

Clinical Efficacy Analysis of Tiotropium Bromide Combined with Budesonide and Formoterol Inhalation in Treating COPD

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Abstract: *Objective:* To analyze the clinical efficacy of tiotropium bromide (TB) combined with budesonide formoterol (BUD/FM) inhalation in treating chronic obstructive pulmonary disease (COPD). *Methods:* 62 COPD patients admitted to the hospital between June 2020 and December 2022 were selected as samples for this study. The patients were divided into a combination group and a conventional group using the random number table method, with 31 cases in each group. The patients in the combination group were treated with TB combined with BUD/FM inhalation, whereas the patients in the conventional group were treated with BUD/FM inhalation only. The treatment efficacy and changes in lung function indicators of both groups were compared. *Results:* The total efficacy of treatment in the combined group was higher than that in the conventional group, and the difference was statistically significant ($P < 0.05$). Before treatment, there was no difference in pulmonary function indicators between the two groups ($P > 0.05$). After three months of treatment, all lung function indicators of the combined group were higher than those of the conventional group, and the difference was statistically significant ($P < 0.05$). *Conclusion:* Combining TB with BUD/FM inhalation therapy increases the efficacy of treatment for patients with COPD. Besides, it also improves lung function and leads to a better prognosis.

Keywords: Tiotropium bromide; Budesonide formoterol; Inhalation therapy; Chronic obstructive pulmonary disease

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1. Introduction

Chronic obstructive pulmonary disease (COPD) is a relatively common respiratory disease. COPD is characterized by airflow restriction, and symptoms include cough, wheezing, and dyspnea ^[1]. Further progression of the disease may lead to severe complications such as respiratory failure or pulmonary heart disease, thus early and symptomatic treatment is essential. This disease is usually treated with drug inhalation therapy, and β_2 adrenoceptor (β_2 -AR) agonists and glucocorticoids (GC) are the commonly used drugs ^[2]. BUD/FM contains budesonide (BUD) and formoterol fumarate (FM), which can reduce airway inflammation and clear airway restrictions. When used with TB, they can improve the contraction rhythm of bronchial smooth muscles, which significantly reduces airway resistance and restores lung function ^[3]. In this study, we selected

62 COPD patients to analyze the therapeutic effect of TB combined with BUD/FM.

2. Materials and methods

2.1. General information

The study was carried out from June 2020 to December 2022, and a total of 62 COPD patients treated in the hospital were included. The patients were divided into a combination group and a conventional group using the random number table method, with 31 cases in each group. The combination group consisted of 18 males and 13 females, aged between 36 and 77 years old, with a mean of 52.32 ± 1.97 years. The course of disease spanned from 5 months to 5 years, with an average of 2.05 ± 0.75 years. On the other hand, the conventional group consisted of 17 males and 14 females, aged 35 to 74 years old, with a mean of 52.15 ± 1.92 years. The course of disease spanned from 6 months to 5 years, with an average of 2.18 ± 0.67 years. There were no significant differences in the baseline data between the two groups ($P > 0.05$).

Inclusion criteria: Persistent airflow limitation was found through pulmonary function tests, that is, forced expiratory volume in 1 second/forced vital capacity (FEV_1/FVC) value of $< 70\%$; over 18 and less than 80 years of age; complete clinical data; the patient and their families were fully informed about this study and signed the informed consent form.

Exclusion criteria: those who had received treatment with GC or antihistamines in the past month, presence of organic lesions, gastrointestinal ulcers, thyroid disease, immune system disease, other pulmonary diseases such as tuberculosis or asthma, or mental disorders. Those who were allergic to the drugs in this study were also excluded.

2.2. Method

The primary therapies for the two groups of patients were the same, such as low-flow oxygen inhalation (oxygen flow set at 1–2 L/min), phlegm reduction, cough relieving, water-electrolyte and pH imbalance treatment, and asthma relief. The conventional group underwent BUD/FM inhalation treatment (produced by AstraZeneca AB, national drug approval number: H20090772): 160 μg /4.5 μg per inhalation, one inhalation each time, two times a day (once in the morning and once in the evening) One course of treatment lasted for a month, and the treatment was performed for three months. The combination group was given TB treatment in addition to conventional treatment. The TB was supplied by Zhejiang Xianju Pharmaceutical, with the national drug approval number of H20090279. The drug was administered as follows: 18 μg per inhalation, one inhalation each time (once a day at noon). One course of treatment lasted for a month, and the treatment was performed for three months.

2.3. Observation indicators

2.3.1. The total effective rate of treatment

Markedly effective: Disappearance of symptoms like cough and asthma, no murmurs in the lungs, and normal pulmonary function. Effective: Improvement in symptoms and pulmonary function with slight murmurs in the lungs and normal. Ineffective: no improvement of symptoms and pulmonary function and presence of lung murmurs. Total efficacy (%) = markedly effective (%) + effective (%).

2.3.2. Pulmonary function indicators

The patients' FEV_1 , FVC, FEV_1/FVC , maximum respiratory flow rate (PEF), and respiratory interruption flow rate (MMEF) were measured and recorded one day before treatment and 3 months after treatment.

2.4. Statistical analysis

The data were processed using SPSS 28.0. The measurement values were compared using a *t*-test, while the count data were compared using a χ^2 -test. Statistical significance was indicated by $P < 0.05$.

3. Results

3.1. Total efficacy

The total efficacy of the treatment in the combination group was higher than that in the conventional group, and the difference was statistically significant ($P < 0.05$).

Table 1. Comparison of the total effective rate between the two groups of patients [n/%]

Group	Number of cases	Markedly effective	Effective	Ineffective	Total efficacy
Combination group	31	18 (58.06)	11 (35.48)	2 (6.45)	93.55 (29/31)
Conventional group	31	12 (38.71)	10 (32.26)	9 (29.03)	70.97 (22/31)
χ^2	-	-	-	-	5.415
<i>P</i>	-	-	-	-	0.020

3.2. Pulmonary function indicators

There was no difference in lung function indicators between the two groups before treatment ($P > 0.05$). After three months of treatment, the pulmonary function indicators of the combined group were better than those of the conventional group, and the difference was statistically significant ($P < 0.05$).

Table 2. Comparison of pulmonary function indicators between the two groups of patients (mean \pm standard deviation)

Group	Number of cases	FEV ₁ (L)		FVC (L)		FEV ₁ /FVC (%)		PEF (L/s)		MMEF (L/s)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Combination group	31	1.31 \pm 0.45	1.72 \pm 0.51	2.35 \pm 0.61	2.79 \pm 0.41	53.26 \pm 4.81	78.95 \pm 6.74	2.12 \pm 0.45	5.79 \pm 0.53	1.08 \pm 0.32	2.98 \pm 0.52
Conventional group	31	1.33 \pm 0.41	1.38 \pm 0.42	2.34 \pm 0.71	2.51 \pm 0.45	53.22 \pm 4.76	63.59 \pm 5.37	2.14 \pm 0.43	4.48 \pm 0.51	1.09 \pm 0.34	1.65 \pm 0.47
<i>t</i>	-	0.183	2.865	0.059	2.561	0.033	9.924	0.179	9.916	0.119	10.565
<i>P</i>	-	0.855	0.006	0.953	0.013	0.974	0.000	0.859	0.000	0.905	0.000

4. Discussion

COPD is a respiratory disease characterized by progressive and long-term airflow limitation. Its pathogenesis is relatively complex. (1) Inflammatory reaction: Smoking, and air pollution stimulate the respiratory mucosa, leading to inflammatory reactions and increased respiratory tract inflammation. The excessive secretion of mucus leads to the narrowing of the airway^[4]. (2) Airway remodeling: Long-term inflammatory response will lead to the thickening of the airway wall, smooth muscle hyperplasia, and the narrowing of the airway lumen, leading to symptoms such as difficulty breathing or wheezing. (3) Destruction of elastic fibers: The damage of elastic fibers in the lung tissue weakens the elasticity of the lung tissue, leading to emphysema and therefore COPD^[5]. This disease is often managed with low-flow oxygen therapy, measures to reduce phlegm and cough relief. These interventions help maintain adequate blood oxygen levels, enhance the function of the respiratory and central systems, clear respiratory mucus, and alleviate airway inflammation. As a result, they effectively

improve the symptoms of the disease. However, the above treatment methods are challenging to treat COPD in a targeted and efficient manner and have limitations. They need to be combined with other therapeutic drugs ^[6]. To this end, this study uses TB combined with BUD/FM to treat patients with COPD and analyzes its therapeutic effects and advantages.

The results showed that the total effective rate of treatment in the combined group was higher than that of the conventional group. This result is consistent with a study in which two groups of patients were administered nutritional support, antiasthmatic, and antispasmodic treatments along with conventional therapies; the control group received TB treatment alone, while the observation group received a combination of TB and BUD/FM treatment. The efficacy of the treatment in the observation group was 95%, which was higher than that of the control group (79.5%) ^[7]. Therefore, it is clear that TB combined with BUD/FM is more effective than BUD/FM alone in treating COPD. This can be attributed to a few reasons. (1) The synergistic effect of different pharmacological mechanisms: TB is an anticholinergic drug that can inhibit the action of acetylcholine, thereby expanding the airway and reducing the degree of airway stenosis ^[8]. BUD/FM consists of a long-acting β_2 -AR agonist and steroid that can expand airways and inhibit inflammatory reactions, thus improving respiratory function. The two drugs can produce synergistic effects through different pharmacological pathways, thereby comprehensively improving the patient's respiratory symptoms and lung function ^[9]. (2) Comprehensive pathophysiological effects: COPD is affected by multiple factors. TB combined with BUD/FM can act on different pathophysiological links at the same time, thereby comprehensively improving airway patency and promoting mucus clearance, ultimately reducing symptoms such as dyspnea, cough, and increased sputum ^[10,11]. (3) Long-lasting effect: TB and BUD/FM are long-acting therapeutic drugs. The dose of the drug administered by inhalation is small, the drug concentration at the lesion site is high, so the drug effect lasts longer. Therefore, the combination of the drugs can achieve an all-around treatment effect – reducing respiratory symptoms during the day, maintaining airway patency at night, and improving sleep quality, leading to an improvement in the quality of life ^[12]. (4) Flexibility of treatment: COPD patients have different conditions and symptoms. The dosage of TB and BUD/FM can be adjusted according to the patient's condition, making the treatment extremely effective ^[13]. In this study, all lung function indicators after treatment in the combination group were higher than those in the conventional group. This result is consistent with the results of a similar study in which these two treatment methods were compared. The study also showed that FVC, FEV₁, and FEV₁/FVC of patients who received BUD/FM combined with TB were higher than those who received BUD/FM alone. Therefore, it is clear that combining the two drugs can improve the patients' lung function. There are several reasons that contributed to this outcome. (1) Expanding the airway: TB has a strong inhibitory effect on acetylcholine, which can expand the airway smooth muscle, and improve the patient's expiratory flow rate, facilitating a smoother flow of gas through the airways. This effect then leads to an improvement in the lung function indicators. (2) Reducing airway inflammation: BUD/FM can expand airway smooth muscles and relieve airway spasms, thereby clearing airway obstruction and improving lung function indicators like FEV₁/FVC. (3) Synergistic effect: TB and BUD/FM have anticholinergic and anti-inflammatory mechanisms, respectively. When used in combination, these drugs synergistically enhance their therapeutic impact, leading to a significant improvement in lung function indicators ^[15]. (4) Advantages of inhalation therapy: Both drugs are administered through inhalation, which allows the drug to directly enter the airways and the lung tissue. This method ensures a consistent and sustained therapeutic effect, leading to an improvement in lung function.

However, it should be noted that patients with COPD are usually older and often have other health issues like high blood pressure and diabetes. Some may also have special situations, like allergies to certain medications or a history of surgeries. Therefore, it is necessary to comprehensively evaluate the patient's

disease status, medical history, and other essential information. Furthermore, the dosage, administration, and course of treatment should be determined based on the patient's condition to achieve the maximum effect of the treatment.

5. Conclusion

TB combined with BUD/FM has a significant therapeutic effect on patients with COPD. Besides, it can effectively restore lung function and help achieve better treatment prognosis.

Disclosure statement

The authors declare no conflict of interest.

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