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Original Article

Clinical efficacy of glucocorticoid and terbutaline in the treatment of acute exacerbation of chronic obstructive pulmonary disease

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Abstract: Background: To investigate the efficacy of glucocorticoid and terbutaline in the treatment of acute exacerbation of chronic obstructive pulmonary disease (AECOPD). Methods: 248 patients with AECOPD were assigned into two groups, 124 patients in the control group were only given terbutaline treatment, while 124 patients in the experimental group were treated with glucocorticoid and terbutaline. The effect on lung function and blood gas indexes were compared between the two groups. Results: The total effective rate of the treatment with glucocorticoid and terbutaline was higher than that of control group ($P < 0.05$). After treatment, the pulmonary function indexes such as FEV_1, FVC and PaO_2 levels in the two groups were significantly higher than those before treatment, $PaCO_2$ levels were significantly lower than that before the treatment ($P < 0.05$). Conclusions: The combined use of glucocorticoid and terbutaline could effectively improve the lung function and blood gas indexes. It's of great significance to promote the rehabilitation of patients with AECOPD, and it provides insights for future clinical practice.

Keywords: Glucocorticoid, terbutaline, acute exacerbation of chronic obstructive pulmonary disease, clinical efficacy

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is clinically a common respiratory disease. It is characterized by air flow restriction. If without treatment in time, respiratory failure may threaten patient's lives [1, 2]. Indeed, the mortality is gradually increasing these years. There will be increased wheezing, expectoration, shortness of breath and other symptoms in the early stage of disease, and the disease will affect other systems of the patients [3]. Some researchers suggested that COPD is a disease that caused chronic inflammatory reaction, activated a variety of inflammatory cells, released inflammatory mediators, and damaged the lung parenchyma and structure [4, 5]. At present, anti-inflammatory and antispasmodic, anti-infective, antitussive and expectorant methods were applied to improve lung function and relieve clinical symptoms, but the effect is unsatisfactory [6]. FEV1 is the gold standard for the diagnosis of COPD. Gold defined COPD as persistent airflow limitation in 2017 [7]. The judgment of severity criteria: on the premise of FEV1/FVC < 70%, 80% predicted value of FEV1 is mild, < 80% predicted value is moderate, < 50% predicted value is severe, and < 30% predicted value is extremely severe [8].

Terbutaline is a β_2 receptor agonist, which can control inflammatory release and improve ventilation function [9]. Glucocorticoid can block the occurrence of pathological immune response and control the immune inflammatory reaction [10]. This study was aimed to investigate effect of glucocorticoid and terbutaline in the treatment of AECOPD.

Materials and methods

Study design

The study was a randomized controlled single center trial. This study was performed at the

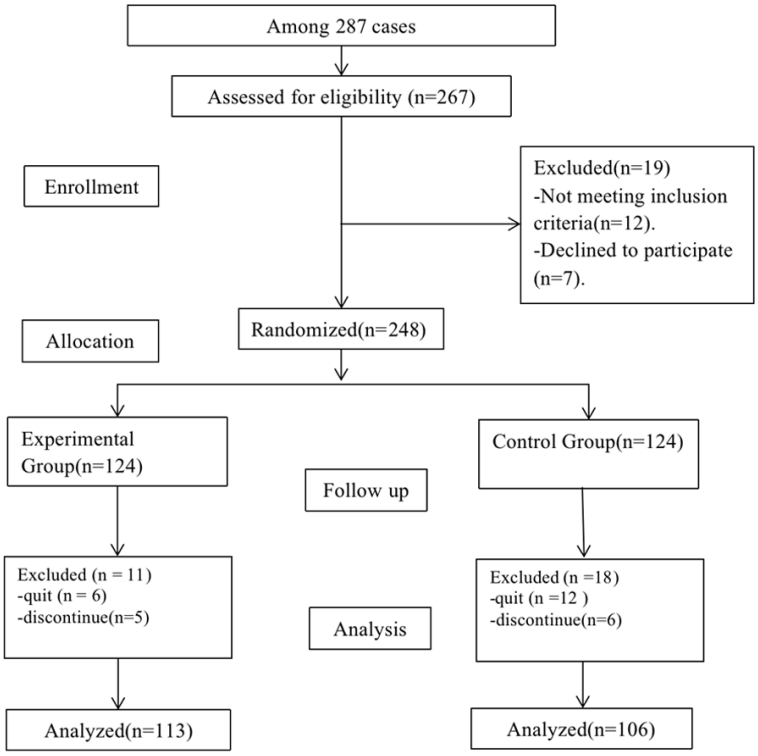

Figure 1. Flow chart showing recruitment through the study.

3rd Affiliated Hospital of Chengdu Medical College from January 2018 to January 2020. Inclusion criteria: 1) The diagnosis of AECOPD is consistent with the standard of the GOLD of 2018 [11]; 2) No glucocorticoid was used within six months; 3) No β_2-receptor agonist or antihistamines were taken within 24 hours; 4) The subjects were willing to cooperate and implement the experiment. Exclusion criteria: 1) Had a history of mental illness; 2) Had a history of blood system diseases; 3) Had a history of chronic diseases such as diabetes, hypertension, nephropathy or coronary heart disease before pregnancy; 5) Had a history of malignant tumor; 6) Had serious cognitive, psychological and hearing impairment; 7) The pregnant woman and the breast-feeding period woman; 8) Drop out researcher. The procedures of this clinical trial are presented **Figure 1**. The researchers systematically explained the role, purpose and process of the study to the patients and their families. The patients and their families voluntarily signed the informed consent form to participate in this study. This study was approved and recognized by the ethics committee of our hospital.

Participants and subgroup

287 participants were admitted to our hospital, and 267 patients were meeting the inclusion and exclusion criteria. Finally, 248 eligible patients were allocated into two group: the experimental group (Glucocorticoid budesonide combined with terbutaline treatment) (n=124) or the control group (Terbutaline alone) (n=124).

Interventions

Control Group (CG): Terbutaline (AstraZeneca Pharmaceutical Co., Ltd) alone. 0.9% normal saline was diluted and added into the atomizer for atomization inhalation, 2 ml each time, it lasts 15-20 minutes each time, inhales twice a day, and uses it for 7 days continuously.

Experimental Group (EG): Glucocorticoid budesonide combined with terbutaline treatment. 2 ml budesonide suspension was added into 0.9% normal saline for 15-20 minutes each time, twice a day. Continuous treatment for 7 days.

During the process of treatment, the two groups were given symptomatic treatment such as anti-infection, vasodilation, phlegm resolving and diuresis.

Primary outcome measure

The primary outcome measure was clinical efficacy, lung function indexes (peak expiratory velocity, forced expiratory volume in the first second, forced vital capacity and so on), arterial blood gas index (Blood oxygen saturation (SpO_2), arterial partial pressure of carbon dioxide ($PaCO_2$) etc) and adverse reactions.

Efficacy evaluation criteria

Significant effect: The basic symptoms such as shortness of breath and dyspnea disappeared after treatment, and the index of SpO_2 and

Table 1. Clinical characteristics of AECOPD patients

	Experimental group (n=113)	Control group (n=106)	t/χ^2	*P*
Age (years)	68±12.26	65±11.47	2.15	0.55
Sex			6.96	0.35
Male (n%)	87 (77%)	79 (74.5%)		
Female (n%)	26 (23%)	27 (25.5%)		
BMI (kg/m^2)	20.4±1.66	21.1±1.76	5.74	0.21
Smoking Status			10.85	0.48
Smoking	95 (84%)	86 (81.1%)		
Never Smoke	13 (11.5%)	14 (13.2%)		
Chronic emphysemaseparated	35 (31%)	27 (25.5%)	2.76	0.69
Asthme	41 (36.3%)	34 (32.1%)	5.72	0.41
Disease severity GOLD Stage			6.17	0.137
A	20 (17.7%)	23 (20.6%)		
B	41 (36.3%)	36 (34%)		
C	35 (31%)	29 (27.4%)		
D	17 (15%)	18 (17%)		

Note: Signiticant difference as P < 0.05. GOLD: Global Initiative for Chronic Obstructive Lung Disease (2019).

$PaCO_2$ were returned to normal. Effective: Cough and expectoration, shortness of breath and dyspnea were significantly improved after treatment, SpO_2 and $PaCO_2$ levels tended to be normal. Ineffective: The symptoms and signs of the disease were not significantly improved, or the symptoms were aggravated [12].

Statistical analysis

All data were analyzed by SPSS 22.0. The statistical results are expressed by mean ± standard deviation (M ± s), the data comparison is conducted by t-test and the correlation analysis is conducted by person linear phase, P < 0.05 was the difference with statistical significance. Analyses were performed using Graph Pad Prism (Graph Pad Software Inc., CA, USA).

Result

Participant recruitment

Figure 1 showed the recruitment of participants in our study. We recruited 287 participants in our hospital; 248 subjects were eligibility for this study, of these, 124 were assigned to the experimental group and 124 to the control group.

Clinical characteristics

The research included 113 patients in the experimental group at last, a mean age (68±12.26) years old, the number of male was 87 (87/113, 77%), and the number of female was 26 (26/113, 23%), while 106 AECOPD patients in the control group at last, a mean age (65±11.47) years old, the number of male was 79 (79/106, 74.5%), and the number of female was 27 (27/106, 25.5%), there was no statistical significance between two group (P > 0.05). The BMI in the experimental group was (20.4±1.66) kg/m^2, and in the control group was (21.1±1.76) kg/m^2, there was no difference between two group (P=0.21, > 0.05). The number of smoking in the experimental group was 95 (95/113, 84%), while the number of never smoking was 13 (13/113, 11.5%), and the number of smoking in the control group was 86 (86/106, 81.1%), the number of never smoking was 14 (14/106, 13.2%), there was no difference between two group (P > 0.05). The number of patients who had history of chronic emphysema, chronic bronchitis and asthme were respectively 35 (31%), 43 (38.1%) and 41 (36.3%) in the experimental group, while that in the control group were respectively 27 (25.5%), 38 (35.8%) and 34 (32.1%). In the two group, the patients were graded for severity of disease severity (GOLD Stage 2019) as A, B, C, D, and there was no difference between two group (X^2=6.17, P=0.137, P > 0.05) (**Table 1**).

Compared clinical efficacy between the two groups

As shown in **Table 2**, the total effective rate of the experimental group was 93.8%, which was higher than that of the control group (61.3%), the differences were statistically significant (P < 0.05). In the experimental group, the markedly effective rate was 60.2% (68 cases), the effective rate was 33.6% (38 cases), and the ineffective rate was 6.2% (7 cases); in the control group, the markedly effective rate was 39.6% (42 cases), the effective rate was 21.7% (23 cases), and the ineffective rate was 38.7% (41 cases).

Table 2. Clinical efficacy

group	Number of cases	Significant effective	Effective	Ineffective	Total effective rate
Experiemntal group	113	68 (60.2%)	38 (33.6%)	7 (6.2%)	106 (93.8%)
Control group	106	42 (39.6%)	23 (21.7%)	41 (38.7%)	65 (61.3%)
t	-	4.128	8.527	14.261	12.348
P	-	0.005	0.031	0.000	0.000

Note: Signiticant difference as P < 0.05.

Table 3. Blood gas index level

Index	time	Experimental group (n=113)	Control group (n=106)	t	*P*
PaO_2	Before treatment	56.31±3.81	55.26±3.67	3.178	0.201
	After treatment	70.63±2.36	64.88±2.14	6.323	0.001
	t	10.358	6.176	-	-
	P	0.000	0.000	-	-
$PaCO_2$	Before treatment	70.70±2.63	71.75±3.58	3.103	0.098
	After treatment	51.85±2.37	63.60±2.81	11.928	0.000
	t	19.228	14.136	-	-
	P	0.000	0.000	-	-

Note: Signiticant difference as P < 0.05.

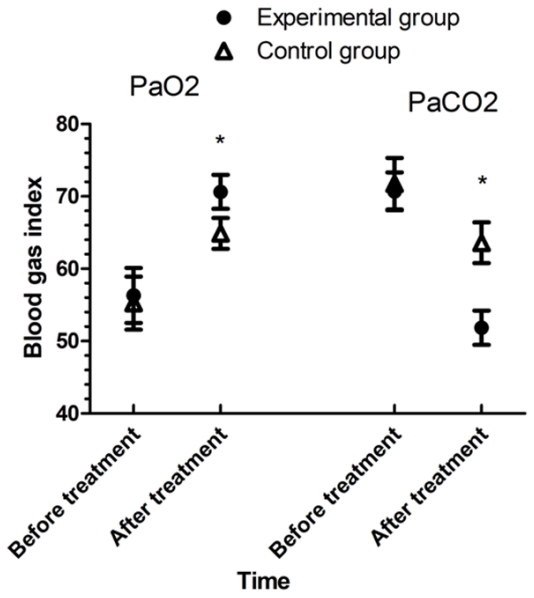

Figure 2. Blood gas index level of two groups. *$P < 0.05$.

Analysis of blood gas index level of two groups

The $PaCO_2$ level after treatment was lower than that before treatment, and the PaO_2 level was higher than that before treatment, $PaCO_2$ and PaO_2 were improved after treatment; after treatment, the $PaCO_2$ level in the experimental group was lower than that in the control group ((51.85±2.37) VS. (63.60±2.81), P=0.001 < 0.05), and the PaO_2 level was higher than that in the control group ((70.63±2.36) VS. (64.88±2.14), P=0.001 < 0.05) (**Table 3** and **Figure 2**).

Lung function indexes in the two groups

As shown in **Table 4**, the level of FEV1 in the experimental group before treatment was (1.11±0.38) L, and that in the control group was (1.17±0.42) L; while the level of FEV1 in the experimental group after treatment was (3.26±0.38) L, and that in the control group was (2.91±0.51) L, the level of FEV1 of two groups afer treatment were higher than those before treatment, and there had statistical significance (P < 0.05). The level of FVC in the experimental group before treatment was (1.47±0.59) L, and that in the control group was (1.45±0.57) L; while the level of FVC in the experimental group after treatment was (3.91±0.53) L, and that in the control group was (2.75±0.48) L, the level of FVC were improved after treatment. The level of FEV1/FVC in the experimental group before treatment was (52.94±5.51)%, and that in the control group was (53.08±5.72)%; while the level of FEV1/FVC in the experimental group after treatment was (63.43±4.32)%, and that in the control group was (58.57±5.41)% the level of FEV1/FVC of two groups afer treatment were higher than those before treatment, and there had statistical significance (P < 0.05).

Discussion

Our research indicated that total effective rate of experimental group was significantly higher than that in control group (P < 0.05). After treatment, the indexes of FEV_1, FVC and PaO_2 levels in the two groups were significantly increased,

Table 4. Lung function indexes

Index	time	Experimental group (n=113)	Control group (n=106)	t	*P*
FEV1 (L)	Before treatment	1.11±0.38	1.17±0.42	1.028	0.320
	After treatment	3.26±0.38	2.91±0.51	3.113	0.001
	t	4.218	3.216	-	-
	P	0.000	0.000	-	-
FVC (L)	Before treatment	1.47±0.59	1.45±0.57	1.201	0.861
	After treatment	3.91±0.53	2.75±0.48	1.939	0.000
	t	3.128	2.416	-	-
	P	0.000	0.000	-	-
FEV1/FVC (%)	Before treatment	52.94±5.51	53.08±5.72	2.113	0.908
	After treatment	63.43±4.32	58.57±5.41	6.138	0.000
	t	8.618	7.216	-	-
	P	0.000	0.000	-	-

Note: Signiticant difference as $P < 0.05$.

and the $PaCO_2$ level was significantly lower than that before treatment ($P < 0.05$). The results also indicated that terbutaline combined with glucocorticoid treatment had a better improvement in the blood gas and lung function indexes.

Terbutaline is a β_2-adrenoceptor agonist, which can promote the activation of related β_2 receptors on bronchial smooth muscle and relax the bronchial smooth muscle. It can increase the movement of airway cilia, reduce vascular permeability, reduce the degree of airway submucosal edema. Moreover, it can improve the levels of PaO_2 and $PaCO_2$, FVC, FEV_1 and FEV_1/FVC [13-15]. Glucocorticoid can play a good anti-inflammatory response, control the release of inflammatory mediators, increase the production of anti-inflammatory factors, reduce the activity of inflammatory mediators and capillary permeability, and also control the secretion of epithelial cell mucus [16]. Budesonide is a kind of glucocorticoid, which can promote sputum excretion, make airway cilia for better movement, reduce the release of inflammatory mediators [17, 18]. Terbutaline combined with glucocorticoid application, which plays a synergistic role, can better improve the treatment effect, improve the symptoms and prognosis of patients [19, 20]. These were consistent with our findings in this study. The total effective rate of the experimental group was 93.8%, which was higher than that of the control group (61.3%). The $PaCO_2$ level of the two groups after treatment was lower than that before treatment, and the levels of PaO_2 and $PaCO_2$ level, and the FVC, FEV_1, FEV_1/FVC values of the experimental group were higher than that before treatment.

Nevertheless, our study had limitations. One limitation is the small number of subjects. The difficulties in the beginning of our study were the age of patients, the COPD patients were acute and hard to cooperate with researches. On the other hand, although our results are promising, the mechanism of this method is unclear. Therefore, our results still require further confirmation by larger scale, randomized, control clinical trials.

In summary, this study provides preliminary evidence that terbutaline combined with glucocorticoid in the treatment of AECOPD. It can effectively control inflammation and improve lung function, shorten the time of inflammation control, and improve effect of treatment.

Disclosure of conflict of interest

None.

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