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Short Communication

Curative Effect of Glucocorticoid Combined with Respiratory Stimulant on AECOPD Patients

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ABSTRACT

As there is a high rate of the treatment failure in patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD) and many studies have tried to specify an effective treatment. Objective of this study was to observe and analyze the therapeutic effect of glucocorticoid combined with respiratory stimulant on patients with AECOPD along with the optimal nursing care required for these patients. Also, tumor necrosis factor-alpha (TNF-a) was assessed as an inflammatory factor to see the response to treatment. In this study, 180 AECOPD patients who had been treated in our hospital were enrolled as research objects, who were given routine respiratory stimulant therapy regimen and intravenous methylprednisolone. According to the dosage of glucocorticoid methylprednisolone, the patients were divided into three groups, each containing 60 patients. The changes of arterial blood gas parameters including pH value, oxygen partial pressure (PaO_2) and carbon dioxide partial pressure ($PaCO_2$) were compared. We found that respiratory stimulant combined with different doses of glucocorticoid methylprednisolone positively improve the pH value of patients with acidosis, increase the partial pressure of oxygen and lower the partial pressure of carbon dioxide ($P<0.05$ in all three groups). Methylprednisolone at 40mg every 12 h proved better than other doses ($p<0.05$). The average length of stay was (12.5±3.0) days, the complication rate was 6.67%, and the overall nursing satisfaction was 97.22%, which shows that this is an auxiliary way to improve the treatment effect of patients.

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Authors' Contributions
Mw selected glucocorticoid experiment and XC made further medical analysis. Both authors carried out the experiment, analyzed and discussed the results, and wrote manuscripts.

Key words
Glucocorticoids, Respiratory stimulants, AECOPD patients, Therapeutic effect, Nursing mode.

Symptoms of chronic obstructive pulmonary disease (COPD) include worsening of cough, shortness of breath or wheezing within a short period of time, increased sputum volume that is purulent or mucous purulent, and fever. In addition, symptoms such as general discomfort, insomnia, lethargy, fatigue, depression and mental disorders can also occur (Liu *et al*., 2004; Eng *et al*., 2019; Nimdet and Techakehakij, 2017). Reduced exercise endurance, fever, and/or abnormal chest imaging may be signs of COPD exacerbation. COPD can be diagnosed with at least 2 of the following 3 criteria: hyperventilation, increased sputum volume, and purulent sputum. Infection is the main cause leading to the acute exacerbation of chronic obstructive pulmonary disease (AECOPD).

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Currently, effective measures for the treatment of AECOPD are oxygen absorption, anti-inflammatory, spasmolysis, antiasthmatic, expectorant, respiratory stimulant and non-invasive ventilator assisted ventilation. Non-invasive ventilator assisted ventilation has been more and more widely used in clinical practice, with definite efficacy. However, some patients cannot tolerate non-invasive ventilator assisted ventilation due to the risk of pulmonary bullae rupture and unacceptable psychological factors of patients. Previous studies have shown (Iacob *et al*., 2017; Liu *et al*., 2014) that the administration of the respiratory stimulant nikezamide by dose of 1.125 g every 12 h can produce a positive improvement in pH value at the fourth day, while increasing oxygen partial pressure and reducing carbon dioxide partial pressure. AECOPE is normally induced by airway infection. According to previous studies and current guidelines, systemic glucocorticoids are indispensable components during the treatment of AECOPD, but the dosage and administration duration of glucocorticoids are not consistent. This study analyzed the therapeutic effect of glucocorticoid combined with respiratory stimulant on AECOPD patients. The novelty of this study was using systematic glucocorticoid

(intravenous methylprednisolone) combined with respiratory stimulant along with assessing nursing method of conduction of this treatment protocol, as it is not investigated in other studies. Also, tumor necrosis factor-alpha (TNF-a) was assessed as an inflammatory factor to see the response to treatment.

Materials and methods

In this study, 180 patients, 102 males and 78 females, ranging in age from 60 to 83 years, with an average age of 68.4±2.0 years old and an average BMI of 22.5±1.8, who had been treated in our hospital for AECOPE complicated with type 2 respiratory failure from June 2015 to May 2019 were enrolled as research objects. Inclusion criteria of this study were patients meeting the diagnostic criteria of the global strategy for chronic obstructive pulmonary disease (revised edition in 2011), being unable to tolerate non-invasive ventilator assisted ventilation due to various factors, receiving the routine treatment of respiratory stimulant. Patients with severe cardiac dysfunction, mental disorders, low treatment compliance were excluded.

All included patients were divided into three groups randomly (each containing 60 cases) according to the dose of glucocorticoid methylprednisolone.

All patients were prescribed routine treatment including anti-infection, antiasthmatic, spasmodic and expectorant treatment, acid-base balance correction, and nutritional support. In addition, patients were treated with the respiratory stimulant nicosum and glucocorticoid methylprednisolone. Nikexamide (Suzhou Pharmaceutical Factory of Jiangsu Wuzhong Pharmaceutical Group Co., Ltd., SFDA approval number: H32022792) was administrated at dose of 1.125g every 12 h, for four consecutive days. 40 mg of glucocorticoid methylprednil (Tianjin Jinyao Pharmaceutical Co., Ltd., SFDA approval number: H20123319) was dissolved in 20ml of 5% glucose solution, and then intravenously injected into patients for 20 min. Treatment was conducted once a day for group I, once every 12 h for group II, and once every 8 h for group III. All of the three groups were treated for four consecutive days.

Patients with AECOPD have a long course of disease, with a large range of changes in the condition, and are prone to recurrent attacks, leading to emotional instability (Ding *et al*., 2014). Nursing staff was involved in effectively channeling the negative emotions of patients, encourage family members to accompany patients, helped passive ROM joint exercise and relieve bad mood.

Blood gas analysis was conducted at different time points before and after treatment, and the changes of pH, PaO_2 and $PaCO_2$ were counted. SF-36 scale was adopted to evaluate the quality of life of patients before and after nursing. At the same time, the length of stay, the rate of complications and nursing satisfaction were calculated.

For TNF-α assessment monocytes were isolated by PBMC method from 10 ml of heparinized blood collected after 12 h fasting of patients. The obtained PBMC was mixed with RPMI-1640 (Gibco, UK) with mM2-L glutamine (Sigma, USA) and incubated at 37°C for 2 h in the presence of 100 U/ml of penicillin, 100 µg/ml of streptomycin and serum AB10% with 90% humidity and 25% CO_2. Sandwich enzyme immunoassay kits were used to detect TNF-alpha levels.

Statistical analysis software of SPSS21.0 was used to process data. Continues data were expressed by mean ± average ($\bar{x}$ ± s), with t test conducted for intergroup comparison. Categorical data were expressed by natural (n) and percentage (%), with X2 used for intergroup comparison. The intergroup difference is of statistical value when $p<0.05$.

Table I.- Comparison of blood gas analysis indexes before and after treatment ($\bar{x}$±s).

Group	pH		PaO_2 (mmHg)		$PaCO_2$ (mmHg)	
	Before treatment	4 days after treatment	Before treatment	4 days after treatment	Before treatment	4 days after treatment
Group I	7.23±0.07	7.36±0.03	46.8±3.2	71.6±3.5	74.8±4.0	56.7±5.2
Group II	7.27±0.04	7.36±0.08	45.3±3.7	76.5±3.2	72.7±5.3	53.4±3.1
Group III	7.27±0.03	7.33±0.06	46.8±4.4	74.5±4.6	73.5±4.0	52.4±3.6

Table II.- Comparison of quality of life before and after nursing ($\bar{x}$±s).

Time	No. of cases	Physiological function	Emotional function	Social function	State of health	Mental function	Energy
Before nursing	180	79.80±3.25	78.96±3.20	82.35±2.18	60.78±3.22	75.63±4.02	65.79±2.04
After nursing	180	72.20±2.46	66.88±2.58	73.20±2.59	49.06±3.01	65.80±2.06	55.49±3.28
t		6.70	20.19	6.79	8.53	11.22	13.27
p		<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

Results

Table I shows that group II had significant advantages in the improvement of pH, PO_2, PCO_2 as compared with group I and group III, $p<0.05$. Table II shows that the quality of life was significantly better after nursing than that before nursing, $p<0.05$. Table III shows the length of stay, rate of complication and nursing satisfaction of the patients.

The TNF-alpha level of monocytes didn't significantly change after treatment, p=0.15. TNF-alpha level before treatment was 10.3±4.35 and after 4 days was 8.9±7.2.

Table III.- Length of stay, rate of complication and nursing satisfaction of the patients.

No. of cases	Length of stay (d)	Rate of complication (%)	Nursing satisfaction (%)
180	12.5±3.0	12 (6.67)	175 (97.22)

Discussion

COPD is a common disease characterized by continuous airflow limitation (CPD), progressive airflow, and increased chronic inflammatory caused by harmful particles and gases in the airways and lungs. As a typical central excitant, the respiratory stimulant nikhoshmi directly or indirectly excites the medulla oblongata respiratory center, exerting an influence on respiratory frequency, promoting the acceleration of respiration, increasing the ventilation volume and increasing the partial pressure of arterial blood oxygen, thus reducing the partial pressure of arterial blood carbon dioxide (Kuti and Oyelami, 2015; Wilmot *et al*., 2016). One of the most common factors for AECOPD is infection, which can lead to an inflammatory airway response. Abnormal chronic inflammatory response in the lungs of patients with COPD is a key factor in promoting disease progression. Glucocorticoids are involved in many aspects of the airway inflammatory response, which had the function of anti-allergy, anti-microvascular leakage, anti-mucosal edema and indirect relaxation of airway smooth muscle. Systemic glucocorticoid therapy can promote the recovery of pulmonary function FEV1 and improve the therapeutic effect. After patients with AECOPD combined with type 2 respiratory failure accepting conventional treatment, the PH, $PaCO_2$ and $PaCO_2$ levels in blood gas analysis can be positively corrected after 4 days of systemic glucocorticoid methylprednisolone treatment combined with respiratory stimulant nissami, and better results can be achieved. As well as our study, prednisone therapy greatly increased the exchange of gases by increasing PaO_2, in the study of the Woods *et al*. (2014). In a meta-analysis study by Dobler *et al*. (2020), 68 randomized clinical trials were reviewed. Systemic corticosteroids were correlated with a less medication failure at the end of the assessment. There were no differences between the one-month readmission or fatality rates between group of patients with systemic corticosteroid therapy with and without inhaled corticosteroids (Pearce *et al*., 2018). While we did not assess these outcomes; they saw a shorter length of hospitalization (about 6 days averaged) than patients in our study. The difference of our results with Pearce *et al*. (2018) may be due to the use of the respiratory stimulants in our study.

Meta-analysis of Wu *et al*. (2020) reviewed studies using systemic corticosteroid therapy and they found that treatment failure happens with a risk ratio of 0.61, as well as our study that 6.67% of patients had complications during or after treatment. Also, our study showed no difference in the level of TNF-a after treatment. A meta-analysis of studies showed that the COPD disease progression and the development of COPD could lead to increased rates of TNF-a. The underlying cause, though, is still unexplained and needs to be analyzed (Uzeloto, 2020).

While most of studies show benefits of systemic corticosteroids for exacerbation of chronic obstructive pulmonary disease; there are limited studies with a long term follow up. In the REDUCE Trial, 40 mg prednisone for 5 days and patients were assessed till 180 days (Leuppi *et al*., 2013). Reexacerbation rate was about 37%. But there are few studies with this long term follow up and as also our study evaluated short term outcomes, we purpose further researches with long term follow ups.

Conclusion

In conclusion, the treatment mode of glucocorticoid combined with respiratory stimulant in patients with AECOPD can achieve good results.

Statement of conflict of interest

The authors have declared no conflict of interests.

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