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CLINICAL STUDY

Effect of Bufei granule on stable chronic obstructive pulmonary disease: a randomized, double blinded, placebo-controlled, and multicenter clinical study

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Abstract

OBJECTIVE: To study the therapeutic effect Bufei granule, which is a traditional Chinese drug that can enhance the immune function of the lung, on patients with stable chronic obstructive pulmonary disease (COPD).

METHODS: This is a randomized, double blinded, placebo-controlled, and multicenter clinical study. Three medical centers in Tianjin, China, participated in the trial. A total of 140 patients with stable COPD were enrolled and randomized into two groups, with 70 patients in each. The treatment group was treated with Bufei granule, while the control group received Bufei placebo. The pharmacological treatment lasted for 12 weeks from the date of enrollment. Then, the indexes of patients were observed. Data were analyzed to study the effect of Bufei granule, with the frequency of acute exacerbation as the primary outcome. Traditional Chinese Medicine syndromes, Modified British Medical Research Council dyspnea scale score, St. George's respiratory questionnaire scores, pulmonary function, and serum inflammatory marker levels [including interleukin-6 (IL-6), interleukin-8, tumor necrosis factor-α, and transformation growth factor-β1] were the secondary outcomes.

RESULTS: During the 12-week treatment, treatment and control groups had no adverse reactions. The analysis of the indexes obtained from all patients showed that the therapeutic effect in the treatment group was significantly better than that in the control group because most of the similar probabilities of primary and secondary outcomes were less than 0.05, except for the level of IL-6.

CONCLUSION: Bufei granule can treat patients with stable COPD by lowering the frequency of acute exacerbation, improving the quality of life, and alleviating the severity of inflammation.

Key words: Bufei Granule; Pulmonary disease, chronic obstructive; Stable stage; Randomized controlled trial

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) af-

flicts 10% of the global population over the age of 40 years[1] and will be the third leading cause of mortality by 2020.[2] COPD is defined as a preventable and treatable respiratory disease characterized by partially reversible chronic airflow obstruction. This obstruction is progressive and characterized by inflammation of the lungs in response to inhalation of noxious particles or toxic gases, especially cigarette smoke.[3] Although COPD is a leading cause of global morbidity and mortality, current therapeutic strategies have shown little success in reliving inflammation and slowing progression. For example, β_2-adrenergic agonists, which benefit asthma by alleviating reversible airflow limitation, have little effect on the irreversible obstruction observed in COPD. Moreover, glucocorticosteroids, another main treatment for COPD, was proven to be largely insensitive to COPD-associated inflammation.[4]

Experts in Traditional Chinese Medicine (TCM) have studied COPD for several decades. Many studies found that traditional Chinese drugs did have positive effects in treating patients with stable COPD.[5-7] However, most studies lack reasonably designed research schemes, all of which were either performed at only one medical center or not placebo-controlled. In this paper, we used Bufei granule, which is a traditional Chinese drug that enhances the lung's immune function, to study the therapeutic effect of TCM in treating patients with stable COPD.

METHODS

Design

This is a randomized and double blinded, placebo-controlled, and multicenter clinical study. The study was conducted in three medical centers (The Second Affiliated Hospital of Tianjin University of TCM, Tianjin Chest Hospital, and Tianjin Haihe Hospital), which are all AAA hospitals in Tianjin, China. The study lasted from May 1st, 2008 to May 31st, 2011.

Ethics

The trial was approved by the Ethics Committee of Tianjin University of TCM, and adhered to the principles of the Declaration of Helsinki. The protocol and its informed consent form were judged by the Committee to be ethically and scientifically satisfactory to the aims. Written informed consent was obtained from all participants or their representatives before enrolling.

Participants

According to the inclusion and exclusion criteria, 140 stable COPD patients were enrolled (50 patients from the Second Affiliated Hospital of Tianjin University of TCM, 50 patients from Tianjin Chest Hospital, and 40 patients from Tianjin Haihe Hospital).

Inclusion criteria: (a) COPD patients who were diagnosed according to the diagnosis criteria in global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease reported by Global Initiative for Chronic Obstructive Lung Disease (GOLD);[8] (b) stable COPD patients, with the severity of airflow limitation based on post-bronchodilator forced expiratory volume in one second (FEV_1) from GOLD2 (moderate) to GOLD3 (severe). (Pulmonary function test: FEV_1/forced vital capacity (FVC)%< 70%, 30%≤FEV_1/predicted value (%)≤80%, tested by Pulmonary Function Testing System, Model: MasterScreen PFT, Supplied by CareFusion-Jaeger);[8] (c) COPD patients who were diagnosed as "deficiency of lung, spleen, and kidney accompanied with retention of phlegm and blood stasis" in TCM;[9] (d) aged 40-75 years; (e) completed and submitted the informed consent form.

Exclusion criteria: (a) patients who suffered from other primary pulmonary diseases such as bronchiectasis, tuberculosis, or idiopathic pulmonary fibrosis; (b) allergic constitution or Chinese herb allergies; (c) pregnancy, planning to be pregnant, or lactating; (d) severe hepatic or renal deficiency; (e) severe primary diseases of the heart, brain, digestive system, or hematopoietic system; (f) mental diseases; (g) those who participated in other clinical studies in the past three months; (h) those who used other medicinal interventions regularly to treat stable COPD in the past three months.

Medications

(a) Bufei granule [Produced by Pharmaceutical Centre of the Second Affiliated Hospital of Tianjin University of TCM, Tianjin, China; Production batch number: 200702003, composed of Dangshen (*Radix Codonopsis*), Shudihuang (*Radix Rehmanniae Praeparata*), Shanzhuyu (*Fructus Corni*), Mahuang (*Herba Ephedra Sinica*), and Chenpi (*Pericarpium Citri Reticulatae*), 8 g/bag]; (b) Bufei placebo (Produced by Pharmaceutical Centre of the Second Affiliated Hospital of Tianjin University of TCM, Tianjin, China; composed of 5% crude drug of Bufei granule and 95% starch, 8 g/bag).

Randomization and blindness

Using the stratified block randomization method, according to a predetermined proportion of 1∶1, the 140 stable COPD patients were randomized to the treatment group or the control group, with 70 patients in each group. Staffs not involved in this clinical study were involved in the randomization process. After enrollment in the trial, the participants were given a fixed prescription and received study medications from pharmacy staff according to the enrollment sequence. Both Bufei granule and Bufei placebo had the same appearance, shape, color, and packaging, so the research physicians and participants were not able to know the difference.

Treatment

During the trial, patients in the treatment group were