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Effects of Combined Inhalation of Budesonide, Formoterol, and Tiotropium Bromide on Arterial Blood Gas and Pulmonary Function Indexes in Patients with Chronic Obstructive Pulmonary Disease

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Abstract: *Objective:* To analyze the effect of combined inhalation of budesonide formoterol and tiotropium bromide on arterial blood gas and pulmonary function indexes in patients with chronic obstructive pulmonary disease (COPD). *Methods:* 100 patients with COPD treated from January to December 2022 were selected as observation objects, and were divided into a control group (n = 50, in which budesonide and formoterol were administered) and an experimental group (n = 50, the treatment drug was budesonide formoterol combined with tiotropium bromide) according to the computer grouping method, and compared the treatment results. *Results:* (i) Before treatment, there was no difference in the partial pressure of carbon dioxide and partial pressure of oxygen between the control group and the experimental group (P > 0.05); after treatment, the partial pressure of carbon dioxide and partial pressure of oxygen in the experimental group were higher than those in the control group, with significant differences (P < 0.05). (ii) Before treatment, there was no difference in forced vital capacity (FVC), forced expiratory volume in one second (FEV1), FEV1/FVC between the control group and the experimental group (P > 0.05); after treatment, the FVC, FEV1, and FEV1 /FVC in the experimental group were significantly higher than those in the control group (P < 0.05). (iii) There was no difference in the levels of CRP, IL-6, and TNF-α between the control group and the experimental group (P > 0.05); after treatment, the levels of CRP, IL-6, and TNF-α in the experimental group were lower than those in the control group, with significant differences (P <0.05). (iv) Compared to the total incidence of adverse reactions in the control group (28.00%), the incidence of total adverse reactions in the experimental group was lower at 10.00%, and the difference was significant (P < 0.05). *Conclusion:* The combined inhalation of budesonide and formoterol with tiotropium bromide has demonstrated a clear therapeutic efficacy and safety in treating chronic obstructive pulmonary disease. This treatment approach effectively enhances arterial blood gas levels and lung function, showing promising potential for widespread application.

Keywords: Budesonide formoterol; Tiotropium bromide; Chronic obstructive pulmonary disease; Arterial blood gas; Lung function

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1. Introduction

Chronic obstructive pulmonary disease (COPD) is a relatively common respiratory disease. The disease is characterized by airflow limitation, and the disease manifests as dyspnea and coughing. This further reduces the quality of life, and COPD will eventually develop into cor pulmonale and respiratory failure, which is life-threatening [1]. COPD has the characteristics of acute onset, slow disease progression, and high mortality. At present, COPD is mainly treated through medication, with β2 receptor agonists and glucocorticoids being the primary option. However, these medications need to be administered for long periods of time, causing adverse reactions, which affects the patient's compliance towards the treatment and the overall treatment effect [2]. Many studies have found that the use of long-acting anticholinergic drugs on the basis of conventional treatment can not only reduce adverse reactions, but also improve the efficacy of drug treatment [3]. Therefore, the effect of combined inhalation of budesonide formoterol and tiotropium bromide on arterial blood gas and pulmonary function indexes in patients with COPD will be discussed in this paper.

2. General information and methods

2.1. General information

A hundred patients with COPD treated during January to December 2022 were selected as the study subjects, and they were divided into a control group and an experimental group through computer grouping. Inclusion criteria: (i) patients who were diagnosed with COPD based on the 2013 Chinese Medical Association's revised guidelines [4], (ii) patients who have been diagnosed with COPD by laboratory tests, (iii) patients who agree to participate in this study. Exclusion criteria: (i) patients who have contraindications to the drugs used in the study, (ii) patients who had been taking narcotic drugs for a long time, (iii) patients with cardiovascular and cerebrovascular diseases.

There were 28 female and 22 male patients respectively in the control group; their age ranged from 46 to 70 years old, with an average of 58.00 ± 3.69 years; and the course of disease ranged from 2–9 years, with an average of 5.50 ± 1.74 years. The patients in the experimental group consisted of 30 males and 20 males, with ages ranging from 46 to 72 years old, with an average of 59.00 ± 3.71 years old; their disease durations ranged from 2 to 10 years, with an average of 6.00 ± 1.77. The data was inputted into statistical software for analysis, which revealed no significant differences. ($P > 0.05$).

2.2. Methods

The control group received budesonide-formoterol as the treatment drug: administered twice a day, with 4.5 μg per inhalation, 1–2 times each session, for a total of 3 months. The experimental group was administered tiotropium bromide in addition to the drugs administered in the control group: 1 capsule per dose, once daily, for a total treatment duration of 3 months.

2.3. Observation indicators

(i) Arterial blood gas parameters were measured using a blood gas biochemical analyzer, covering partial pressure of carbon dioxide and partial pressure of oxygen. (ii) Lung function was evaluated through a portable spirometer, measuring forced vital capacity (FVC), forced expiratory volume in the first second (FEV_1), and FEV_1/FVC ratio. (iii) Fasting venous blood samples (5 mL) were collected for ELISA analysis of acute blood gas and biomarkers, including C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α). (iv) The incidence of adverse reactions was compared between groups.

2.4. Statistical method

SPSS 22.0 was used to analyze the data, the measurement data was expressed by mean ± standard deviation, the data of the two groups were compared through a *t*-test, the count data was expressed as [*n*(%)], and the comparison between groups was expressed by x^2 test, with $P < 0.05$ indicating statistical significance.

3. Results

3.1. Comparison of arterial blood gas index changes in patients in each group

Before treatment, there was no difference in the partial pressure of carbon dioxide and partial pressure of oxygen between the control group and the experimental group ($P > 0.05$); after treatment, the partial pressure of carbon dioxide and partial pressure of oxygen in the experimental group were significantly higher than those in the control group ($P < 0.05$), as shown in **Table 1**.

Table 1. Comparison of arterial blood gas index changes in patients in each group (mean ± standard deviation, mmHg)

Group	Partial pressure of carbon dioxide		Partial pressure of oxygen	
	Before treatment	After treatment	Before treatment	After treatment
Control group	55.64 ± 5.11	51.08 ± 4.78	0.54 ± 0.46	71.08 ± 5.38
Experimental group	55.61 ± 5.08	46.11 ± 4.63	0.53 ± 0.45	78.11 ± 5.60
t	0.029	5.281	0.110	6.401
P	> 0.05	< 0.05	> 0.05	< 0.05

3.2. Comparison of changes in pulmonary function indexes of patients in each group

Before treatment, there was no difference in FVC, FEV_1, FEV_1/FVC between the control group and the experimental group ($P > 0.05$); after treatment, the FVC, FEV_1, FEV_1/FVC in the experimental group were significantly higher than those in the control group ($P < 0.05$), as shown in **Table 2**.

Table 2. Comparison of changes in pulmonary function indexes of patients in each group (mean ± standard deviation)

Group	FVC (L)		FEV_1 (L)		FEV_1/FVC (%)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	1.63 ± 0.18	2.04 ± 0.28	1.60 ± 0.14	1.86 ± 0.23	8.47 ± 1.26	58.33 ± 3.01
Experimental group	1.65 ± 0.20	2.30 ± 0.35	1.61 ± 0.15	2.21 ± 0.31	8.45 ± 1.23	64.24 ± 3.97
t	0.526	4.102	0.345	6.412	0.080	8.388
P	> 0.05	< 0.05	> 0.05	< 0.05	> 0.05	< 0.05

3.3. Comparison of changes in serum inflammatory factor levels of patients in each group

Before treatment, there was no difference in the levels of CRP, IL-6, and TNF-α between the control group and the experimental group ($P > 0.05$); after treatment, the levels of CRP, IL-6, and TNF-α in the experimental group were significantly lower than those in the control group ($P < 0.05$) as shown in **Table 3**.

Table 3. Comparison of changes in serum inflammatory factor levels of patients in each group (mean ± standard deviation)

Group	CRP (mg/L)		IL-6 (pg/L)		TNF-α (pg/L)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	22.30 ± 4.16	16.91 ± 3.49	36.26 ± 5.01	18.55 ± 3.76	45.34 ± 5.89	21.62 ± 3.89
Experimental group	22.33 ± 4.19	12.30 ± 3.31	36.23 ± 4.98	11.70 ± 3.03	45.36 ± 5.91	16.31 ± 3.40
t	0.036	6.777	0.030	10.031	0.017	7.268
P	> 0.05	< 0.05	> 0.05	< 0.05	> 0.05	< 0.05

3.4. Comparison of adverse reactions in patients in each group

The total incidence of adverse reactions in the control group (28.00) higher than that in experimental group (10.00%), and the difference was significant ($P < 0.05$), as shown in **Table 4**.

Table 4. Comparison of adverse reactions in patients in each group [n(%)]

Group	Headache	Palpitations	Nausea	Rash	Tremors	Total incidence
Control group	3 (6.00)	2 (4.00)	3 (6.00)	4 (8.00)	2 (4.00)	14 (28.00)
Experimental group	2 (4.00)	0 (0.00)	1 (2.00)	2 (4.00)	0 (0.00)	5 (10.00)
x^2						5.263
P						< 0.05

4. Discussion

COPD is a prevalent and life-threatening condition, marked by symptoms like chest tightness and chronic cough with mucus production, which significantly impact the patients' quality of life [5]. The combination of budesonide and formoterol can promote bronchodilation, inhibit and relieve airway inflammation, and at the same time strengthen local anti-inflammatory activity in lung tissue, thereby improving lung function. Budesonide and formoterol exert a potent local anti-inflammatory effect, which can impact the production of immune response antibodies and endothelial cells [6]. Budesonide and formoterol inhibit inflammatory factors released by neutrophils, rapidly alleviating edema caused by inflammation in lung tissue's small airways and respiratory mucosa after administration. This helps restore normal respiratory system function and maintain airway patency.. Budesonide-formoterol is a commonly used drug in the treatment of COPD. However, the effect of single-use budesonide-formoterol in the treatment of COPD is not very satisfactory due to its mechanism of action [7]. Tiotropium bromide, a selective anticholinergic drug, exerts a potent cholinergic receptor tissue effect [8]. Its dissociation from M1 and M3 receptors is relatively slow, with a duration of up to 34.7 hours. This enables tiotropium bromide to provide prolonged bronchial smooth muscle relaxation by blocking cholinergic nerve-mediated bronchial contraction [9]. Tiotropium bromide has high specificity once it enters the body. Upon inhalation, tiotropium bromide adheres to the respiratory tract due to its strong affinity for mucin receptors on bronchial smooth muscle cells. This interaction inhibits the binding of acetylcholine to the end of parasympathetic nerves, leading to bronchial smooth muscle relaxation. This effect helps prevent bronchial spasms, resulting in stabilized respiratory rates for patients [10]. In addition, tiotropium bromide can not only block M receptors, but also M1, M2, and M3 receptors. Tiotropium bromide effectively controls bronchial smooth muscle tension, leading to bronchial dilation and improved ventilation function. Its effect is more long-lasting, and the dosage required is relatively low, thus reducing the incidence of adverse drug reactions [11].

In COPD patients, airway damage and irritation are common, elevating the risk of airway remodeling during the recovery phase. Swift improvement of lung function is crucial for disease control and the regulation of respiratory system function [12]. Although budesonide and formoterol can improve lung function and stabilize vital signs, it is not very effective in restoring the respiratory system and lung function. M3 receptors are primarily located in the submucosal glands of the human airway. Stimulation of M3 receptors promotes mucus secretion and smooth muscle contraction, potentially alleviating asthma symptoms [13]. Tiotropium bromide's effect lasts for more than 24 hours after administration, helping to maintain open airways for around 24 hours. This contributes to reduced lung hyperventilation and a high level of safety [14]. Our study demonstrated that combining tiotropium bromide with budesonide and formoterol is more effective in treating COPD compared to using budesonide and formoterol alone. This is evident in the improved arterial blood gas and pulmonary function indicators along with a high level of safety. The combination therapy harnesses complementary and synergistic effects, addressing the limitations of individual drug use and yielding a more favorable outcome [15].

5. Conclusion

In short, inhalation of budesonide and formoterol combined with tiotropium bromide is a safe and effective treatment for COPD. It can also effectively improve arterial blood gas and lung function.

Disclosure statement

The authors declares no conflict of interest.

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