ORIGINAL ARTICLE

Application of Non-invasive Positive Pressure Ventilation Combined with $PetCO_2$ Monitoring for Patients with Chronic Obstructive Pulmonary Disease Combined with Severe Respiratory Failure

Fu-Tao Cao, Yu Cui, Jia Mao, Fang Wan and Su Tu

ABSTRACT

Objective: To investigate the role of $PetCO_2$ monitoring in non-invasive positive pressure ventilation (NPPV) treatment for chronic obstructive pulmonary disease (COPD) patients combined with severe respiratory failure.

Study Design: A clinical retrospective study.

Place and Duration of Study: The ICU Emergency Department, Wuxi Second People's Hospital, Wuxi, China, from February 2015 to February 2016.

Methodology: A total of 60 COPD patients with respiratory failure were selected. All patients received non-invasive positive pressure ventilation and conventional treatment. $PetCO_2$ values were recorded two hours before and after NPPV treatment. At the same time, blood was collected for arterial blood gas analysis. Changes in $PetCO_2$, $PaCO_2$ and the difference between $PaCO_2$ and $PetCO_2$ (Pa-etCO_2) were also monitored to determine the correlation between $PetCO_2$ and $PaCO_2$.

Results: After two hours of initial NPPV treatment, among the 60 patients, the $PaCO_2$ and Pa-etCO_2 of 40 patients were significantly decreased (66.7%), the $PaCO_2$ and Pa-etCO_2 of 20 patients were not significantly decreased (33.3%). The correlation analysis revealed that $PaCO_2$ and $PetCO_2$ were negatively correlated (correlation coefficient r = -0.537, p=0.001, p<0.001). Furthermore, there were no significant correlations between $PaCO_2$ and $PetCO_2$ in the ineffective group (correlation coefficient r = -0.253, p=0.116, p>0.05).

Conclusion: $PaCO_2$ monitoring could not be replaced by $PetCO_2$ monitoring for patients with COPD combined with severe respiratory failure. Nevertheless, dynamic monitoring can instantly feedback the respiration state, which can guide the respiration, and improve the success rate of NPPV treatment and prognosis.

Key Words: *End tidal carbon dioxide partial pressure, Non-invasive positive pressure ventilation, Respiratory failure, Chronic obstructive pulmonary disease.*

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common and frequently occurring disease characterised by persistent airflow limitation. This disease can seriously affect the quality of life of patients and has a high mortality rate.[1,2] COPD is usually combined with respiratory failure in the acute exacerbated period, and endanger the life of a patient. The pathophysiological characteristics of COPD combined with respiratory failure are increased oxygen consumption and respiratory loading resulting from high airway resistance and endogenous positive end-tidal pressure, which exceed the compensatory ability of the respiratory muscles. This would eventually cause carbon dioxide retention and hypoxia, and lead to respiratory failure. Therefore, improving the ventilation function of patients is the most important treatment measure to improve COPD combined with respiratory failure.

Department of Emergency, The Affiliated Wuxi No.2 People's Hospital of Nanjing Medical University, Wuxi, China

Correspondence: Dr. Su Tu, Department of Emergency, The Affiliated Wuxi No.2 People's Hospital of Nanjing Medical University, Wuxi, China
E-mail: tus021438@163.com

Received: April 10, 2018; Accepted: January 15, 2019

Common treatments in clinical practice included promoting respiratory muscle training for patients, dilating the bronchus, and the application of ventilator assisted ventilation,[3] and non-invasive positive pressure ventilation (NPPV). Early intervention could reduce the values of $PaCO_2$, decline breathe frequency and severity of dyspnea, reduce the complications of ventilator-associated pneumonia and hospitalisation time, and decrease mortality rate and intubation rate.[4,5] End-tidal carbon dioxide partial pressure ($PetCO_2$) monitoring is a non-invasive method for monitoring arterial blood carbon dioxide partial pressure ($PaCO_2$), which has been widely used in patients undergoing anesthesia, endotracheal intubation and pre-hospital care.[6-8]

Therefore, this study was conducted to investigate the role of $PetCO_2$ monitoring in NPPV treatment for chronic obstructive pulmonary disease (COPD) patients combined with severe respiratory failure.

METHODOLOGY

All patients were inducted from the ICU Emergency Department, Wuxi Second People's Hospital, Wuxi,

China, from February 2015 to February 2016. The study was approved by the Ethics Committee of the hospital. The patients or their family members provided an informed consent. Data collection was conducted by using a predefined standardised data collection form, including age, changes in $PetCO_2$, $PaCO_2$ and the difference between $PaCO_2$ and $PetCO_2$ ($Pa\text{-}etCO_2$). The sample size was estimated by the statistical software based on the previous studies.

Inclusion criteria were patients suffered from chronic obstructive pulmonary disease (COPD), combined with severe respiratory failure; and age over 18 years who had signed the informed consent form. Exclusion criteria were patients in coma with poor autonomous protection ability of the airways; weak autonomous respiration (with low breathing rate and PaO_2); unstable hemodynamics; unable to wear a respiratory mask or the mask did not fit the patient's face, resulting in leakage; and patients combined with function failures of other organs.

The ventilation mode was S/T, and the reserve frequency was set at 12 times per minute. The initial inspiratory positive airway pressure (IPAP) was set at 8 cmH_2O, and the expiratory positive airway pressure (EPAP) was set at 4 cmH_2O. Then, IPAP and EPAP were adjusted according to the patient's tolerance, allowing the tidal volume to reach 7-10 ml/kg and maintain a SpO_2 of >90%. The appropriate ventilation masks, which combined the nasal cavity and oral cavity, were provided to the patients, and connected with the plateau valve expiratory device to avoid air leakage.

Direct current $PetCO_2$ monitor was connected between the non-invasive mask and ventilation pipeline in series. The value of $PetCO_2$ was recorded at two hours before and after the NPPV treatment. At the same time, blood was collected for arterial gas analysis. The difference between $PaCO_2$ and $PetCO_2$ was marked as $Pa\text{-}etCO_2$. The NPPV treatment was counted as ineffective for cases where the pH value of arterial blood continued to decline and the $PaCO_2$ continued to increase after two hours of initial treatment.

A VENTImotion30 ventilator (Weinmann, Germany) was used during the NPPV treatment, a B20 ECG monitor (GE) was used for ECG and blood oxygen saturation monitoring. A Solar 8000M mainstream carbon dioxide analyser (GE, USA) was used for $PetCO_2$ monitoring, and instrument correction was performed before sampling, according to manufacturer's instructions. The blood gas analyser type was GEM 3500 (USA).

Data were analysed using SPSS 17.0 statistical software. Measurement data were expressed as mean ± standard deviation (x ±SD). Paired t-test was used for comparison between groups, while linear regression analysis was used for correlation analysis. $P<0.05$ was considered statistically significant.

RESULTS

A total of 60 patients with COPD combined with respiratory failure, who were admitted in the ICU Emergency Department of the Hospital from February 2015 to February 2016, were enrolled for the study. All cases were in line with the guidelines of the 2014 Global Initiative for Chronic Obstructive Lung Disease (GOLD),[9] and had a $PaCO_2$ of >80 mmHg or pH of <7.25. Among these patients, 32 patients were males and 28 patients were females, and the age of these patients ranged within 65-85 years, with an average age of 62.5 ±9.8 years. The course of the disease ranged within 5-30 years, with an average of 15.5 ±3.4 years. BMI was 18.02 ±4.02 Kg/m^2, smoking index was 781 ±268.25 branches/year, mean arterial pressure was 93.92 ±6.82 mmHg, and heart rate was 102.26 ±8.68 bpm.

After two hours of initial NPPV treatment, the indexes of both $PaCO_2$ and $Pa\text{-}etCO_2$ decreased (Table I), and the differences were statistically significant (both $p<0.001$). Furthermore, the difference in $PetCO_2$ before and after the treatment was not statistically significant ($p=0.896$, $p>0.05$).

According to the results of the arterial blood gas analysis at two hours before and after NPPV treatment, among these 60 patients, 40 patients (66.7%) were treated effectively, while 20 patients (33.3%) were treated ineffectively. These patients were grouped according to the effects of the treatment. The differences in $PaCO_2$ $PetCO_2$ and $Pa\text{-}etCO_2$ before and after the treatment between the effective group and ineffective group were statistically significant ($p<0.001$, $p<0.001$; $p=0.001$, and $p<0.01$ respectively, Table II).

Table I: Comparison of $PaCO_2$, $PetCO_2$, and $Pa\text{-}etCO_2$ before the NPPV treatment and 2 hours after the NPPV treatment.

	$PaCO_2$	$PetCO_2$	$Pa\text{-}etCO_2$
Before the NPPV treatment	92 ±7.1	33.8 ±9.2	58.1 ±11.8
2 hours after the NPPV treatment	85.3 ±12.9	33.9 ±11.6	51.4 ±23.4
t-value	4.818	1.183	3.746
p-value	0.000	0.896	0.000

Table II: Comparison of $PaCO_2$, $PetCO_2$, and $Pa\text{-}etCO_2$ between the effective NPPV treatment group and the ineffective NPPV treatment group.

	$PaCO_2$	$PetCO_2$	$Pa\text{-}etCO_2$
The effective NPPV treatment group (n=40)			
Before treatment	91.6 ±7.0	39.3±5.0	52.2 ±8.3
2 hours after treatment	78.4 ±7.5	41.4 ±5.1	37.0 ±11.1
t-value	36.230	-3.428	13.902
p-value	0.000	0.001	0.000
The ineffective NPPV treatment group (n=20)			
Before treatment	91.7 ±5.6	22.8 ±4.29	68.8 ±6.4
2 hours after treatment	97.9 ±8.6	18.9 ±3.3	78.9 ±10.1
t-value	-5.670	3.769	-6.284
p-value	0.000	0.001	0.000

The correlation analysis revealed that among the 60 patients, there was a negative correlation between $PaCO_2$ and $PetCO_2$ before and after treatment (correlation coefficient r = -0.537, p<0.001, and p<0.01 respectively). Furthermore, in the effective treatment group, $PaCO_2$ was negatively correlated with $PetCO_2$ (correlation coefficient r = -0.294, p=0.008, p<0.01). However, there was no significant correlation between $PaCO_2$ and $PetCO_2$ in the ineffective group (correlation coefficient r = -0.253, p=0.116, p>0.05).

DISCUSSION

The results of the present study revealed that for COPD patients with severe respiratory failure, both $PaCO_2$ and Pa-$etCO_2$ decreased after two hours of NPPV treatment (p<0.05), and the proportion of patients who underwent effective treatment reached 66.7%. Therefore, with the results of the present study that included patients with severe respiratory failure, if careful screening and selection were performed to appropriate patients, NPPV treatment would have a good effect, with the condition of close monitoring and adequate assessment. For patients who had no significant improvement after two hours of treatment, IPPV treatment should be applied. Therefore, in the process of NPPV treatment, the selection of appropriate monitoring means is a very important aspect of treatment.

NPPV has presently become a routine treatment for acute exacerbations of chronic obstructive pulmonary disease (AECOPD), and the success rate of AECOPD can reach 80-85%. Most studies have suggested that effective NPPV treatment can increase pH value, decrease $PaCO_2$ value, decrease the degree of dyspnea, reduce tracheal intubation rate, and shorten hospitalisation time in the short term.[1,10] For patients with severe respiratory failure caused by AECOPD, studies have shown that NPPV failure rate and mortality rate are higher.[11-13] For these patients, invasive positive pressure ventilation (IPPV) is more effective.

$PaCO_2$ detection by blood gas analysis is an invasive operation. It not only increases the suffering of patients, increases the incidence of related complications and aggravates the workload of the medical staff; but also has certain limitations of not being able to continuously and dynamically monitor patients. With mainstream type $PetCO_2$ monitoring, as a non-invasive monitoring technology, it can continuously and non-invasive monitor the pressure or concentration of carbon dioxide in human alveolar.[14] This makes it a very critical respiratory care indicator. This has commonly been used for monitoring patients in anesthesia care, pre-hospital emergency care and tracheal intubation. $PetCO_2$ refers to the partial pressure of carbon dioxide in the human body, which is exhaled from the end-tide in one breath. Since the end-tidal gas of the human body is derived from alveolar gas, $PetCO_2$ can reflect the level of carbon dioxide pressure of alveolar gas ($PACO_2$) in human body, and the pressures of $PACO_2$ and $PaCO_2$ are almost equal after full gas exchange.[15] Therefore, it is clinically possible to estimate the $PaCO_2$ of the human body by monitoring $PetCO_2$, achieving the goal of non-invasive monitoring of $PaCO_2$.

In normal physiological conditions and in COPD patients without respiratory failure, $PetCO_2$ is closely correlated to $PaCO_2$.[16] However, in COPD patients combined with respiratory failure, $PetCO_2$ cannot represent $PaCO_2$, because $PetCO_2$ is often significantly lower than $PaCO_2$ due to the imbalance between alveolar ventilation/ perfusion (VA/Q) and shunting changes (Qs / Qt), which greatly limits its clinical application.[17-19]

In the present study, it was found that for severe respiratory failure patients, there was no significant difference in $PetCO_2$ before and after two hours of NPPV treatment (p>0.05). For patients grouped according to the effect of treatment, the differences were statistically significant in $PaCO_2$, $PetCO_2$ and Pa-$etCO_2$ before and after treatment in both the effective group and ineffective group (p<0.05). Therefore, the investigators consider that for patients with severe respiratory failure, $PetCO_2$ cannot accurately reflect the level of $PaCO_2$, and cannot completely replace the role of $PaCO_2$. Furthermore, respiratory depression, asphyxia, poor ventilation and other respiratory adverse reactions could be detected in time. Through the dynamic monitoring of $PetCO_2$, the medical staff can directly open the airway, guide patient breathing and adjust the ventilator parameters well. All these have important roles for improving the ventilation effect and reducing the rate of endotracheal intubation.

Some studies have shown that in critically ill patients, as the alveolar dead space increased, the correlation between $PetCO_2$ and $PaCO_2$ became worse, and Pa-$etCO_2$ increased with the increase in VD/VT (dead space volume/tidal volume).[20] The present study revealed that $PaCO_2$ was negatively correlated with $PetCO_2$ (r = -0.537, p<0.01), which is not consistent with its relationship in normal physiological conditions. This may be due to the existence of significant ventilation disorder in severe respiratory failure patients, CO_2 in the body could not be smoothly excreted through the alveolar, which resulted in significant CO_2 retention. Furthermore, there was no significant correlation between $PaCO_2$ and $PetCO_2$ (p>0.05) in patients in the ineffective treatment group (p>0.05). This further indicates that $PetCO_2$ could not replace blood gas analysis in critically ill patients. For these patients, even with the intervention during the monitoring process, according to the waveform and pressure parameters of $PetCO_2$, the ventilation could not be improved. For patients in the ineffective group, who were evaluated by arterial blood gas analysis after two hours of treatment,

tracheal intubation should be performed to allow for timely invasive ventilation and prevent delayed treatment.

CONCLUSION

$PaCO_2$ monitoring could not be replaced by $PetCO_2$ monitoring for patients with COPD combined with severe respiratory failure. Nevertheless, dynamic monitoring can instantly feedback the respiration state, which can guide the respiration, and improve the success rate of NPPV treatment and prognosis.

REFERENCES

1. Nishiyama O, Tohda Y. Diagnostic differences in asthma and chronic obstructive pulmonary disease. *Rinsho Byori* 2014; **62**: 457-63.
2. Berg KM, Clardy P, Donnino MW. Non-invasive ventilation for acute respiratory failure: A review of the literature and current guidelines. *Intern Emerg Med* 2012; **7**:539-45.
3. Sørensen D, Frederiksen K, Groefte T, Lomborg K. Striving for habitual well-being in noninvasive ventilation: A grounded theory study of chronic obstructive pulmonary disease patients with acute respiratory failure. *J Clin Nurs* 2014; **23**:1726-35.
4. Windisch W, Storre JH, Köhnlein T. Nocturnal non-invasive positive pressure ventilation for COPD. *Expert Rev Respir Med* 2015; **9**:295-308.
5. Stein M, Joannidis M. Ventilation strategies for chronic obstructive pulmonary disease. *Med Klin Intensivmed Notfmed* 2012; **107**:613-21.
6. Mebrate Y, Willson K, Manisty CH, Baruah R, Mayet J, Hughes AD, *et al*. Dynamic CO_2 therapy in periodic breathing: A modeling study to determine optimal timing and dosage regimes. *J Appl Physiol (1985)* 2009; **107**:696-706.
7. Mora Capín A, Míguez Navarro C, López López R, Marañón Pardillo R. Usefulness of capnography for monitoring sedo-analgesia: Influence of oxygen on the parameters monitored. *An Pediatr (Barc)* 2014; **80**:41-6.
8. Hiller J, Silvers A, McIlroy DR, Niggemeyer L, White S. A retrospective observational study examining the admission arterial to end tidal carbon dioxide gradient in intubated major trauma patients. *Anaesth Intensive Care* 2010; **38**:302-6.
9 Pauwels RA, Buist AS, Calverley PM, Jenkins CR, Hurd SS. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. NHLBI/WHO global initiative for chronic obstructive lung disease (GOLD) workshop summary. *Am J Respir Crit Care Med* 2001; **163**:1256-76.
10. Antonelli M, Pennisi MA, Montini L. Clinical review: Non-invasive ventilation in the clinical setting-experience from the past 10 years. *Crit Care* 2005; **9**:98-103.
11. Squadrone E, Frigerio P, Fogliati C, Gregoretti C, Conti G, Antonelli M, *et al*. Noninvasive *vs* invasive ventilation in COPD patients with severe acute respiratory failure deemed to require ventilatory assistance. *Intensive Care Med* 2004; **30**: 1303-10.
12. Passarini JN, Zambon L, Morcillo AM, Kosour C, Saad IA. Use of noninvasive ventilation in acute pulmonary edema and chronic obstructive pulmonary disease exacerbation in emergency medicine: predictors of failure. *Rev Bras Ter Intensiva* 2012; **24**:278-83.
13. Sun F, Li C, Fu Y, Tan D, Shao S, Xu J, *et al*. Predictive value of continuous monitoring end-tidal carbon dioxide partial pressure on in-hospital resuscitation outcome: Secondary analysis of the data from a multicenter observational study. *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue* 2018; **30**:29-33.
14. Nickol AH, Dunroy H, Polkey MI, Simonds A, Cordingley J, Corfield DR, *et al*. A quick and easy method of measuring the hypercapnic ventilatory response in patients with COPD. *Respir Med* 2009; **103**:258-67.
15. Nassar BS, Schmidt GA. Estimating arterial partial pressure of carbon dioxide in ventilated patients: How valid are surrogate measures? *Ann Am Thorac Soc* 2017; **14**:1005-14.
16. Colasanti A, Esquivel G, den Boer E, Horlings A, Dandachi A, Oostwegel JL, *et al*. Effects of tryptophan depletion and tryptophan loading on the affective response to high-dose CO_2 challenge in healthy volunteers. *Psychopharmacology (Berl)* 2011; **215**:739-48.
17. Liu SY, Lee TS, Bongard F. Bongard. Accuracy of capnography in nonintubated surgical patients. *Chest* 1992; **102**:1512-5.
18. Bongard F, Wu Y, Lee TS, Klein S. Capnographic monitoring of extubated postoperative patients. *J Invest Surg* 1994; **7**:259-64.
19. Bräunlich J, Beyer D, Mai D, Hammerschmidt S, Seyfarth HJ, Wirtz H. Effects of nasal high flow on ventilation in volunteers, COPD and idiopathic pulmonary fibrosis patients. *Respiration* 2013; **85**:319-25.
20. McSwain SD, Hamel DS, Smith PB, Gentile MA, Srinivasan S, Meliones JN, *et al*. End-tidal and arterial carbon dioxide measurements correlate across all levels of physiologic dead space. *Respir Care* 2010; **55**:288-93.