD) and acute exacerbations were treated with noninvasive ventilation. Elliott et al. [12] reported on 6 patients, Brochard et al. [13] on 11 and Folgio et al. [14] on 49. Then Benhamou et al. [15] documented the successful treatment also of patients suffering from cardiac insufficiency. Although the first descriptions of noninvasive ventilation for pulmonary oedema date back to the 1930's [16], this knowledge was neglected for a long time.

Bott et al. [17] and Brochard et al. [4] have shown in randomised studies that noninvasive ventilation can prevent endotracheal intubation and reduces mortality and duration of hospital stay in patients with acute exacerbations of COPD. Two further randomised studies also included patients with pulmonary oedema. Wysocki et al. [18] and Kramer et al. [19] studied the use of noninvasive ventilation for acute respiratory failure of different origins. They found that the rate of intubation and mortality is reduced. Wysocki et al. observed the reduction only among hypercapnic patients. In this study 8 patients with pulmonary oedema were included. Kramer included 2 patients. In neither studies was their outcome specified separately.

How a rapid improvement occurs remains speculative. Pathophysiological surveys do not exist. We postulate that at least two different mechanisms work together: improved work of breathing and normalisation of cardiac output. NIPSV is able to reduce the diaphragmatic work of breathing [20, 21] and induce a decline in oxygen consumption of respiratory muscles. This might explain why hypercapnic patients especially respond well to NIPSV. Hypercapnia is in these cases the consequence of an overload of respiratory work. As the work of breathing is reduced, hypercapnia normalises. In addition, IPAP increases lung volume and reduces right-to-left shunting by recruiting previously hypoventilated alveoli. Cardiac output rises due to improved myocardial oxygenation. Increased intrathoracic pressure diminishes right ventricular preload and left ventricular afterload. As a result, a lower right ventricular filling pressure [22] has to be postulated. The paradoxical movement of the interventricular septum, which is secondary to the abnormal distension of the right ventricle, comes to a halt [23] and left ventricular stroke volume rises.

An important advantage of NIPSV may be the decreased risk of nosocomial pulmonary infection, which becomes a problem after the first day of intubation [2]. Since NIPSV can be terminated without weaning whenever respiratory function is stabilised, the duration of NIPSV is shorter than that of invasive ventilation. In addition, the function of the nose and throat as a natural barrier against infection is retained. Undesired side effects were rare and minor. We cannot support the conclusion of Mehta et al. [7], who found a higher incidence of myocardial infarction among patients being treated with NIPSV in contrast to those receiving CPAP ventilation. In our study, myocardial infarction was suspected in several cases before NIPSV and confirmed in 5 cases during follow-up.

Great care in selecting patients for NIPSV is necessary. One patient in our study, who had to be intubated, suffered from pneumonia. The overall positive effect of NIPSV in our study is limited to patients with severe pulmonary oedema of different cardiac origins. In general, NIPSV is not difficult to perform, if the patient is closely supervised. We conclude that NIPSV can be highly successful in patients with severe cardiogenic pulmonary oedema. It is strongly recommended as an addition to conventional therapy, especially if conventional therapy is not able to induce a significant improvement and orotracheal intubation is likely.

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