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Analysis of factors influenced by the effectiveness of non-invasive ventilation in the treatment of acute exacerbation of chronic obstructive pulmonary disease with different severities

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Abstract. – OBJECTIVE: To investigate the correlation of levels of procalcitonin (PCT) and blood lactic acid with the effectiveness of the non-invasive ventilation (NIV) in the treatment of acute exacerbation of chronic obstructive pulmonary disease (AECOPD) with different severities.

PATIENTS AND METHODS: We used a case-control method to study patients who were admitted for AECOPD to the ICU at the Second Affiliated Hospital of Soochow University from January 1, 2012, to December 31, 2014. The patients had shown no response to conventional therapy or NIV treatment. The patients who had been treated with NIV before ICU admission were excluded. According to the pH value of arterial blood gas analysis after ICU admission, the AECOPD patients were divided into a mild group (pH ≥ 7.30) and a severe group (pH < 7.30). On the basis of whether a patient needed an artificial airway after NIV therapy, the two groups of patients were divided into two subgroups: an effective group and an ineffective group. A total of 153 patients were screened for the study. Of the 62 patients in the mild group, 38 cases were in the effective group, while 24 cases were in the ineffective group. Through the comparative analysis of clinical features of the patients in the two subgroups before NIV therapy, the single factor analysis between groups was applied to find the factor that influenced the effectiveness of NIV in the treatment of AECOPD with different severities. The logistic regression for multi-factor analysis was applied.

RESULTS: The results implied that the level of procalcitonin (PCT) in patients of the effective group was significantly lower than the level in the ineffective group (0.95 ± 0.54 *vs.* 1.34 ± 0.70, *p* = 0.016). Of 89 patients in the severe group, 33 cases were in the effective group, while 56 cases were in the ineffective group. The results indicated that levels of PCT (0.99 ± 0.57 *vs.* 1.46 ± 0.81, *p* = 0.004) and blood lactic acid (1.5 ± 0.5 *vs.* 1.9 ± 0.8, *p* = 0.008) in patients of the effective group were significantly lower than levels of the ineffective group.

CONCLUSIONS: The PCT and blood lactic acid, which reflect the infection severity, are factors influenced by the effectiveness of NIV in the treatment of AECOPD of different severities.

Key Words:

Non-invasive ventilation (NIV), Acute exacerbation of chronic obstructive pulmonary disease (AECOPD), Procalcitonin (PCT), Lactic acid.

Introduction

As a common respiratory system disease, chronic obstructive pulmonary disease (COPD) is characterized by airflow limitation that can be prevented and treated. This airflow limitation mainly involves the lungs but also can cause adverse effects on the whole body (also known as non-pulmonary). This can seriously endanger a patient's physical and mental health[1]. An attack of COPD is the outcome of the combined action of genetic and environmental pathogenic factors. COPD causes high mortality and a heavy social and economic burden, and has become an important public health problem. Therefore, how to effectively prevent and timely treat COPD is among the most active areas of medical research. In recent years, non-invasive ventilation (NIV) has become a routine means of treatment for acute exacerbation of chronic obstructive pulmonary disease (AECOPD). Clinical studies have reported that effective non-invasive positive pressure ventilation (NIPPV) can decrease $PaCO_2$, increase pH,

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alleviate dyspnea and ensure stable vital signs in a short period. The long-term application of NIPPV can decrease endotracheal intubation rate, shorten hospital length of stay and decrease hospital mortality[2]. But, for AECOPD patients, who can benefit from NIV therapy? Domestic and foreign studies have reported the factors that influence the effectiveness of NIV in the treatment of AECOPD. However, a study from a perspective based on the disease severity of AECOPD patients and the factors that influence the effectiveness of NIV in the treatment of patients had yet to be completed. Multiple studies[3-6] suggested that the pH value of arterial blood gas is an independent risk factor that influences the prognosis of patients with AECOPD. As the patients were grouped by the pH value of arterial blood gas, our study was designed to find the factors that influenced the effectiveness of NIV in the treatment of AECOPD with different severities, so as to provide an effective clinical basis for further improvements in the success rate of NIV in the treatment of AECOPD.

Patients and Methods

Patients

From January 1, 2012, to December 31, 2014, patients who were admitted for AECOPD to the ICU of the Second Affiliated Hospital of Soochow University were selected. Inclusion criteria were as follows: (1) age ≥ 18 years old; (2) the patients conformed to the diagnostic criteria of AECOPD[7]; (3) the patients failed to respond to conventional therapy[8-10] (after the treatment of controlled oxygen therapy, bronchodilator agents and glucocorticoid drugs, AECOPD patients still manifested as acute respiratory function failure); and (4) the patients were approved for treatment with NIV therapy. Patients who had been treated with NIV before ICU admission were excluded.

Research Methods and Grouping

To collect the clinical data, a retrospective analysis of AECOPD patients who conformed to inclusion criteria was used. According to the pH value of arterial blood gas, the patients were divided into a mild group (pH ≥ 7.30) and a severe group (pH ≥ 7.30). Each group was further divided into two subgroups – an effective group and an effective group – according to their response to NIV therapy, namely whether the patient eventually needed endotracheal intubation (Figure 1).

Observation Index

An observation index was based on the following parameters: (1) the basic data of ICU transferred patients, including gender, age, body mass index (BMI) and other materials; and (2) the clinical data of patients before they were received for NIV therapy, including laboratory test results such as blood inflammation index and arterial blood gas analysis.

Implementation of NIV

The implementation of NIV was performed by an NIV therapy team comprised of a physician and nurses in the ICU. A BiPap Vision respirator (Philips Respironics, Amsterdam, The Netherlands), which is a non-invasive mechanical ventilator, was used. The specific steps regarding the use and fitting of the NIV connection were as follows: (1) assisted patients to set their proper position in relation to the respirator; (2) chose each facial mask suitable for each patient; (3) placed each mask on each face and secured it with a fillet; and (4) regulated the position of each mask to ensure the tightness was comfortable to the patient and any air leakage was minimalized.

Setting and Adjusting the Ventilation Parameters of NIPPV

Parameter initialization is the parameter that has been set at the beginning of treatment. Due to a patient's need for an adaptive process, the transition from complete spontaneous breathing to positive pressure ventilation begins with a relatively low inspiratory pressure. Regulation refers to the process after a patient gradually adapts to positive pressure ventilation. A gradual increase in inspiratory pressure is conducive to enhanced comfort and compliance and to ensure adequate assisted ventilation. The whole process of NIV therapy is based on adjustments to ventilation parameters according to the change in a patient's condition, such as to relieve shortness of breath, slow the respiratory rate, increase tidal volume and improve the arterial blood gas. Detailed respiratory parameters of NIPPV were shown in Table I.

Failure with NIV Therapy

When certain situations occur, NIV therapy needs to include establishing an artificial airway. These situations can include the following: (1) mental deterioration or dysphoria; (2) inability to remove secretions; (3) inability to tolerate connection method; (4) hemodynamic instability; (5) oxygenation function deterioration; and (6) CO_2 retention aggravation. All these situations can define an ineffective group.

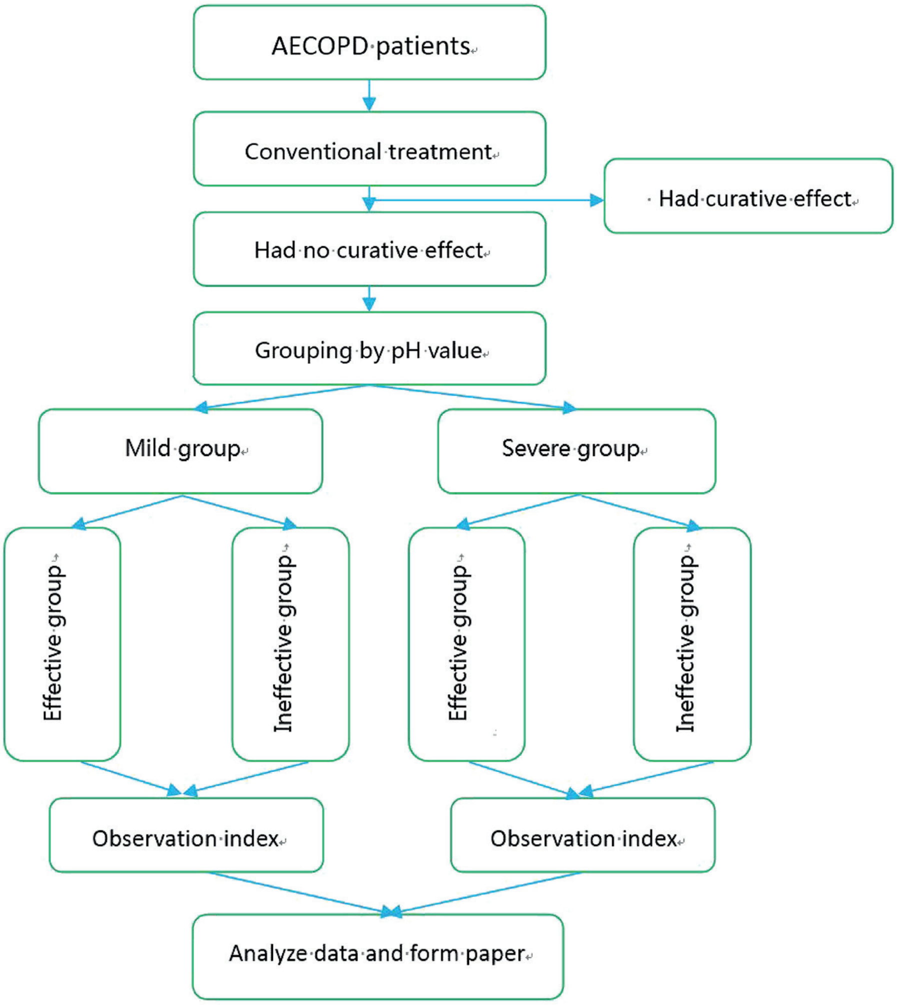

Figure 1. The flow chart of the study.

Table I. Respiratory parameters of NIPPV for patients in two groups.

Group	Number of cases	IPAP (cmH_2O)	EPAP (cmH_2O)	RR (/min)	I/E	FiO_2 (%)
Mild	62	14.39±1.33	5.32±0.47	13.84±1.03	0.568±0.070	43.9±4.4
Severe	89	14.79±1.25	5.30±0.46	13.63±1.06	0.563±0.067	43.3±5.0

IPAP: Inhale Positive Airway Pressure; EPAP: Exhale Positive Airway Pressure; RR: respiratory rate; I/E: inspiratory/expiratory ratio; FiO_2: fraction of inspiration O_2

Statistical Analysis

SPSS 13.0 software (Softonic, Barcelona, Spain) was used for data processing. The value was expressed as a mean ± standard deviation ($\bar{x}$ ± s) if the data analysis of measurement data showed a normal distribution. Measurement data between groups were used by a *t*-test for single factor analysis. Enumeration data between groups were used by an x^2-test for single factor analysis. Logistic regression was used for multivariate analysis after single factor analysis (p < 0.05 means the difference has statistical significance).

Results

Source of Research Objects

Of 2,007 patients selected during 3 years in this study, 151 cases conformed to the research. Of these cases, 62 were in the mild group, while 89 cases were in the severe group.

Table II. The clinical data of the group of with mild AECOPD.

	Effective group	Ineffective group	*t* or x^2	*p*
Gender (M/F)	25/13	15/9	0.070a	0.792
Age (y)	68.3±45.1	69.2±48.5	-0.401	0.693
BMI (kg/m^2)	22.2±1.0	22.6±1.6	-1.371	0.176
Inducing factor of AECOPD (Pneumonia/Total factor)	27/11	16/8	0.133a	0.715
Heart rate	108.6±9.1	104.4±8.4	1.774	0.089
Mean arterial pressure	74.9±5.0	76.7±5.6	-0.1.336	0.187
Breathing rate	29.8±3.1	31.3±3.1	-1.913	0.170
White blood cell (×10^9)	11.5±2.8	12.9±3.3	-1.684	0.112
CRP (mg/L)	70.7±25.2	74.5±25.8	-0.591	0.557
PCT (ng/ml)*	0.95±0.54	1.34±0.70	-2.47	0.016
Blood glucose (mmol/L)	11.2±1.8	10.7±2.6	1.006	0.318
Serum phosphate (mmol/L)	1.03±0.08	1.01±0.07	0.611	0.543
LAC (mmol/L)	1.5±0.5	1.6±0.5	-0.894	0.375
PH	7.36±0.02	7.35±0.02	1.669	0.100
PaO_2 (mmHg)	96.9±16.3	103.2±15.0	-1.528	0.132
$PaCO_2$ (mmHg)	70.8±6.2	72.9±5.2	-1.367	0.177
Actual HCO_{3-} (mmol/L)	27.8±1.7	28.5±1.4	-1.550	0.126

PCT: procalcitonin; CRP: C reactive protein; LAC: blood lactic acid; *represents $p < 0.05$; x^a means Chi-square x^2.

Comparison of Effective and Ineffective Groups in Patients with Mild AECOPD

By comparison of the two subgroups of patients with mild AECOPD, we found PCT levels in the NIV effective group were lower than levels in the ineffective group. The difference had statistical significance ($p < 0.05$), while there were no significant differences in the comparison of respiratory parameters, and other factors between two groups (Table II).

Comparison of Effective and Ineffective Groups in Patients with Severe AECOPD

By comparison of the two groups of severe patients, we found the PCT and blood lactic acid levels in the effective group were lower than levels in the ineffective group. The difference had statistical significance ($p < 0.05$), while there were no significant differences in the comparison of respiratory parameters, and other factors between two groups (Table III).

Table III. The clinical data of the group with severe AECOPD.

	Effective group	Ineffective group	*t* or x^2	*p*
Gender (M/F)	22/11	39/17	0.085^a	0.816
Age (y)	77.9±69.3	78.3±65.8	1.50	0.693
BMI (kg/m^2)	22.1±1.7	21.9±1.6	0.608	0.545
Inducing factor of AECOPD (Pneumonia/Total factor)	22/11	36/20	0.052^a	0.820
Heart rate	113.9±8.8	118.2±13.7	-1.482	0.142
Mean arterial pressure	76.0±6.4	74.3±6.1	1.288	0.201
Breathing rate	30.2±3.2	30.7±3.8	-0.807	0.434
White blood cell (×10^9)	12.6±4.1	13.4±4.6	-0.849	0.398
CRP (mg/L)	53.3±24.1	49.5±23.2	0.749	0.456
PCT (ng/ml)*	0.99±0.57	1.46±0.81	-2.922	0.004
Blood glucose (mmol/L)	11.1±1.8	10.8±2.3	0.778	0.439
Serum phosphate (mmol/L)	1.03±0.08	1.02±0.08	0.268	0.790
LAC (mmol/L)*	1.5±0.5	1.9±0.8	-2.697	0.008
PH	7.18±0.06	7.17±0.06	0.548	0.585
PaO_2 (mmHg)	97.7±16.7	100.3±16.3	-0.722	0.472
$PaCO_2$ (mmHg)	74.4±7.9	75.1±8.5	-0.422	0.674
Actual HCO_{3-} (mmol/L)	27.7±1.7	28.3±1.9	-1.376	0.172

PCT: procalcitonin; CRP: C reactive protein; LAC: blood lactic acid; *represents $p < 0.05$; x^a means Chi-square x^2.

Table IV. The results of multiple factor analysis of the group with severe AECOPD.

	B	SE	Wald	df	Sig	Exp (B)	95.0% C.I Lower	95.0% C.I Upper
PCT (ng/ml)	0.865	0.358	5.840	1	0.016	2.374	1.177	4.786
LAC (mmol/L)	0.879	0.394	4.974	1	0.026	2.408	1.112	5.214
Constant	-1.991	0.790	6.374	1	0.012	.0.137		

In patients in the group with severe AECOPD, the variable, which was significant in single factor analysis, helped to provide logistic regression analysis of multiple factors (Table IV).

Discussion

The non-invasive ventilation is an effective and safe therapy technology that has been widely applied in the treatment of respiratory failure caused by various diseases[7,10-13]. With the rise of COPD incidence, non-invasive ventilation has become a routine means of therapy for acute periods of COPD, but after treatment, the condition of some patients has no remission, or even worse, the patients need to receive endotracheal intubation[14,15]. While looking at different severities of the disease, the study was designed to find the factors that influenced the effectiveness of NIV in the treatment of AECOPD. A total of 151 patients were screened for the research.

Several studies[3-5] indicate that the pH value of blood is the independent risk factor influencing the prognosis of patients with AECOPD. Our research focused on blood pH levels to hierarchically analyze AECOPD patients and find the factors that influenced the effectiveness of NIV in the treatment of AECOPD. This provided a clinical basis for enhancing the success rate of NIV in the treatment of AECOPD patients.

PCT is the calcitonin propeptide with no hormonal activity and contains 116 amino acids. In a healthy physiological state, the blood concentration of PCT is <0.1 ng/ml, so it can hardly be detected. However, when in the pathology of severe infection, PCT is heavily stimulated by bacterial toxins and inflammatory cytokines in thyroid tissue. PCT levels rapidly rise after being induced, which can reflect the early systemic infection in the body[16,17]. The change of PCT levels also is associated with clinical prognosis[10]. At least one study indicated that infection severity relates to the clinical prognosis of patients with AECOPD – the heavier the infection, the worse the prognosis[14,18]. Despite whether a patient was in the mild or severe group of this study, the PCT levels of patients in the ineffective group were

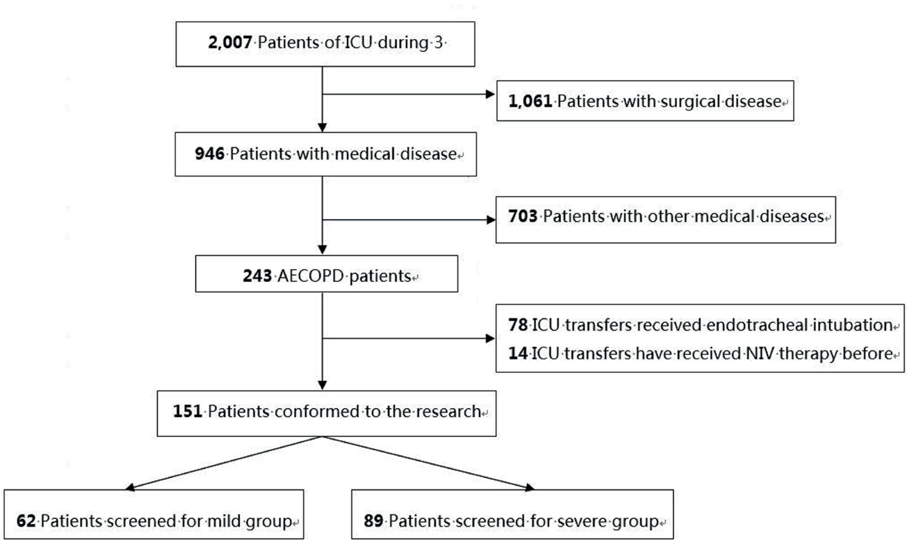

Figure 2. Source of disease category of patients during the past 3 years in the study.

significantly higher than levels in the effective group. This implied that the level of PCT was closely associated with the success rate of AECOPD patients receiving noninvasive ventilation therapy. This may be related to the fact that pulmonary infection was the main inducing factor that led to an acute attack in COPD patients who were screened for this research.

Lactic acid is an intermediate of glucose metabolism. It is reduced by pyroracemic acid when hypoxia or pyroracemic acid has insufficient oxidation. This can produce too much lactic acid. When arterial blood lactic acid, which has a reference value of 1.0-1.5 mmol/L, mildly or moderately increases and has no metabolic acidosis, it is called hyperlactacidemia. When lactic acid was more than 5 mmol/L and has metabolic acidosis, it is referred to as lactic acidosis[19]. At least one study[20] has indicated that arterial blood lactic acid can reflect hypoxia as well as disease severity. Another report[21] has implied that lactic acid can be used as an important indicator to determine the prognosis of patients with respiratory failure. Dynamic monitoring of lactic acid as well as observing the curve of lactic acid levels over time has great clinical value for the detection of a change in a patient's condition. Decreasing lactic acid levels can reflect the effective intervention and improvement of a patient's condition[22]. Our work has found that the blood lactic acid levels of patients in the ineffective group was significantly higher than that of the effective group. This suggests that lactic acid can be used as a factor to predict the success of NIV therapy. One mitigating factor to consider is that the patients who screened for this study had different degrees of respiratory failure. The more severe the illness, the longer the hypoxia time and the higher the blood lactic acid levels. Also, we reported that there was no significant difference in respiratory parameters between the two subgroups of patients, suggesting that the associated respiratory parameters were not predictive of the success of NIV treatment.

The shortcomings of this paper were as follows, for example, the lack of usual pulmonary function of most patients; no observation of the final clinical prognosis of patients, including hospital length of stay, hospital expenses, mortality and other indexes; and no collection of data regarding blood lactate clearance to evaluate lactic acid as an influencing factor. Hypoxia-inducible factor 1 (HIF-1) was newly discovered; it played an important role in changing the oxygen concentration. Through the detection of HIF-1 levels in different groups, the study could research the function of HIF-1 in treating patients with AECOPD. Therefore, the team plans to conduct another study to address these shortcomings.

Conclusions

PCT, which reflects the severity of infection, is the factor that influenced the effectiveness of NIV in the treatment of patients with AECOPD. In addition, blood lactic acid levels also can influence the effectiveness of NIV in the treatment of patients with severe AECOPD.

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Conflict of Interests

The Authors declare that they have no conflict of interests

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