JOURNAL OF PHYSIOLOGY AND PHARMACOLOGY 2007, 58, Suppl 5, 539–549
www.jpp.krakow.pl

T. PLADECK[1,2], C. HADER[2], A. VON ORDE[3], K. RASCHE[2], H.W. WIECHMANN[1]

NON-INVASIVE VENTILATION: COMPARISON OF EFFECTIVENESS, SAFETY, AND MANAGEMENT IN ACUTE HEART FAILURE SYNDROMES AND ACUTE EXACERBATIONS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

[1]St. Barbara-Klinik, Abteilung für Innere Medizin, Bereich Schlaflabor und Innere Intensivmedizin, Hamm, Germany; [2]Kliniken St. Antonius, Akademisches Lehrkrankenhaus der Heinrich-Heine-Universität Düsseldorf, Zentrum für Innere Medizin, Schwerpunkt Pneumologie, Wuppertal, Germany; [3]Universität Bielefeld, Fakultät für Gesundheitswissenschaften, Bielefeld, Germany

Continuous positive airway pressure ventilation (CPAP) and non-invasive positive pressure ventilation (NPPV) are accepted treatments in acute cardiogenic pulmonary edema (ACPE) and acute exacerbation of chronic obstructive pulmonary disease (AECOPD). The aim of the study was a comparison of effectiveness, safety, and management of NPPV in ACPE and AECOPD trying to find an approach for standard management in intensive care. Thirty patients with acute respiratory failure (14 due to ACPE, 16 due to AECOPD) were prospectively included into the study. If clinical stability could not be achieved by standard therapy (pharmacological therapy and oxygen) patients were treated by non-invasive ventilation (NPPV) using a BiPAP®-Vision™ device in S/T-mode. During the first 90 min after the onset of NPPV respiratory and vital parameters were documented every 30 min. Additional relevant outcome parameters (need for intubation, duration of ICU stay, complications and mortality) were monitored. We found that 85.7% of the ACPE patients and 50.0% of the AECOPD patients were treated successfully with NPPV. Intubation rate was 31.2% in the AECOPD group and 14.3% in the ACPE group. 78.6% of the ACPE patients and 43.8% of the AECOPD patients were regularly discharged from hospital in a good condition. In the first 90 min of NIV, there was a significant amelioration of respiratory and other vital parameters. In ACPE patients there was a significant increase in PaO_2 from 58.9 mmHg to 80.6 mmHg and of oxygen saturation (SaO_2) from 85.1% to 93.1% without changing the inspiratory O_2 concentration. This effect was comparable in the AECOPD group, but only could be achieved by increasing the inspiratory ventilation pressure. In the ACPE group inspiratory ventilation pressure could be reduced. In conclusion, in acute respiratory failure, ACPE patients comparably profit from NPPV as do patients with AECOPD, but the algorithm of titration for non-invasive ventilation pressure is different.

Key words: *cardiogenic pulmonary edema, chronic obstructive pulmonary disease, non-invasive ventilation*

INTRODUCTION

A major interest in using non-invasive ventilation is to avoid complications of invasive ventilation. Although invasive mechanical ventilation is highly effective, endotracheal intubation has numerous well known risks of complications. These complications are related directly to intubation (injury of the vocal cord or trachea), to aspiration of gastric content, irritation or injury due to the endotracheal tubus, edema, inflammation and increased mucus production. Furthermore patients need more sedatives and analgetics.

Although non-invasive ventilation dates back to 1930, it was not used widely till the 1980s. Since the introduction of CPAP in the treatment of obstructive sleep apnea syndrome (OSAS) with a full face or nasal mask, non-invasive ventilation a gained widespread acceptance in several conditions of acute respiratory failure. Using masks as interfaces is the most important advantage of non-invasive positive pressure ventilation (NPPV). NPPV preserves normal swallowing, speaking, cough, air warming, and humification. (1, 2). In patients with COPD and hypercarbic respiratory failure several studies show high success rates in avoiding intubation (60-90%), reducing respiratory rate and dypsnea scores, improving gas exchange and in reducing mortality rate (3-6). CPAP and BIPAP have been shown to be effective as well in ACPE with hypoxemic respiratory failure. Patients without myocardial infarction or hemodynamic complications showed excellent response to CPAP therapy (7-13). The use of NPPV in patients with pneumonia or acute respiratory distress syndrome (ARDS) showed conflicting results (14, 15). The aim of our study was a comparison of the effectiveness, safety, and management of NPPV under two different circumstances, acute exacerbation of COPD and acute cardiogenic pulmonary edema. Previous data confirm a better effect of NPPV in AECOPD patients. We tried to find a standard approach for management of patients with ACPE and AECOPD in intensive care.

PATIENTS AND METHODS

This study was performed according to the guidelines set by the Declaration of Helsinki for Human Research, concerning safety and ethics of human experimentation. It was a prospective observational study. Thirty patients with acute respiratory failure were consecutively enrolled in the study. Data were collected prospectively for 21 months. The criteria for eligibility were acute respiratory distress that had deteriorated despite aggressive medical management. Severe dyspnea at rest was determined by a clinician. Inclusion criteria are summarized in *Table 1* and the exclusion criteria are summarized in *Table 2*. These criteria were selected according to evidence based guidelines (1). Anthropometric and clinical measurements were taken: gender, age, body-mass-index (BMI) and APACHE II -Score (acute physiology and chronic health evaluation score) (18).

All patients with acute respiratory failure considered eligible for the study were admitted to intensive care unit and received standard basic care and received oxygen through a venturi mask.

Table1. Criteria for eligibility.

AECOPD	ACPE
Symptoms: amount of sputum, purulent sputum, dyspnea. Minor symptoms: wheezing, painful throat cough, cold, obstructed nasal breathing. >2days: 2 major or 1 major and 1 minor symptom (16).	Findings on chest X-ray: pulmonary edema Clinical examination: • fine and high pitched crepitations • added heart sound (17)
• Severe dypnea at rest • Contraction of accessory muscles of respiration or paradoxical abdominal motion • Deterioration of pulmonary gas exchange: • $PaCO_2$ >45 mmHg and/or SaO_2 <90% during O_2 therapy • Respiratory rate >30 breaths/min • Acidosis (pH <7.35) • Ratio PaO_2/F_iO_2 <200 (1)	

Table 2. Exclusion criteria.

• deterioration in neurogic status according to Glasgow coma scale • history or high risk of aspiration • mask intolerance • ARDS (clinical diagnosis) • requirement of urgent intubation (refractory hypoxemia) • acute coronary syndrome, myocardial infarction • hemodynamic instability, defined as a systolic blood pressure ≤90 mmHg • clinically significant ventricular arrhythmias • gastrointestinal bleeding • respiratory arrest • cardiac arrest (1)

Inspiratory oxygen concentration (FiO_2) was adjusted to achieve a level of arterial oxygen saturation (SaO_2) >90%.

Heart rate (electrocardiography) and respiratory rate were monitored continuously, blood pressure was measured invasively. A bedside pulsoximeter was used to control arterial oxygen saturation. The head of the bed was kept elevated at a 45-degree angle. Medication included antibiotics, diuretics (furosemide or torasemide), bronchodilators (reproterol, aminophylline), heparine, corticosteroids, morphine, cardiovascular drugs, and therapy for comorbidities if necessary. Volume and electrolyte abnormalities were corrected. The diagnosis of acute exacerbation of COPD was established according to the criteria of Semungal et al (16) and that of ACPE according to the definition of the Framingham study (17).

All patients received NPPV treatment in a semirecumbent position with the head raised 45° using a well fitting full face mask as an interface (King Systems Cooperations™). The mask was secured with head straps to avoid an excessively tight fit and connected to a ventilator (BiPAP®-Vision™ ventilory support system, Respironics, Murrysville, PA). Non-invasive ventilation was used in a pressure-controlled spontaneous-timed mode (S/T mode) via the BiPAP®-Vision ventilory support system.

The level of pressure support (inspiratory positive airway pressure, IPAP) was chosen between 12 and 16 cmH_2O. Expiratory positive airway pressure (EPAP) was varied between 4 and 6 cmH_2O. Pressure support was progressively increased and adjusted for every patient to obtain an expired tidal volume of more than 7 ml/kg, a respiratory rate of fewer than 25 breaths/min and a clinical disappearance of accessory muscle activity. F_iO_2 was adjusted to achieve a level of SaO_2 >90%. IPAP was then increased repeatedly by 1 to 2 cmH_2O until the F_iO_2 requirement was 0.6 or less. The patients were not sedated.

Respiratory rate, expired tidal volume (V_T), IPAP, EPAP, and F_iO_2 were monitored every 15 min and arterial-blood gases were determined. Close monitoring was performed for 90 min, because several studies demonstrated that success of NPPV can be judged in this period (14, 19).

NPPV was continuously maintained until oxygenation and clinical status improved. Subsequently, each patient was evaluated breathing supplemental oxygen without ventilatory support. NPPV was reduced progressively in accordance with the degree of clinical improvement. NPPV was stopped in one of the following conditions:

- NPPV and therapy successful: SaO_2 >90% during F_iO_2 <35%, respiratory rate <20 breaths/min;
- Therapy successful, intermittent NIV necessary. Therapy was considered successful if the patient was stable under oxygen therapy (2-4 l/min) and persistent intermitted NPPV, without any need for intubation;
- Intubation: intubation was performed if respiratory rate after 2 h of NPPV was >30 breaths/min, persistent hypoxemia, in hemodynamic instability (systolic blood pressure <70 mmHg), in agitation or worsened neurological status, inability to tolerate the mask or aspiration of gastric content.

The criteria were selected according to evidence based guidelines.(1, 5, 20).

Outcome variables included the length of stay in the intensive care unit, duration of ventilatory assistance, mortality, the need for endotracheal intubation, and complications during the treatment such as sepsis, pneumonia (evidenced by radiographic findings), myocardial infarction.

Statistical analysis

The two groups were compared using the Chi^2 test for dichotomous variables and an independent sample *t*-test. A P value <0.05 was considered to be significant. Repeated measurements in NPPV were performed according to the method of generalized linear models (GLM) in a multivariate analysis to compare treatment effects from measurement points T_0 (0 minutes) to T_4 (90 minutes) differences between both groups.

RESULTS

A total of 30 patients were admitted to the intensive care unit with acute hypoxemic or hypercapnic respiratory failure, 16 patients due to AECOPD, 14 patients due to ACPE. Baseline characteristics are shown in *Table 3*. There were no significant differences in gender, age, body mass index, and APACHE II Score.

Respiratory rate, heart rate, systolic and diastolic blood pressure improved in both groups during NPPV therapy. In the first 90 min of NPPV, there was a significant amelioration of respiratory parameters. Patients showed an initial and sustained improvement of the mean PaO_2 and SaO_2 in both groups without significant differences. In ACPE patients, there was a significant increase in PaO_2 from 58.9 mmHg to 80.6 mmHg and of SaO_2 from 85.1% to 93.1% without changing the inspiratory O_2 concentration. The effect in AECOPD patients was comparable (as shown in *Fig. 1*).

There was a significant increase of pH in both groups during the first 90 minutes of NIV (*Fig. 2*). Although there was a steeper increase in the ACPE

Table 3. Baseline characteristics of patients with AECOPD and ACPE (**t*-test, **Chi^2; NS=non-significant).

	AECOPD	ACPE	P value
	n=16	n=14	
Gender			NS**
male	8 (50%)	11 (78.6%)	
female	8 (50%)	03 (21.4%)	
Age (years)	73.3 ±9.9	73.2 ±7.8	NS*
BMI (kg/m^2)	24.0 ±4.4	26.2 ±2.4	NS*
APACHE II-Score	20.8 ±3.6	22.8 ±4.4	NS*

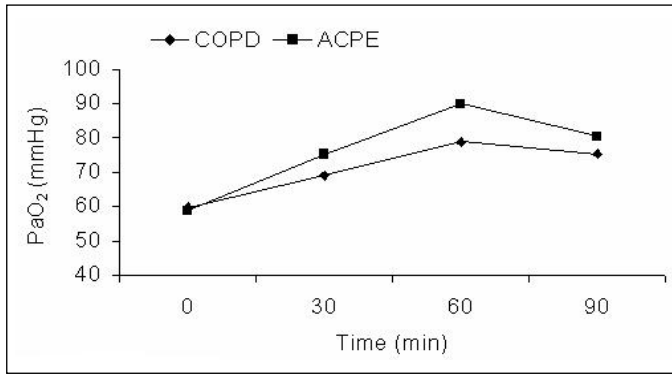

Fig. 1. Mean PaO_2 during NIV treatment. Significant differences were found (GLM with retest) during the first 90 min in both groups (P=0.0001). No significant differences were found between the two groups.

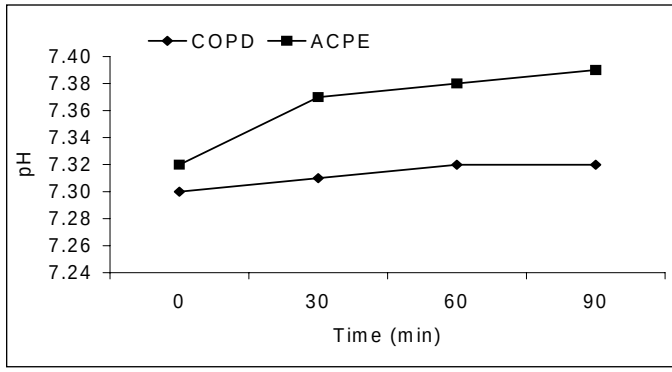

Fig. 2. pH values during NIV. Significant differences were found (GLM with retest) during the first 90 min in both groups. No significant differences were found between the two groups.

group, no significant differences between both groups were found. Although NIV was performed with good results, no significant changes in $PaCO_2$ could be detected during the first 90 min. $PaCO_2$ was significantly higher in patients with AECOPD (*Fig. 3*).

The improvement of respiratory parameters was comparable in both groups. As shown in *Figures 4-6*, this was mainly achieved by the increased inspiratory ventilation pressure (IPAP) in the AECOPD group. In the ACPE group, inspiratory ventilation pressure could be reduced along with F_iO_2. 85.7% of the

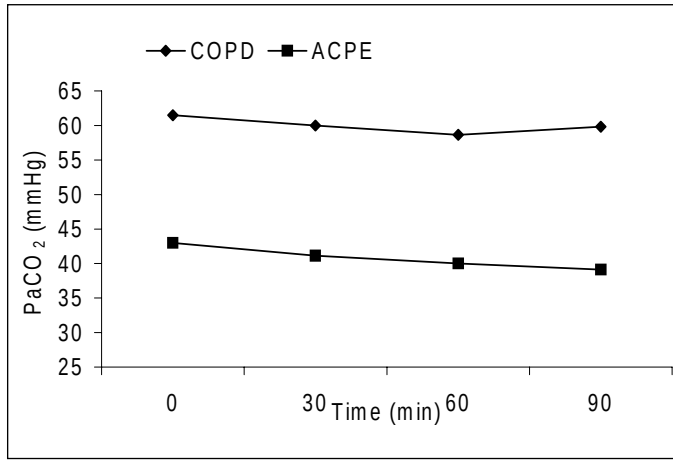

Fig. 3. $PaCO_2$ during NIV. No significant differences were found (GLM with retest) during 90 minutes in either group. Significant differences were found between the two groups.

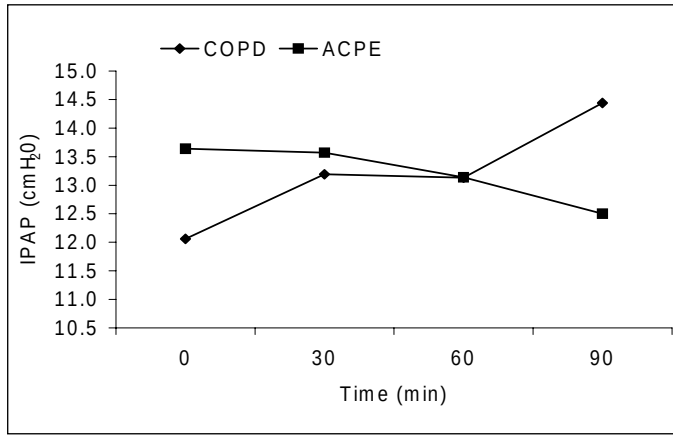

Fig. 4. IPAP during NIV. No significant differences were found (GLM with retest) during 90 minutes in either group or between the two groups.

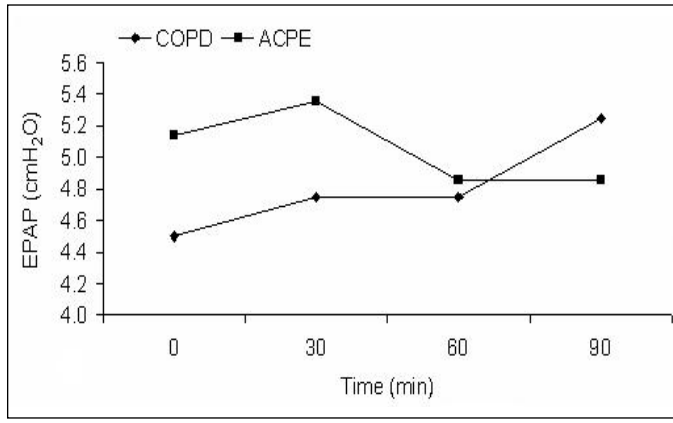

Fig. 5. EPAP during NIV. No significant differences were found (GLM with retest) during 90 minutes in either group or between the two groups.

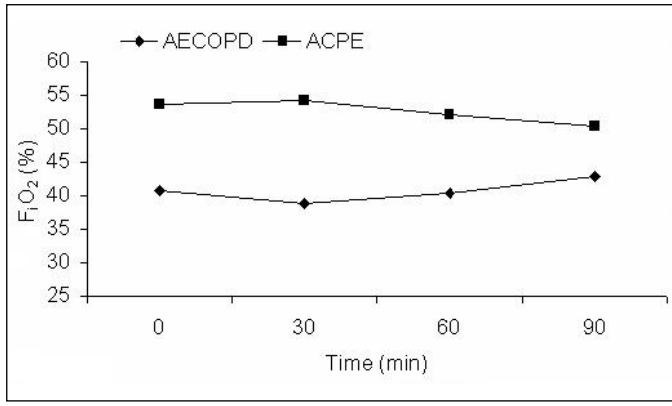

Fig. 6. F_iO_2 during NIV. No significant differences were found (GLM with retest) during 90 minutes in either group. Significant differences were found between the two groups (P=0.019).

Table 4. Outcome of NPPV treatment after discharge from intensive care unit.

	AECOPD	ACPE	Total
	n=16	n=14	n=30
NIV successful	8 (50%)	12 (85.7%)	20 (66.7%)
NIV not successful (intubation)	5 (31.2%)	2 (14.3%)	7 (23,3%)
Intermittient NIV	3 (18.8%)	--	3 (10%)

Table 5. Outcome of NPPV treatment at the time of discharge from hospital.

	AECOPD	ACPE	Total
	n=16	n=14	n=30
Discharged from hospital	7 (43.8%)	11 (78.6%)	18 (60%)
Discharged on intermittent NIV	4 (25%)	--	4 (13.3%)
Readmission to ICU, no admission at the end of study	1 (6.2%)	--	1 (3.4%)
Mortality	4 (25%)	3 (21.4%)	7 (23.3%)

Table 6. Serious complications during NPPV therapy in intensive care unit.

	AECOPD	ACPE	Total
	n=16	n=14	n=30
No complications	3 (18.8%)	4 (28.6%)	7 (23.3%)
Mycardial infarction	1 (6.2%)	3 (21.4%)	4 (13.3%)
Pneumonia	8 (50%)	4 (28.6%)	12 (40%)
Ventricular arrhythmias	2 (12.5%)	2 (14.3%)	4 (13.4%)
More than one complication	2 (12.5%)	1 (7.1%)	3 (10%)

ACPE patients and 50% of the AECOPD patients were treated successfully with NPPV.

Intubation rate was 31.2% in the AECOPD group and 14.3% in the ACPE group. 78.6% of the ACPE patients and 43.8% of the AECOPD patients were regularly discharged from hospital in a good condition. The rate of serious complications was 23 out of 30 (77%); pneumonia was the most common complication in both groups. The ACPE group had a significantly more myocardial infarctions (20%). All patients with myocardial infarction were

Table 7. Duration of ventilatory assistance and length of stay in intensive care (*t*-test, NS= non-significant).

	AECOPD	ACPE	P value
	n=16	n=14	
Duration of ventilatory assistance (hours)	19.9 ±22.6	7.8 ±8.0	NS
Length of stay on the intensive care unit (hours)	114.3 ±18.8	59.7 ±60.6	P=0.03

regularly discharged from hospital. Patients with AECOPD stayed longer on the intensive care unit and received longer NPPV treatment. Mortality was 25.0% in the AECOPD group and 21.4% in the ACPE group. This difference was not significant.

DISCUSSION

Ventilation pressure

The study was designed to compare effectiveness, safety, and management of NPPV in ACPE and AECOPD trying to find an approach for the standard management in intensive care. Studies from Benhamou et al (8), Brochard et al (3, 20), and Plant et al (21) strongly support that non-invasive positive-pressure ventilation is an effective treatment for patients with acute hypercarbic respiratory failure in AECOPD. In ACPE, NPPV, especially CPAP therapy, has been shown in controlled trials by Bersten et al (9), Hoffmann and Welte (22), and von Rusterholtz et al (12) to be an effective therapy improving oxygenation, decreasing respiratory work, and reducing the rate of endotracheal intubation. Nevertheslees, the effect of NPPV in acute respiratory failure on outcomes, such as the need for endotracheal intubation, length of stay in the intensive care unit (ICU), duration of ventilation, and survival, varies among the studies. The above mentioned studies, in accordance with our present results, have shown a significant increase of PaO_2 in the first few hours of non-invasive ventilation.

The influence of NPPV on hypercarbia itself is controversial in patients with AECOPD or pulmonary edema. In this study, the mean IPAP was increased up to 14.4 mbar and the mean EPAP was 5 mbar. This protocol did not affect hypercarbia significantly. Similarly to our results, Brochard et al (3, 20) could not improve hypercarbia, either with an inspiratory pressure support of 12 cmH_2O or 20 cmH_2O. In conflict with these data, there is growing evidence that the benefit of NPPV seems greatest in patients with almost pure hypercarbic respiratory failure. This condition is most common in patients with AECOPD. On the other hand, Bersten et al (9), Hoffmann and Welte (22), and Rusterholtz et al (12) have succeeded in reducing $PaCO_2$ significantly using an IPAP between 15 and 20 mbar in the first hour of treatment.

Blood pressure in patients with ACPE was reduced significantly in our study, which was in line with the trials of Hoffmann and Welte (22) and Rusterholtz et

al (12). Nava et al (11) treated patients with ACPE *via* NPPV with an IPAP of 14.5 mbar and an EPAP of 6.1 mbar. Respiratory rate, heart rate and mean blood-pressure decreased significantly.

Need for endotracheal intubation

Intubation rate in our study patients with AECOPD was 31.2%. A meta-analysis of Keenan et al (23) has shown that the addition of NPPV to standard therapy in patients with acute respiratory failure decreases the need for endotracheal intubation. The effect was restricted to patients whose cause of acute respiratory failure was AECOPD. The intubation rate was 35% in that study. Our data are in good accordance with those findings.

Intubation rate in our ACPE patients with was 14.3%. Several studies found a significant reduction of endotracheal intubation in patients with ACPE treated with NPPV in comparison with conventional treatment. The intubation rate varied between 0% and 21% (3, 6, 8, 9, 12, 24). In a meta-analysis from Pang et al (19) consisting of three randomized controlled trials NPPV, especially CPAP, was associated with a decreased intubation rate (mean 12.5%) compared with standard therapy alone. Apart from of a study by Kramer et al (5), the intubation rate in patients with ACPE is, in general, lower than in patients with AECOPD. Again our data are in good accordance with these findings.

Mortality

The present study showed an in-hospital mortality of 32.3%, with no significant difference between both groups. Previous studies showed mortality rates between 9% and 30% in NPPV treated patients with AECOPD (8, 20, 21, 23) and between 8% and 27% in NPPV treated patients with ACPE (12, 19).

Complications

Brochard et al (20) have found a trend toward a decrease in the rate of nosocomial pneumonia in patients treated with NPPV (relative risk, 0.28; 95% confidence interval 0.06-1.27). The authors have found that 9 out of 43 patients with AECOPD treated with NPPV (21%) developed several complications. The type of complication was comparable with the findings in our study. In contrast, the complication rate in our study was much higher in AECOPD (81.2%) and ACPE (71.4%) patients. Rusterholtz et al (12) have reported complications in 6 out of 26 patients (23%) with ACPE.

The fact that our ACPE group had a higher rate of myocardial infarction (3 out of 14) causes concern about bilevel ventilation for therapy of acute pulmonary edema. A randomized trial of Mehta et al (25) compared bilevel *vs*. CPAP in acute pulmonary edema. A higher rate of myocardial infarction was found in the bilevel ventilation group. On the basis of these findings we would recommend to use

either CPAP or to begin BiPAP with low pressures and titrate the pressure according to the patient's clinical condition.

Further studies should be performed to identify those patients with hypoxemic respiratory failure who most likely will benefit from NPPV, and those who are at the highest risk of adverse consequences. Despite the fact that there was no influence of NPPV on hypercarbia, the benefit of NPPV seems greatest for patients with hypercarbic respiratory failure. We conclude that in acute respiratory failure, ACPE patients comparably profit from NPPV as do patients with AECOPD, but the algorithm of titration for non-invasive ventilation pressure is different.

REFERENCES

1. Burchardi H, Kuhlen R, Schönhofer B, Müller E, Criée CP, Welte T. Konsensus-Statement zu Indikation, Möglichkeiten und Durchführung der nicht-invasiven Beatmung bei der akuten respiratorischen Insuffizienz. *Intensivmed* 2001; 38: 611-621.
2. Meduri GU, Turner RE, Abou-Shala N, Wunderink R, Tolley E. First-line intervention in patients with acute hypercapnic and hypoxemic respiratory failure. *Chest* 1996; 109: 179-193.
3. Brochard L. Isabey D, Piquet J et al. Reversal of acute exacerbations of chronic obstructive lung disease by inspiratory assistance with face mask. *N Engl J Med* 1990; 323: 1523-1530.
4. Elliott MW, Steven MH, Phillips GD, Branthwaite M.A. Non-invasive mechanical ventilation for acute respiratory failure. *Br Med J* 1990; 300: 358-360.
5. Kramer N, Meyer TJ, Meharg J, Cece RD, Hill NS. Randomised, prospective trial of noninvasive positive pressure ventilation in acute respiratory failure. *Am J Respir Crit Care Med* 1995; 151: 1799-1806.
6. Meduri GU, Abou-Shala N, Fox RC, Jones CB, Leeper KV, Wunderink R. Noninvasive face mask mechanical ventilation in patients with acute hypercapnic respiratory failure. *Chest* 1991; 100: 445-454.
7. Antonelli M, Conti G, Rocco M et al. A comparison of positive-pressure ventilation and conventional mechanical ventilation in patients with acute respiratory failure. *New Engl J Med* 1998; 339: 429-435.
8. Benhamou D, Girault C, Faure C, Portier F, Muir J.F. Nasal mask ventilation in acute respiratory failure. Experience in elderly patients. *Chest* 1992; 102: 912-917.
9. Bersten AD, Holt AW, Vedig AE, Skowronski G, Baggoley CJ. Treatment of severe cardiogenic pulmonary edema with continuous positive airway pressure delivered by face mask. *N Engl J Med* 1991; 325: 1825-1830.
10. Lin M, Yang YF, Chiang HAT, Chang MS, Chiang BN, Cheitlin MD. Reappraisal of continuous positive airway pressure therapy in acute cardiogenic pulmonary edema: short-term result and long-term follow up. *Chest* 1995; 107: 1379-1386.
11. Nava S, Carbone G, DiBattista N et al. Noninvasive ventilation in cardiogenic pulmonary edema: a multicenter randomized trail. *Am J Respir Crit Care Med* 2003; 168: 1432-1437.
12. Rusterholz T, Kempf J, Berton C et al. Noninvasive pressure support ventilation (NIPSV) with face mask in patients with acute cardiogenic pulmonary edema (ACPE). *Intensive Care Med* 1999; 25: 21-28.
13. Wysocki M, Tric L, Wolff MA, Millet H, Herman B. Noninvasive pressure support ventilation in patients with acute respiratory failure. *Chest* 1995; 107: 761-768.

14. Ferrer M, Esquinas A, Leon M, Gonzales G, Alarcon A, Torres A. Noninvasive ventilation in severe hypoxemic respiratory failure: a randomized clinical trial. *Am J Respir Crit Care Med* 2003; 168: 1438-1444.
15. Miletin MS, Detsky AS, Lapinsky SE, Mehta S. Non-invasive ventilation in acute hypoxemic respiratory failure. *Intensive Care Med* 2000; 26: 242-245.
16. Knaus WA, Draper EA, Wagner DP, Zimmermann JE. APACHE II: A severity of disease classification system. *Crit Care Med* 1985; 13: 818-829.
17. Seemungal TAR, Donaldson GC, Bhowmik A, Jeffries DJ, Wedzicha JA. Time course and recovery of exacerbations in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2000; 161: 1608-1613.
18. Marantz .R, Tobin JN, Wassertheil-Smoller S et al. The relationship between left ventricular systolic function and congestive heart failure diagnosed by clinical criteria. *Circulation* 1988; 77: 607-612.
19. Pang D, Keenan SP, Cook DJ, Sibbald WJ. The effect of positive pressure airway support on mortality and the need for intubation in cardiogenic pulmonary edema. *Chest* 1998; 114: 1185-1192.
20. Brochard L, Mancebo J, Wysocki M et al. Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. *N Engl J Med* 1995; 333: 817-822.
21. Plant PK, Owen JL, Elliott MW. Early use of non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease on general respiratory wards: a multicentre randomised controlled trial. *Lancet* 2000; 355: 1931-1935.
22. Hoffmann B, Welte T. Die Anwendung einer nichtinvasiven druckunterstützten Beatmung zur Behandlung des kardiogenen Lungenödems. *Med Klin 94 Sondernr* 1999; 1: 58-61.
23. Keenan SP, Kernermann PD, Cook DJ, Martin CM, McCormack D, Sibbald WJ. Effect of noninvasive positive pressure ventilation on mortality in patients admitted with acute respiratory failure: a meta-analyse. *Crit Care Med* 1997; 25: 1685-1692.
24. Meduri GU, Conoscenti CC, Menashe P, Nair S. Noninvasive face mask ventilation in patients with acute respiratory failure. *Chest* 1989; 95: 865-870.
25. Mehta S, Jay GD, Woolard RH et al. Randomised, prospective trial of bilevel versus continuous positive airway pressure in acute pulmonary edema. *Crit Care Med* 1997; 25: 620-628.

Author's address: T. Pladeck, Kliniken St. Antonius, Akademisches Lehrkrankenhaus der Heinrich-Heine-Universität Düsseldorf, Zentrum für Innere Medizin, Schwerpunkt Pneumologie/Allergologie Schlaf- und Beatmungsmedizin Klinik, Vogelsangstrasse 106, 42109 Wuppertal, Germany.