

Clinical analysis of optimal timing for application of noninvasive positive pressure ventilation in treatment of AECOPD patients

H.-Y. YAN, Y. YANG, Y.-L. WU

Department of Respiratory Diseases, Sichuan Provincial People's Hospital, Chengdu, Sichuan Province, P.R. China

Intensive Care Unit, Hospital of Guangxi Medical University, Nanning City, China

Abstract. – OBJECTIVES: This study is conducted to investigate an optimal timing of sequential noninvasive positive pressure ventilation (NPPV) applied for patients with acute exacerbations of chronic obstructive pulmonary disease (AECOPD).

PATIENTS AND METHODS: Application of NPPV for 102 patients was randomly observed in the conditions of a 2-hour spontaneous breathing trial (SBT-2) and pulmonary infection control (PIC) window. Efficiency of NPPV in treatment of the patients, an incidence rate of tracheal reintubation, length of time for patients received invasive mechanical ventilation, and a morbidity rate of ventilator-associated pneumonia were examined in each group of 51 patients.

RESULTS: The incidence rates for the patients treated successfully with NPPV and for tracheal reintubation were shown as 88.2 and 60.8, and 11.8 and 39.2 in SBT-2 and PIC, respectively (both $p < 0.05$). Length of time (hour) for use of the invasive ventilation was 116 and 82.5 in SBT-2 and PIC, respectively ($p < 0.05$). There was a similar morbidity rate of ventilator-associated pneumonia seen in both groups.

CONCLUSIONS: SBT-2 would be the optimal timing considered to use NPPV for AECOPD patients based on a high success rate and a low risk of tracheal reintubation.

Key Words:

NPPV, AECOPD, 2-hour spontaneous breathing trial, Pulmonary infection control (PIC) window.

Introduction

The noninvasive positive pressure ventilation (NPPV), the provision of ventilatory assistance without airway invasion, has seen increasing use in critical care units, to avoid endotracheal intubation and its attendant complications^{1,2}. Research has showed timely use of NPPV in the treatment of acute pulmonary edema could decrease the need of endotracheal intubation and mechanical ventilation, meanwhile reduce medical cost and

mortality rate of patients³. Accumulating evidence and experience have demonstrated that NPPV has an important role in managing chronic obstructive pulmonary disease (COPD) exacerbations through markedly reducing need for intubation and improving outcomes of patients including relieving dyspnoea, lowering complication and mortality rates, as well as shortening hospital stay⁴⁻⁶.

The application of NPPV in weaning patients from invasive ventilation has been investigated by few studies in which the use of NPPV has been submitted to the conditions of either pulmonary infection control (PIC) or 2 hours spontaneous breathing trial (SBT-2)^{7,8}. Although effects of NPPV on AECOPD (acute exacerbations of chronic obstructive pulmonary disease) patients has been examined in its clinical significance^{9,10} and the tolerance of a 30-120 min SBT has been reported with the adequacy of gas exchange and subjective comfort¹¹, it is still lacking in a comparison of data obtained from the application of NPPV in SBT-2 and PIC. Since an appropriate timing switched to the application of NPPV is a key to the successful treatment of COPD patients, so the selection process takes into consideration a number of factors, including the clinical characteristics and ventilator-acquired complications, and ultimately becomes a clinical judgment depending largely on physician experience.

This study is to explore an optimal timing for NPPV applied for AECOPD patients and adds new knowledge in understanding its clinical interests observed in the conditions of SBT-2 and PIC window, respectively.

Patients and Methods

Patient Inclusion Criteria

Patients taken for this study have to satisfy all of the conditions: (1) COPD and acute exacerbation

tion of COPD (AECOPD) diagnosed according to the standards made by American Thoracic Society and European Respiratory Society¹²; (2) Combination of hypercapnic respiratory failure; (3) Mechanical ventilation provided either by endotracheal or tracheostomy tube, and activity of spontaneous breathing available; (4) No atelectasis, hemoptysis, pleural effusion and other serious diseases of heart, brain, liver, kidney. (5) No NPPV contraindications.

Contraindications for Sequential NPPV Treatment

Contraindications for NPPV include the following: (1) Respiratory inhibition or stop; (2) Abnormalities of the cardiovascular system; (3) Drowsiness, disorders of consciousness with high aspiration risk due to incompetent breathing mechanism; (4) Large amounts of thick and tenacious (purulent) sputum in the airway of a patient; (5) Recent facial or gastroesophageal surgery; (6) Craniofacial trauma and/or fixed nasopharyngeal abnormality; (7) Extreme obesity and severe flatulence in the gastrointestinal tract.

Age, Gender and Group

102 male patients aged from 60-85 years (median, 68.8 years) were randomized into two parallel groups using a random number table, and assigned by study nurse with 51 patients per group. The effects of sequential NPPV treatment on these patients were determined in two groups designed for the conditions of either SBT-2 that invasive mechanical ventilation was disconnected or PIC window that pulmonary infection was controlled by treatments. In the SBT-2 group the ages of the patients were ranged from 63-85 years (median, 67.8 years) and 65-81 years (median, 67.2 years) in the PIC group, respectively. There was no statistical difference in the distribution of ages between these two groups ($p > 0.05$).

Ventilator Settings

Inspiratory and expiratory pressure settings for all patients were initially set up at 3 and 5 cm H₂O. The pressure settings were adjusted up by 1 cm H₂O increment every 5-15 minute intervals. The maximal pressures for expiration and inspiration were designed to be lower than 5 and 25 cm H₂O in the process of the application of NPPV in treatment of the patients, respectively.

Criteria for Pulmonary Infection Control Window

PIC window was established with the symptoms: (1) Absorption of bronchial and pulmonary infection with no fusion patch shown in chest x-ray examination; (2) Significantly reduced sputum volume and sputum purulence with the sputum color changed to be white; (3) One of the indications found with lowering body temperature or $\leq 38^{\circ}\text{C}$, white blood cell count (WBC) of $\leq 10 \times 10^9/\text{L}$ or a decrease of $\geq 2 \times 10^9/\text{L}$ as compared to the previous findings; (4) The mode of mechanical ventilation adjusted to synchronized intermittent mandatory ventilation at 10-12 times/min and to pressure support ventilation at a range of 10-12 cm H₂O (1 cm H₂O = 0.098 kPa).

Efficiency of Sequential NPPV Treatment

NPPV can be considered successful when arterial blood gas and pH improve, dyspnoea is relieved, the acute episode resolves without the need of endotracheal intubation, mechanical ventilation can be discontinued and the patient is discharged from the hospital.

Criteria for Tracheal Reintubation After Disconnection of Invasive Ventilation

Criteria for tracheal reintubation after the patients disconnected from invasive mechanical ventilation may be considered as: (1) A pH value ≤ 7.20 associated with a progressive increase in PaCO₂; (2) Serious hypoxia (PaO₂ < 50 mmHg) even in sufficient supply of oxygen; (3) Serious disturbance of consciousness such as coma, drowsiness and delirium; (4) Respiratory abnormalities with respiratory rate < 8 or > 40 times/min; (5) Respiratory or cardiac arrest.

Diagnosis of Ventilator-Associated Pneumonia

The ventilator-acquired pneumonia was diagnosed with the indications: (1) Pneumonia occurred more than 48 hours after tracheal intubation and connection of ventilator; (2) A pulmonary infiltrate with new inflammatory lesions shown in a chest x-ray; (3) Signs of pulmonary consolidation with or without moist rales in a physical exam; (4) One of the findings including WBC $> 10 \times 10^9$ or $< 4 \times 10^9/\text{L}$ with and without an increased percentage of neutrophils, body temperature $> 37.5^{\circ}\text{C}$, increase in purulent airway secretions with new pathogens found in the secretions.

Statistical Analysis

Values were expressed as a percentage of data from the investigated patients and Mean \pm Standard Deviation (SD) on some of the results, respectively. Statistical analysis was performed using Statistical Package for the Social Science (SPSS Inc., version 12.0, Chicago, IL, USA). Comparisons from groups observed with individual measurements were performed by Student's paired t test in between of two groups. The Chi-square test (χ^2) was conducted to analyze the significance of a parameter within groups. A p value of < 0.05 was considered significant.

Results

Effect of Sequential NPPV Treatment on AECOPD Patients

The patients in both groups received NPPV treatment following invasive mechanical ventilation and the results are shown in Figure 1. An effective treatment was shown in 45 of 51 patients in the SBT-2 group (A) with a 88.2% success rate in the NPPV-treated patients. However, there were 31 of 51 patients in the PIC group (B) and a 60.8% success rate was seen in the treatment. In contrast, the success rate for the NPPV-treated patients in the SBT-2 group was a 28% increase over that in the PIC group. There was significant difference in the treatment effects between these two groups of the patients (χ^2 test, $p < 0.05$).

Prevalence Rate of Tracheal Reintubation in Grouped Patients

Prevalence rate of tracheal reintubation was examined in both groups and the results are shown in Figure 2. Only two patients in the SBT-2 group (A) experienced the tracheal reintubation with a prevalence rate of 11.8%. In contrast, there were 13 of 51 patients in the PIC group (B) with prevalence rate of 39.2% which was about a 3-fold higher than that in the SBT-2 group. There was statistically significant difference in occurrence of the repeated tracheal intubation in these two groups of the patients (χ^2 test, $p < 0.05$).

Measurement for Length of Time for Invasive Mechanical Ventilation

A time-period used for invasive mechanical ventilation was assessed prior to the patients treated with NPPV and the results are shown in Figure 3. The time-period was prolonged in the patients treated with the invasive ventilation

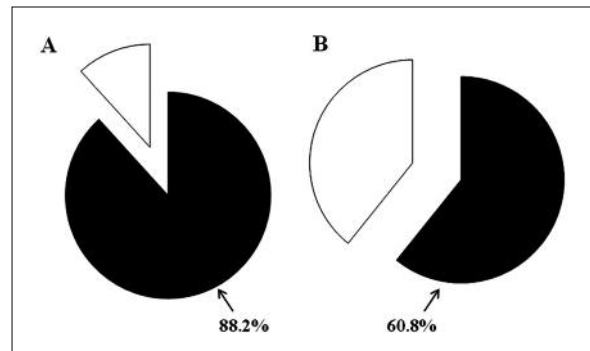


Figure 1. NPPV applied for the patients in SBT-2 increases a success rate of treatment. Efficiency of NPPV in treatment of AECOPD patients was examined in SBT-2 (A) and PIC (B). The success rates (black) of the patients treated with NPPV were expressed with a percentage in each group. A χ^2 test showed a p -value of < 0.05 .

and the length of the time may be reached up to the range of 93-139 hours with a median value of 116 hours in the SBT-2 group. The time-period measured for the patients in the PIC group showed a range of 57-98 hours with a median value of 82.4 hours which was about a 30-hour decrease as compared to that in the PIC group. There was a significant difference in the length of the time observed in the patients using invasive ventilation between these two groups ($p < 0.05$).

Morbidity of the NPPV-Associated Pneumonia

Prevalence rate of the NPPV-associated pneumonia was examined in the patients treated with

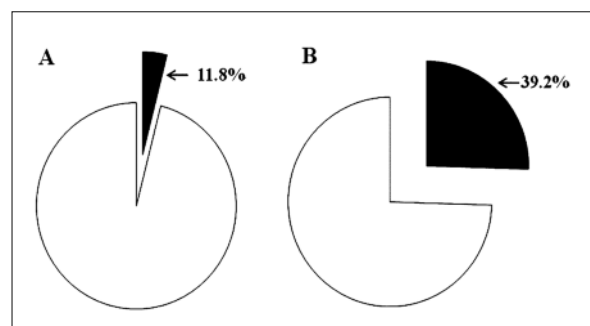


Figure 2. The patients treated with NPPV in SBT-2 shows a low risk of tracheal reintubation. Prevalence rate of tracheal reintubation in AECOPD patients was observed in SBT-2 (A) and PIC (B). The prevalence rate (black) of the repeated intubation was expressed with a percentage in each group. A p -value is < 0.05 as compared to the prevalence rate found between these two groups.

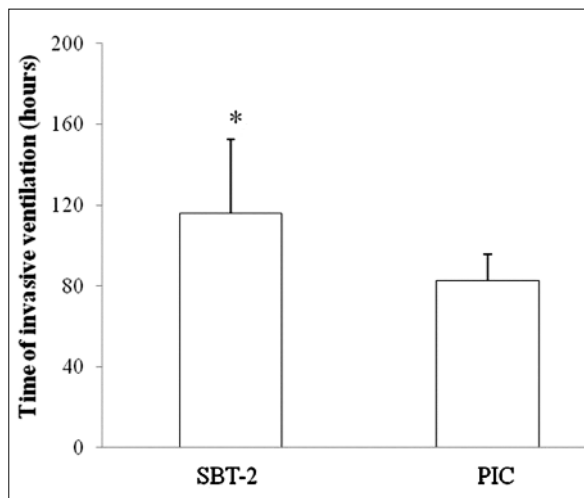


Figure 3. Length of time for the use of invasive ventilation increases in SBT-2. Length of time for patients received invasive ventilation prior to application of NPPV was examined in SBT-2 and PIC. A significant increase in the duration of the use of the ventilation was detected in SBT-2. * $p < 0.05$ vs PIC.

NPPV in both groups and the results are shown in Figure 4. The patients received the NPPV treatment showed a morbidity rate of 7.8% in the STB-2 group (A) and a 5.9% in the PIC groups (B). There was a similar prevalence of the ventilator-acquired pneumonia clearly observed in both groups of the patients. In contrast, there was no statistical difference seen in the occurrence of the pneumonia between these two groups ($p > 0.05$).

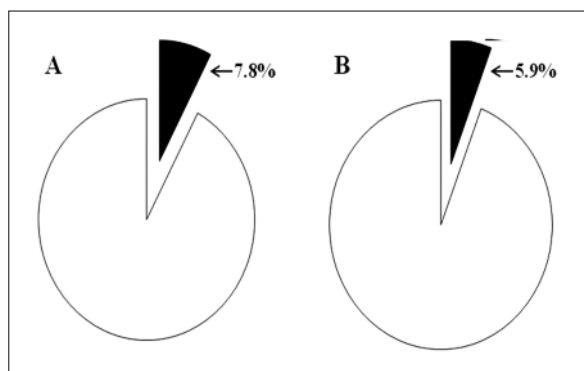


Figure 4 Morbidity of NPPV-acquired pneumonia is similar in STB-2 and PIC. Prevalence rate population of NPPV-associated pneumonia was examined in the NPPV-treated patients. A similar morbidity rate (black) of the pneumonia was detected in SBT-2 (A) and PIC (B). A p -value is > 0.05 as compared to the rate between these two groups.

Discussion

Timely alternative to sequential NPPV can effectively alleviate the sufferings of patient and prevent reintubation in patients who develop overt respiratory failure after extubation^{13,14}. Therefore, an appropriate timing selected for the use of NPPV would be critically important in relieving dyspnoea, lowering need of endotracheal intubation and shortening hospital stay.

In this randomized controlled study, NPPV was applied for AECOPD patients after extubation and discontinuation of invasive mechanical ventilation. The effect of NPPV on the patients was examined with a success rate of 88.2% in SBT-2 patients and a 61.88% in PIC, indicating the efficiency of NPPV treatment in the SBT-2 patients was superior to PIC with a 26% increase in the treatment effect. The result supported the consideration that an optimized timing switched to the application of NPPV in treatment of AECOPD should be selected at SBT-2 in which the actual process of weaning a patient from mechanical ventilation was carried out by allowing a 2-hour spontaneous breathing attempt. As spontaneous breathing activity may integrate intrinsic feedback mechanisms contributed to improving cardiorespiratory stability¹⁵, maintained SBT-2 patients at a long duration followed by adequate mechanical support as a natural ventilation strategy should, in terms of pulmonary gas exchange¹⁶, be superior to PIC patients. The benefits from the SBT-2 patients treated with NPPV were presented probably due to an increased efficiency of ventilation systems including mitigation of respiratory muscle fatigue because severe COPD places the respiratory muscles at a mechanical disadvantage that becomes potentially catastrophic¹⁷, whereas related to increased airway resistance and hypoxemia, the demand for the work of breathing increases while the capacity to supply the work becomes further compromised in COPD patients⁴. It is conceivable that the improved clinical outcomes of SBT-2 patients with NPPV treatment could account for lowering respiratory muscle fatigue caused by AECOPD.

The replacement of a tracheal tube may exacerbate the existing injury to the tracheal mucosa¹⁸. NPPV by full face (nasal) mask is a method of providing mechanical ventilatory support in the absence of tracheal intubation, and it has been employed in patients with respiratory failure, effectively improving oxygenation and ventilation¹⁹. To determine whether NPPV ap-

plied to SBT-2 patients may reduce a risk for repeated tracheal intubation in AECOPD patients, prevalence rate of tracheal reintubation was examined in SBT-2 and PIC groups. The results showed that the occurrence rate of reintubation was 11.8% in SBT-2 and 39.2% in PIC with a 27% decrease seen in the SBT-2 patients, suggesting that the use of NPPV in the patients may diminish the trauma to the trachea associated with the repeated insertion and maintenance of a tracheal tube. This finding from the patients treated with NPPV could provide an important clue to SBT-2' role in such reintubation rate, and thus may provide a novel therapeutic opportunity for clinicians who want to facilitate early extubation after bouts of acute respiratory failure and to avoid extubation failure when the condition of a patient deteriorates following extubation. According to the reintubation rate observed in the SBT-2 patients treated with NPPV, it is reasonable to speculate that NPPV applied for the patients may reduce a risk of lung infection as well as the hospital length of stay.

Mechanical ventilation is the most widely used supportive technique to assist or replace spontaneous breathing in intensive care units (ICU)²⁰. Some patients with chronic illnesses require long-term ventilation assistance^{21,22}. In this study, duration of invasive mechanical ventilation was assessed prior to patients treated with NPPV in SBT-2 and PIC, respectively. In contrast, a time-period for the patients received invasive ventilation showed a 30-hour increase in SBT-2 over the time in PIC. There was significant difference in the observed durations between these two groups of the patients. The data on the duration of invasive mechanical ventilation suggested the clinical activity of NPPV used in SBT-2 for the invasively ventilated patients. It has been reported that approximately 25% of patients intubated for acute respiratory failure require at least 7 days of mechanical ventilation, and up to 10% are intubated for more than 3-weeks²³. In many patients much of that period is consumed by weaning from ventilator support. One study found that 40% of ventilator time was devoted to weaning in a 60% of COPD patients²⁴. Our finding revealed that the use of sequential NPPV in SBT-2 may be suitable to the patients who experienced long-term invasive ventilation.

Ventilator-associated pneumonia is the hospital-acquired infection developing more than 48 hours after the introduction of mechanical ventilation. The estimated frequency is 9-27%, with a mortality rate of 25-50%^{25,26}. It has been known

that a morbidity rate of ventilator-associated pneumonia is positively related to the duration of invasive mechanical ventilation²⁷ and a main advantage of sequential NPPV in treatment of the ventilated patients has been considered as lowering the morbidity of the pneumonia²⁸, which is achieved through shortening duration of endotracheal tube and mechanical ventilation. In this study, a morbidity rate of the pneumonia was demonstrated at a level of 7.8% in SBT-2 and 5.9% in PIC, respectively. There was no statistical difference seen in these two groups, indicating that SBT-2 designed to use NPPV did not lead to an increase in the morbidity rate of the pneumonia as compared to that in PIC. Since much controversy exists about the mortality attributable to the pneumonia²⁹, the finding led us to conclude that the application of NPPV for the SBT-2 patients should be safe. NPPV used in SBT-2 may not only ensure a successful treatment but also avoid occurrence of the pneumonia

Conclusions

This study suggests that STB-2 may be selected as the optimal timing for the use of NPPV which shows a high success rate in treatment of AECOPD patients with less need for tracheal reintubation.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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