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# Effect of Fudosteine Combined with Bisoprolol on Blood Gas Indexes and Inflammatory Factors in Patients with Stable Chronic Obstructive Pulmonary Disease

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**Abstract**

**Objective:** To explore the clinical efficacy of fordostane combined with bisoprolol in the treatment of patients with stable chronic obstructive pulmonary disease (COPD), and their effects on blood gas indexes and inflammatory factors. **Methods:** 104 patients with stable COPD admitted to our hospital from July 2018 to June 2020 were divided into a control group (n = 52) and an observation group (n = 52) by random number table method. Besides conventional treatment in both groups, control group patients were given bisoprolol and observation group patients received fudosteine combined with Bisoprolol. Clinical efficacy, blood gas indexes, serum indexes and adverse reaction incidence of patients in two groups were compared before and after treatment. **Results:** The total effective rate in observation group patients was higher than that in control group patients. After treatment, levels of arterial partial pressure of oxygen ($PaCO_2$), serum amyloid A (SAA), interleukin-6 (IL-6) and malondialdehyde (MDA) in patients in both groups were increased, and the levels in the observation group were higher than those in the control group. Arterial partial pressure of oxygen ($PaCO_2$), serum amyloid A (SAA), interleukin-6 (IL-6) and malondialdehyde (MDA) levels in both groups of patients were declined after treatment and those in the observation group were lower than those in the control group. The comparison of adverse reaction incidence between patients in two groups was not statistically significant. **Conclusion:** The clinical efficacy of fordostane with bisoprolol in the treatment of patients with stable COPD is significant, as it improves blood gas index levels and attenuates body inflammatory response.

## 1 Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a respiratory disease characterised by recurrent respiratory symptoms and persistent airflow obstruction. Patients with COPD suffer from chronic cough, sputum and dyspnoea, which brings great physical and mental pain to patients and seriously affects the quality of life of patients [1,2]. Clinically, COPD is classified into stable and exacerbation phases and patients in the stable phase are often treated with bronchodilators, anti-infectives and expectorants. Studies have shown that COPD patients are in a state of chronic hypoxia, which leads to pulmonary artery hypoxia, and further induces myocardial injury [3]. Bisoprolol, a selective $\beta_1$ receptor blocker, is frequently adopted in the treatment of cardiovascular diseases such as heart failure and coronary artery disease. Bisoprolol can reduce the myocardial burden and decrease myocardial oxygen consumption, and functions as a therapeutic approach for the treatment of COPD [4]. In addition, as patients with stable COPD are chronically hypersecretory, expectorant drugs are widely used in COPD treatment. Fudosteine is a new type of expectorant with the ability to lower sputum viscosity and promote airway plasma secretion [5]. This study investigates the clinical efficacy of fudosteine combined with bisoprolol in the treatment of patients with stable COPD and their effects on blood gas indexes and inflammatory factors, with an aim to explore an effective method for the treatment of stable COPD.

## 2 Materials and methods

### 2.1 Clinical data

A random number table method was adopted to divide 104 patients with stable COPD admitted into our hospital from July 2018 to June 2020 into a control group (n = 52) and an observation group (n = 52).

Control group: gender: 28 males and 24 females; age: 52-69 years old, average age: 58.24 ± 6.45 years old; course of disease: 2-9 years, average course of disease: 4.85 ± 1.06 years; body mass index (BMI): 18.46-24.22 kg/m$^2$ , average BMI: 21.16 ± 3.55 kg/m$^2$.

Observation group: gender: 25 males and 27 females; age: 55-71 years old, average age: 57.48 ± 7.04 years old; course of disease: 2-8 years, average course of disease: 5.01 ± 1.12 years; BMI: 18.73-24.58 kg/m$^2$ , average BMI: 21.04 ± 4.02 kg/m$^2$.

General data of patients in two groups including gender, age, course of the disease and BMI were not statistically significant and comparable ($p > 0.05$). The study was approved by the Ethics Committee of our hospital and the written informed consent was signed by all study participants.

### 2.2 Inclusion and exclusion criteria

Inclusion criteria: Patients meet the diagnostic criteria for COPD in the *Guidelines for the diagnosis and management of chronic obstructive pulmonary disease* [6] and are diagnosed with stable COPD; Patients with clear consciousness and are capable of normal communication.

Exclusion criteria: Patients with psychiatric disorders; Patients who are allergic to fudosteine or bisoprolol; Patients with bronchial asthma or bronchiectasis; Patients with malignancy or immune disorders.

### 2.3 Treatments

Patients in both groups were given a conventional treatment of calming asthma, dispelling expectoration and anti-infection upon admission.

#### 2.3.1 Control group

Patients in the control group were administered with Bisoprolol tablets (Easton Biopharmaceuticals, Chengdu, China, Guodianzhi H20083008,

Specification: 5 mg × 18 tablets) orally, 5 mg/time, once/d, for consecutive 3 months.

### 2.3.2 Observation group

Patients in the observation group orally taken fordostane tablets (Disha Pharmaceutical, Weihai, China, State medical permitment number: H20110037, Specification: 0.2 g × 12 tablets) on top of patients in the control group, 0.4 g/time, 3 times/d for consecutive 3 months.

### 2.4 Observation indexes

(1) Clinical efficacy: The clinical efficacy of the two groups of patients was assessed with reference to the efficacy criteria in the *Internal Medicine* [7]. Obvious effect: clinical symptoms and lung wet rales disappeared, sputum amount declined and no dyspnea occurred; Effective: clinical symptoms and lung wet rales were improved, sputum amount reduced and dyspnea occurred occasionally; Ineffective: no change in clinical symptoms and lung wet rales and dyspnea occurred. Total efficiency of treatment = (effective + obvious effect) cases/total cases × 100%.

(2) Blood gas indexes: Arterial oxygen saturation ($SaO_2$) and arterial partial pressure of carbon dioxide ($PaCO_2$) were detected in patients in both groups using a blood gas analyzer (Radiometer, Shanghai, China).

(3) Serum indexes: Fasting venous blood was collected from both groups of patients before and after treatment. Levels of serum amyloid A (SAA) and interleukin-6 (IL-6) in patients in two groups were assessed by enzyme-linked immunosorbent assay (ELISA), while Malondialdehyde (MDA) level was measured by colourimetric assay.

(4) Adverse reactions: Adverse reactions including nausea, vomiting, skin rash, dizziness and tinnitus in patients in both groups were observed.

### 2.5 Statistical analysis

Statistical analysis was performed using the SPSS 20.0. software, count data were compared using the $x^2$ test and results were presented as the mean ± standard deviation. Differences between the two groups were assessed with an independent sample *t*-test and statistical significance was established at $p < 0.05$.

## 3 Results

### 3.1 Comparison of clinical efficacy between patients in two groups

The total effective rate of treatment for patients in the control group and patients in the observation group were 73.08% and 92.31% respectively, and that in the observation group was remarkably higher than that in the control group (Table 1, $p < 0.05$).

**Table 1** Comparison of clinical efficacy of patients [cases (%)].

| Group | Cases | Obvious effect | Effective | Ineffective | Total effective rate |
|---|---|---|---|---|---|
| Control group | 52 | 21 (40.38) | 17 (32.69) | 14 (26.92) | 38 (73.08) |
| Observation group | 52 | 32 (61.54) | 16 (30.77) | 4 (7.69) | 48 (92.31) |
| $X^2$ | | | | | 6.718 |
| *p* | | | | | 0.010 |

### 3.2 Comparison of blood gas indexes between patients in two groups

No statistical significance was observed in the comparison of $SaO_2$ and $PaCO_2$ levels between patients in the two groups before treatment ($p > 0.05$). After treatment, the $SaO_2$ level in patients in both groups was upregulated with that in the observation group higher than that in the control group ($p < 0.05$).

$PaCO_2$ level was diminished due to treatment in patients in both groups and lower $PaCO_2$ level was observed in patients in the observation group, as compared with the control group (Table 2, $p < 0.05$).

### 3.3 Comparison of serum indexes between patients in two groups

Before treatment, there was no statistically significant difference in the levels of SAA, IL-6 and MDA between patients in the two groups ($p > 0.05$). However, after treatment, the levels of SAA, IL-6 and MDA all dropped in patients in both groups ($p < 0.05$), and those in the observation group were lower than those in the control group (Table 3, $p < 0.05$).

### 3.4 Comparison of adverse reactions between patients in two groups

No significant difference was observed in the incidence of adverse reactions between patients in the control group and the observation group (Table 4, $p > 0.05$).

**Table 2** Comparison of blood gas indexes of patients in two groups (mean ± standard deviation).

| Group | Cases | $SaO_2$ (%) | | $PaCO_2$ (mmHg) | |
|---|---|---|---|---|---|
| | | Before treatment | After treatment | Before treatment | After treatment |
| Control group | 52 | 83.44 ± 4.62 | 90.74 ± 5.57 * | 65.94 ± 8.08 | 52.73 ± 6.14 * |
| Observation group | 52 | 84.13 ± 6.20 | 96.87 ± 6.18 * | 66.39 ± 9.35 | 46.15 ± 5.53 * |
| *t* | | 0.644 | 5.313 | 0.263 | 5.742 |
| *p* | | 0.521 | 0.000 | 0.793 | 0.000 |

* vs. before treatment, * $p < 0.05$.

**Table 3** Comparison of serum indexes between patients in two groups (mean ± standard deviation).

| Group | Cases | SAA (mg/L) | | IL-6 (ng/L) | | MDA (mmol/L) | |
|---|---|---|---|---|---|---|---|
| | | Before treatment | After treatment | Before treatment | After treatment | Before treatment | After treatment |
| Control group | 52 | 53.57 ± 6.53 | 48.76 ± 5.66 * | 35.34 ± 5.08 | 27.95 ± 2.12 * | 6.48 ± 1.16 | 4.08 ± 0.54 * |
| Observation group | 52 | 53.05 ± 8.58 | 37.21 ± 4.64 * | 34.79 ± 4.35 | 22.24 ± 2.63 * | 6.82 ± 1.29 | 2.64 ± 0.35 * |
| *t* | | 0.348 | 11.380 | 0.593 | 12.189 | 1.413 | 16.137 |
| *p* | | 0.729 | 0.000 | 0.554 | 0.000 | 0.161 | 0.000 |

* vs. before treatment, * $p < 0.05$.

**Table 4** Comparison of adverse reactions between patients in two groups [cases (%)].

| Group | Cases | Nausea and vomiting | Rash | Dizziness | Tinnitus | Incidence of adverse reactions |
|---|---|---|---|---|---|---|
| Control group | 52 | 2 (1.92) | 1 (1.92) | 2 (3.85) | 0 (0.00) | 5 (9.62) |
| Observation group | 52 | 3 (5.77) | 1 (1.92) | 2 (3.85) | 1 (1.92) | 6 (11.54) |
| $X^2$ | | | | | | 0.102 |
| *p* | | | | | | 0.750 |

## 4 Discussion

COPD in the stable phrase is a respiratory disease with high morbidity and mortality rates. Patients often suffer from dyspnoea and cough, which brings huge pain and economic burden to patients. Therefore, the treatment of patients with stable COPD should focus on attenuating clinical symptoms and improving the quality of life of patients. Reasonable and effective methods should be applied for stable COPD treatment

and early recovery of patients. Bisoprolol has been adopted in the treatment of stable COPD as it helps to improve lung function and reduce the release of inflammatory factors in patients. The treatment of Fudosteine combined with tiotropium bromide for patients with stable COPD reduces the viscosity of sputum and facilitates the expulsion of sputum, thereby reducing the clinical symptoms of patients [8,9]. In this study, patients in both groups were given common basic treatment. Additionally, patients in the control group and patients in the observation group were treated with bisoprolol and fudosteine combined with bisoprolol respectively. The results showed that the total effective rate of treatment in patients in the observation group was significantly higher than that in the control group, indicating that the efficacy of co-administration enjoys better therapeutic effects when treating patients with stable COPD.

Patients with stable COPD suffer from long-term hypoxia and carbon dioxide retention, which leads to pulmonary injury and pulmonary ventilation dysfunction [10]. The blood gas index levels of $SaO_2$ and $PaCO_2$ can objectively and timely reflect the pulmonary ventilation and respiratory function of the body. The present study found boosted $SaO_2$ level and declined $PaCO_2$ level in both groups after patients received corresponding treatment. Moreover, higher $SaO_2$ level and lower $PaCO_2$ level were observed in patients in the observation group, as compared to those in the control group. These findings indicate that fudosteine with bisoprolol therapy helps to improve blood gas index levels of patients with stable COPD. This is due to the fact that bisoprolol can increase blood oxygenation, reduce carbon dioxide retention, alleviate lung injury and thus improve respiratory function. Meanwhile, bisoprolol is able to reduce airway spasms by selectively lowering the affinity of bronchial smooth muscle and capillaries, improving pulmonary ventilation as well as allowing smooth breathing [11]. In addition, fudosteine functions as a phlegmolytic drug to facilitate the release of sputum-excluding proteins, induce the breakage of disulfide bonds of mucins in bronchial secretions, alter the composition and rheological properties of secretions, decrease sputum viscosity, stimulate sputum expulsion, improve mucociliary clearance, alleviate symptoms such as cough and dyspnoea, and thereby improve respiratory function.

Stable COPD has been proven to be a chronic airway inflammatory disease [12]. SAA, an immunomodulatory apolipoprotein, can trigger neutrophils, macrophages and other cytokines to increase the release of inflammatory factors and exacerbate the inflammatory response of the body [13]. IL-6 is an essential pro-inflammatory cytokine that induces the body's inflammatory response. MDA is an oxidative stress product, and its level reflects the degree of oxidative stress in the body [14]. The results of this study revealed that the treatment of bisoprolol/fudosteine combined with bisoprolol resulted in a decline in SAA, IL-6 and MDA levels of patients in both groups. Of note, these levels in the observation group were lower than those in the control group. These suggest that fudosteine combined with bisoprolol treatment can reduce the inflammatory response of patients with stable COPD. Meng et al. [11] found that bisoprolol possesses an inhibitory effect on the inflammatory response of the body. This might be explained by bisoprolol's effects on improving hypoxemia and hypercapnia, attenuating hypoxia and reducing tissue damage in the body. Fudosteine also contributes to the alleviation of the inflammatory response by reducing sputum viscosity, accelerating sputum expulsion and mitigating airway damage. Besides, fudosteine can also relieve inflammation and oxidative stress in the body via scavenging free radicals to activate α 1-antitrypsin and further suppress pulmonary elastin activity as well as reduce lung injury [15]. In addition, the present study found no significant difference in the

incidence of adverse reactions between patients in the control group and the observation group, which suggests fudosteine combined with bisoprolol is a safe therapy in the treatment of patients with stable COPD.

In conclusion, the combination of fodosteine and bisoprolol has shown significant efficacy in treating patients with stable COPD, improving blood gas index levels and reducing the inflammatory response of the body.

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Not applicable.

**Conflicts of Interest**

The authors declare no conflicts of interest.

**Author Contributions**

Conceptualization, J.G.; Data curation, J.Z.; Formal analysis, J.G.; Methodology, J.Z.; Writing-original draft, J.G.; Writing-review and editing, J.Z. All authors have read and agreed to the published version of the manuscript.

**Ethics Approval and Consent to Participate**

The study was approved by the Ethics Committee of our hospital and the written informed consent was signed by all study participants.

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**Availability of Data and Materials**

The data presented in this study are available on request from the corresponding author.

**Supplementary Materials**

Not applicable.

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