Journal of Hainan Medical University

http://www.hnykdxxb.com/

Assessment of blood gas parameters and the degree of inflammation in noninvasive positive pressure ventilation combined with aminophylline treatment of COPD complicated with type II respiratory failure

Jin−Ru Zhang[1]✉, Hao Fu[2], Shao−Long Li[2], Chun−Fang Guo[1]

[1]*Shenmu County Hospital of Shaanxi Province, Shenmu County, Shaanxi Province, 719300*
[2]*Xi'an Medical College, Xi'an City, Shaanxi Province, 710021*

ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
COPD
Type II respiratory failure
Noninvasive positive pressure ventilation
Aminophylline

ABSTRACT

Objective: To analyze the effect of noninvasive positive pressure ventilation combined with aminophylline therapy on blood gas parameters and the degree of inflammation in patients with COPD and type II respiratory failure. **Methods:** A total of 80 patients with COPD and type Ⅱ respiratory failure were randomly divided into observation group and control group (n=40), control group received symptomatic treatment + aminophylline treatment, observation group received symptomatic treatment + aminophylline + noninvasive positive pressure ventilation treatment, and then differences in blood gas parameters, pulmonary function parameters, hemorheology parameters and inflammatory factor levels were compared between two groups of patients after treatment. **Results:** Radial artery pH and PO_2 values of observation group after treatment were higher than those of control group while PCO_2, Cl^- and CO_2CP values were lower than those of control group; pulmonary function parameters FVC, FEV1, FEF_{25-75}, MMF, PEF and FRC values of observation group after treatment were higher than those of control group; whole blood viscosity (150 s- and 10 s-), plasma viscosity, fibrinogen, erythrocyte aggregation index and erythrocyte rigidity index values in peripheral venous blood of observation group after treatment were lower than those of control group; serum IL-17, IL-33, TREM-1, sICAM-1 and PGE2 levels of observation group after treatment were lower than those of control group. **Conclusion:** Noninvasive positive pressure ventilation combined with aminophylline can optimize the respiratory function of patients with COPD and type II respiratory failure and improve blood gas parameters and the degree of inflammation.

1. Introduction

Acute exacerbation of chronic obstructive pulmonary disease (COPD) infection can lead to respiratory muscle dysfunction, simultaneous occurrence of hypoxia and carbon dioxide retention, and the appearance of type II respiratory failure. COPD combined with type Ⅱ respiratory failure is with more complex illness and greater treatment difficulty, studies have found that the final case fatality rate in these patients is significantly higher than that in patients with COPD alone, so the COPD patients with type Ⅱ respiratory failure should take early active treatment[1,2]. Aminophylline is a common clinical bronchodilator for COPD and also has the effect of exciting respiratory center, but the effect of aminophylline alone is little under the state of respiratory muscle fatigue. Noninvasive positive pressure ventilation is the more respected ventilation way for patients with severe COPD, can enhance the patients' ventilation and gas exchange function, alleviate the degree of respiratory muscle fatigue, actively restore effective alveolar ventilation and oxygen supply while discharge the carbon dioxide retention[3,4]. In the study, aminophylline and noninvasive positive pressure ventilation were used together for the treatment of patients with COPD and type II respiratory failure in

✉Corresponding author: Jin-Ru Zhang, Shenmu County Hospital of Shaanxi Province, Shenmu County, Shaanxi Province, 719300.
Tel: 18091266489
Fund Project: Shaanxi Provincial Science and Technology Bureau NO: 2012K16-06-02.

order to clarify the significance of the treatment in reversing patients' condition.

2. Information and methods

2.1 General information

A total of 80 patients with COPD and type II respiratory failure treated in our hospital between December 2013 and December 2015 were included, and the inclusion criteria were: (1) in accordance with the criteria for chronic obstructive pulmonary disease (COPD) and type Ⅱ respiratory failure established by WHO; (2) with typical clinical symptoms; (3) the patients and families signed informed consent; (4) with complete clinical data. Exclusion criteria: (1) with acute lung infection; (2) with malignant tumor diseases of the respiratory system; (3) with severe heart, liver and kidney dysfunction; (4) allergic to aminophylline; (5) with mental illness and couldn't cooperate with treatment. 80 patients conformed to the above inclusion criteria and divided into observation group and control group (n=40) according to random number table. Control group included 23 male cases and 17 female cases, they were 42-70 years old and (59.37±7.15) years old in average, the body weight was 46-78 kg and (58.39±8.12) kg in average, and the course of COPD was 4-11 years and (7.39±0.85) years in average; observation group included 22 male cases and 18 female cases, they were 40-73 years old and (60.65±7.09) years old in average, the body weight was 44-79 kg and (58.72±8.09) kg in average, and the course of COPD was 5-13 years and (7.98±0.93) years in average. The two groups of patients were not statistically different in the distribution of gender, age, body weight and course of COPD (P>0.05) and they were comparable.

2.2 Treatment methods

Both groups received anti-infection, phlegm dispelling, anti-inflammation, nutritional support, water-electrolyte correction and other symptomatic treatment. Control group received symptomatic treatment + aminophylline, specifically as follows: intravenous micro-pump injection of aminophylline, loading dose 4-6 mg/kg and maintenance dose 0.6-0.8 mg/(kg•h). Observation group received symptomatic treatment + aminophylline + noninvasive positive pressure ventilation therapy, specifically as follows: Bi-PAP vision ventilator (Respironics Inc) was used, bi-level positive airway pressure S/T mode was selected, inspiratory pressure was set to 10 cmH_2O, expiratory pressure was set to 4 cmH_2O, the first 5-20 min was the adjustment stage, the pressure was gradually increased to the ideal state, and the ventilation parameters were adjusted in real time according to the patients' condition and blood gas parameter values. The dosage and usage of symptomatic treatment and aminophylline treatment were the same as those of control group.

2.3 Observation indexes

2.3.1 Blood gas parameters

1 week after treatment, 2 mL of radial artery blood was collected from both groups, and blood-gas analyzer was used to measure pH value, oxygen partial pressure (PO_2), partial pressure of carbon dioxide (PCO_2), chloride (Cl^-) and carbon dioxide combining power (CO_2CP) levels.

2.3.2 Pulmonary function parameters

The lung function analysis system was used to detect the pulmonary function parameters of the two groups 1 week after treatment, including forced vital capacity (FVC), forced expiratory volume in 1 s (FEV1), forced mid-expiratory flow (FEF_{25-75}), maximal mid-expiratory flow rate (MMF) and peak expiratory flow (PEF) and functional residual capacity (FRC).

2.3.3 Hemorheology parameters

1 week after treatment, 3 mL of fasting cubital venous blood was collected from both groups and anticoagulated with heparin, automatic cone-plate viscometer was used to determine whole blood viscosity (150 s- and 10 s-), capillary viscometer was used to determine plasma viscosity, microcalorimetric sedimentation centrifuge method was used to detect the fibrinogen levels, and the erythrocyte aggregation index, erythrocyte rigidity index were further calculated.

2.3.4 Inflammatory factors

1 week after treatment, 3 mL of fasting cubital venous blood was collected from both groups, let stand at room temperature and then centrifuged to get supernatant, and ELISA kits were used to determine interleukin-17 (IL-17), interleukin-33 (IL-33), triggering receptor expressed on myeloid cells-1 (TREM-1), soluble intercellular adhesion molecule-1 (sICAM-1) and prostaglandin E2 (PGE2) levels in it.

2.4 Statistical methods

Data in the study was input in SPSS 23.0 software, measurement data was by t test and P<0.05 indicated statistical significance in differences.

3. Results

3.1 Blood gas parameters of two groups after treatment

1 week after treatment, analysis of radial artery blood gas parameters pH, PO_2, PCO_2, Cl- and CO_2CP between two groups was as follows: radial artery pH and PO_2 levels of observation group were

significantly higher than those of control group while PCO_2, Cl- and CO_2CP levels were significantly lower than those of control group. Differences in pH, PO_2, PCO_2, Cl- and CO_2CP were statistically significant between two groups 1 week after treatment (P<0.05), shown in Table 1.

3.2 Pulmonary function parameters of two groups after treatment

1 week after treatment, analysis of pulmonary function parameters FVC, FEV1, FEF25-75, MMF, PEF and FRC between two groups was as follows: pulmonary function parameters FVC, FEV1, FEF25-75, MMF, PEF and FRC of observation group were significantly higher than those of control group. Differences in pulmonary function parameters FVC, FEV1, FEF25-75, MMF, PEF and FRC were statistically significant between two groups 1 week after treatment (P<0.05), shown in Table 2.

3.3 Hemorheology parameters

1 week after treatment, analysis of hemorheology parameters low-shear whole blood viscosity, high-shear whole blood viscosity, plasma viscosity, fibrinogen, erythrocyte aggregation index and erythrocyte rigidity index between two groups was as follows: low-shear whole blood viscosity, high-shear whole blood viscosity, plasma viscosity, fibrinogen, erythrocyte aggregation index and erythrocyte rigidity index in peripheral venous blood of observation group after treatment were significantly lower than those of control group. Differences in low-shear whole blood viscosity, high-shear whole blood viscosity, plasma viscosity, fibrinogen, erythrocyte aggregation index and erythrocyte rigidity index were statistically significant between two groups 1 week after treatment (P<0.05), shown in Table 3.

3.4 Inflammatory factors

1 week after treatment, analysis of serum inflammatory factors IL-17, IL-33, TREM-1, sICAM-1 and PGE2 between two groups was as follows: serum IL-17, IL-33, TREM-1, sICAM-1 and PGE2 levels of observation group were significantly lower than those of control group. Differences in serum inflammatory factors IL-17, IL-33, TREM-1, sICAM-1 and PGE2 levels were statistically significant between two groups 1 week after treatment (P<0.05), shown in Table 4.

Table 1.
Comparison of radial artery blood gas parameters between two groups after treatment.

Groups	n	pH	PO_2 (mmHg)	PCO_2 (mmHg)	Cl^- (mmol/L)	CO_2CP (mmol/L)
Observation	40	7.32±0.27	79.72±8.13	40.74±5.38	104.38±10.39	25.82±3.11
Control	40	7.21±0.38	57.63±7.29	53.81±6.97	112.67±14.12	30.17±3.49
t		5.382	9.842	7.182	8.394	7.394
P		<0.05	<0.05	<0.05	<0.05	<0.05

Table 2.
Comparison of pulmonary function parameters between two groups after treatment.

Groups	n	FVC (L)	FEV1 (L)	FEF25-75 (L)	MMF (L/s)	PEF (L/s)	FRC (L)
Observation	40	3.52±0.41	2.93±0.25	3.17±0.38	3.04±0.27	4.83±0.51	2.43±0.22
Control	40	2.81±0.32	2.27±0.21	2.53±0.32	2.27±0.23	3.97±0.43	2.03±0.21
t		6.493	5.872	5.273	5.192	6.384	5.283
P		<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

Table 3.
Comparison of hemorheology parameter values between two groups after treatment.

Groups	n	Blood viscosity indexes (mPa•s)			Fibrinogen (g/L)	Erythrocyte aggregation index	Erythrocyte rigidity index
		Low-shear whole blood viscosity	High-shear whole blood viscosity	Plasma viscosity			
Observation	40	8.73±0.92	3.96±0.42	1.42±0.17	3.52±0.39	2.11±0.23	4.53±0.53
Control	40	9.21±0.97	4.49±0.52	1.58±0.18	4.76±0.53	2.57±0.34	5.17±0.62
t		5.834	5.723	5.093	6.293	5.182	6.342
P		<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

Table 4.
Comparison of serum inflammatory factor levels between two groups after treatment.

Groups	n	IL-17 (ng/mL)	IL-33 (ng/mL)	TREM-1 (ng/mL)	sICAM-1 (ng/mL)	PGE2 (pg/mL)
Observation	40	73.28±8.19	6.38±0.72	95.36±9.12	98.46±9.12	9.73±0.95
Control	40	87.61±9.55	10.92±1.85	112.64±13.52	131.53±15.73	12.69±1.73
t		8.493	7.192	12.495	15.382	8.934
P		<0.05	<0.05	<0.05	<0.05	<0.05

4. Discussion

Those with poor control of chronic obstructive pulmonary disease (COPD) easily develop type Ⅱ respiratory failure, COPD patients complicated with type Ⅱ respiratory failure are often more difficult to treat, and those with respiratory dysfunction in late stage are with multiplied mortality rate. Anti-infection, phlegm dispelling, anti-inflammation and adjustment of water-electrolyte disorder are all typical symptomatic treatment methods for COPD, but after it is complicated with type II respiratory failure, the above treatment methods have been unable to reverse the progress of disease, and other treatment methods are also needed to prevent the deterioration of disease[5]. Aminophylline is the compound salt of theophylline and ethylenediamine, the main pharmacological effect is from theophylline, and ethylenediamine can increase its water solubility. Aminophylline can inhibit the phosphodiesterase and improve intracellular cAMP levels, thus dilating the bronchi. At the same time, theophylline can enhance diaphragm contractility and help to improve patients' respiratory function. The positive role of aminophylline in treatment of patients with COPD has been reported by a large number of studies, but it is useless for lung ventilation/ gas exchange dysfunction and ventilator fatigue of patients with COPD. Acute exacerbation stage of COPD can show respiratory muscle dysfunction, independent ventilation and gas exchange function are weakened and it leads to hypoxia and carbon dioxide retention in the body, which is the root cause of type II respiratory failure in such patients[6,7]. In view of the severe consequences severity and complex treatment of COPD with type II respiratory failure, some scholars have proposed to add noninvasive positive pressure ventilation in the treatment, which optimizes the disease by alleviating respiratory muscle fatigue.

In the study, noninvasive positive pressure ventilation combined with aminophylline was used in the treatment of COPD complicated with type Ⅱ respiratory failure in our hospital, radial artery blood gas parameters of two groups were tested after treatment, and it was found that radial artery pH and PO_2 values of observation group were higher while PCO_2, Cl^- and CO_2CP values were lower after treatment, indicating that noninvasive positive pressure ventilation combined with aminophylline can reduce the carbon dioxide retention in patients and further reverse the acidosis caused by hypoxia and carbon dioxide retention. Mechanical ventilation can significantly improve the patients' pulmonary ventilation and gas exchange, and is an important way for the treatment of COPD with respiratory failure. Noninvasive positive pressure ventilation to provide bi-level positive airway pressure, inspiratory stage overcomes airway resistance, increases pulmonary ventilation and improves alveolar gas exchange, and expiratory stage confronts the airway collapse through positive end-expiratory pressure, promotes carbon dioxide discharge and eventually improves the patients' respiratory failure state[8]. So in the study, pulmonary function parameters of the two groups were tested after treatment, and it was found that FVC, FEV1, FEF25-75, MMF, PEF and FRC values of observation group were larger after treatment, further confirming the improving effect of noninvasive positive pressure ventilation on respiratory function in patients with COPD and type Ⅱ respiratory failure. Aminophylline can excite respiratory center and respiratory muscle, noninvasive positive pressure ventilation can improve pulmonary ventilation function, and the combination of the two can further prompt the patients to discharge the retention of CO_2 and fundamentally ease the respiratory muscle fatigue, prompting the improvement of COPD [9-10].

Both hypoxia and carbon dioxide retention can lead to increased blood viscosity in patients, and severe cases can lead to pulmonary hypertension and microcirculation disorder, resulting in the occurrence of thrombotic events. Study has found that there is ubiquitous increase of blood plasma viscosity and hematokrit in patients with COPD, and it is one of the reliable indicators to measure disease severity [11]. It was found in the study that whole blood viscosity (150s- and 10s-), plasma viscosity, fibrinogen, erythrocyte aggregation index and erythrocyte rigidity index values in peripheral venous blood of observation group were smaller after treatment, indicating that aminophylline combined with noninvasive positive pressure ventilation can reduce the patients' blood viscosity, reduce the occurrence risk of thrombotic events and significantly reduce the severity COPD and respiratory failure in patients. Related studies have found that noninvasive positive pressure ventilation can make more than 70% of COPD patients avoid endotracheal intubation, which indicates its excellence in improving the patients' lung ventilation and gas exchange function. The important cause of respiratory failure in patients with COPD is the occurrence of acute respiratory tract infection, respiratory failure can further aggravate the difficulty in treatment of airway inflammation, the two form a vicious circle, so detecting the serum levels of inflammatory factors in patients can act as the effective means to judge the disease severity, evaluate therapeutic effect and forecast treatment outcome. Interleukin-17 (IL-17), interleukin-33 (IL-33), triggering receptor expressed on myeloid cells-1 (TREM-1), soluble intercellular adhesion molecule 1 (sICAM-1) and prostaglandin E2 (PGE2) are all clinically confirmed inflammatory factors that are closely related to the occurrence and development of with COPD [12-13]. IL-17 is highly expressed in the lung of patients with COPD, and its level is negatively correlated with patients' lung function and positively correlated with the amount of smoking. Research has confirmed that IL-33 is highly expressed in the bronchial epithelium of mice with COPD, and can promote the release of IL-6, IL-8 and other pro-inflammatory factors and induce the occurrence of inflammatory cascade. TREM-1 often acts as an infection index, its combination with ligand can cause inflammation amplification, and TREM-1 level increases rapidly when COPD is aggravating[14,15]. PGE2 can dilate blood vessels and reduce vascular permeability, and as COPD occurs, inflammatory and hypoxic stimuli can prompt the endothelial cell injury and secretion of a large number of PGE2 [16]. It was found

in the study that serum IL-17, IL-33, TREM-1, sICAM-1 and PGE2 levels of observation group were lower after treatment, indicating that aminophylline combined with noninvasive positive pressure ventilation can optimize patients' airway function and promote the inflammatory airway mucous discharge so as to eventually reduce the systemic inflammatory response and block the inflammatory cascade.

To sum up, it is concluded as follows: noninvasive positive pressure ventilation combined with aminophylline can optimize the respiratory function of patients with COPD and type II respiratory failure and promote the improvement of blood gas parameters and the degree of inflammation, it is a reliable way to optimize patients' treatment outcome, and it's worth popularization and application in clinical practice in the future.

References

[1] Amri Maleh V, Monadi M, Heidari B, Maleh PA, Bijani A. Efficiency and outcome of non-invasive versus invasive positive pressure ventilation therapy inrespiratory failure due to chronic obstructive pulmonary disease. *Caspian J Intern Med* 2016; **7**(2): 99-104.

[2] Pejkovska S,Kaeva BJ, Goseva Z, Arsovski Z, Janeva JJ, Zeynel S. Predictive factors for the effect of treatment by noninvasive ventilation in patients with respiratory failure as a result of acute exacerbation of the chronic obstructive pulmonary disease. *Open Access Maced J Med Sci* 2015; **3**(4): 655-660.

[3] Pan Wei-sheng, Lan Guang-jun. Observation of the curative effect of aminophylline combined with noninvasive positive pressure ventilation treatment of chronic obstructive pulmonary disease combined with type Ⅱ respiratory failure. *Chongqing Med* 2015; **44**(19): 2733-2736.

[4] Fan L, Zhao Q, Liu Y, Zhou L, Duan J. Semiquantitative cough strength score and associated outcomes in noninvasive positive pressure ventilation patients with acute exacerbation of chronic obstructive pulmonary disease. *Respir Med* 2014; **108**(12): 1801-1807.

[5] Ko BS, Ahn S, Lim KS, Kim WY, Lee YS, Lee JH. Early failure of noninvasive ventilation in chronic obstructive pulmonary disease with acute hypercapnic respiratory failure. *Intern Emerg Med* 2015; **10**(7): 855-860.

[6] Huang Zhi-xin. Effect of Naloxone combining with noninvasive positive pressure ventilation therapy on blood gas indexes and serum indexes of COPD complicated with respiratory failure patients. *J Hainan Med Univ* 2015; **21**(6): 754-757.

[7] Fiorino S, Bacchi-Reggiani L, Detotto E, Battilana M, Borghi E, Denitto C, et al. Efficacy of non-invasive mechanical ventilation in the general ward in patients with chronic obstructive pulmonary disease admitted for hypercapnic acute respiratory failure and pH=7.35: a feasibility pilot study. *Intern Med J* 2015; **45**(5): 527-537.

[8] Xie Wen-ying, Shang Li-zhi, Pan Xiao-li, Zhang Liang-zhi, Chang Xue-hui, Hu Wen-hao, et al. Study of effects lung function, blood gas indexes and pathological changes of ailuo kechuanning on COPD model rats. *Chin J Exp Tradit Med Formulae* 2014; **20**(22): 117-120.

[9] Neame M, Aragon O, Fernandes RM, Sinha I. Salbutamol or aminophylline for acute severe asthma: how to choose which one, when and why? *Arch Dis Child EducPract Ed* 2015; **100**(4): 215-222.

[10]Mekov EV, Slavova YG, Genova MP, Tsakova AD, Kostadinov DT, Minchev DD, et al. Diabetes mellitus type 2 in hospitalized COPD patients: impact on quality of life and lung function. *Folia Med (Plovdiv)* 2016; **58**(1): 36-41.

[11]Asker S, Ozbay B, Ekin S, Yildiz H, Sertogullarindan B. Two-year survival of severe chronic obstructive pulmonary disease subjects requiring invasive mechanical ventilation and the factors affecting survival. *J Pak Med Assoc* 2016; **66**(5): 498-503.

[12]Wang Sheng, Xiong Lingling, Deng Xue, Zhou Qun, Li Chunying, Ren Wei, et al. Effect of aminophylline and simvastatin on airway inflammation and mucus hypersecretion in rats with chronic obstructive pulmonary disease. *J Central South Univ (Med Sci)* 2016; **41**(1): 37-40.

[13]Barnes PJ. Inflammatory mechanisms in patients with chronic obstructive pulmonary disease. *J Allergy Clin Immunol* 2016; **138**(1): 16-27.

[14]Wu Juan, Sha Hang. The detection and clinical value of soluble triggering receptor expressed on myeloid cells-1in patients with stable chronic obstructive pulmonary disease. *J Pract Med* 2016; **32**(10): 1609-1612.

[15]Guo Weiwei, Wang Lihui, Yang Jiong. Effect of IL-33/ST2 on pulmonary hypertension of chronic obstructive pulmonary disease. *Med J Wuhan Univ* 2016; **37**(2): 331-334.

[16]Hall SC, Agrawal DK. Toll-like receptors, triggering receptor expressed on myeloid cells family members andreceptor for advanced glycation end-products in allergic airway inflammation. *Expert Rev Respir Med* 2016; **10**(2): 171-184.