

Analysis on the adjuvant treatment of Jianpi Xiaoyu Recipe on the improvement of clinical symptoms and lung function in patients with stable Chronic Obstructive Pulmonary Disease

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Keywords

Jianpi Xiaoyu recipe, Stable chronic obstructive pulmonary disease, Lung function, Spleen and lung deficiency

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Abstract

Background To determine the efficacy of Jianpi Xiaoyu Recipe in patients with chronic obstructive pulmonary disease (COPD), we performed the analysis on its effects on clinical symptoms and lung function. **Methods:** 80 patients with COPD from January 2017 to January 2019 were divided into research (n=40) and control (n=40) groups by the random number table method. Patients in the control group were given routine treatment (bronchodilation, expectorant, anti-asthmatic therapies), and those of the research group received Jianpi Xiaoyu Recipe on the basis of control group. The scores for COPD assessment test (CAT), life quality, 6-minute walking test, clinical symptoms (cough, sputum, dyspnea, and suffocation), and lung function [forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), one second rate (FEV1 / FVC)] were measured, in addition to serum lipid peroxide (LPO), superoxide dismutase (SOD) activity. **Results:** After treatment, the scores for CAT, life quality and various clinical symptom of patients in the research group were significantly lower than those in the control group, and the distance of 6-minute walking test was significantly longer than that in the control group. After treatment, the levels of FVC, FEV1, FEV1 / FVC and serum SOD activity in patients of the research group were higher yet serum LPO level was lower than that of the control group. **Conclusion:** Jianpi Xiaoyu Recipe has a significant clinical effect on patients with stable COPD, which reduces clinical symptoms, improves the exercise endurance and life quality of patients, and alleviates lung dysfunction and oxidative stress response..



1. Introduction

Characterized by the progressive continuous limitation on airflow accompanied with the inflammation within the airway, chronic obstructive pulmonary disease (COPD) is a clinically prevalent airway disease associated with high rates of disability and mortality [1]. The clinical manifestations of patients with stable COPD include persistent cough, sputum, dyspnea and other symptoms, as well as dysfunctional motor activity to a certain extent, decreased lung function, and even muscle atrophy and cardiopulmonary failure, which seriously endanger the life quality and safety of patients [2]. At present, the clinical treatment of COPD is mainly based on bronchodilator, oral hormone and anti-inflammatory and expectorant drugs. However, COPD is a chronic long-term disease, and long-term use of western medicine may result in the drug resistance within the body, leading to diminished therapeutic effect, in addition to the strong toxic and side effects. Therefore, it is of great significance to seek safer and more effective therapeutic methods to improve the clinical symptoms and life quality of patients with COPD.

According to the beliefs of traditional Chinese medicine (TCM), the basic pathogenesis of COPD lies in the blockage of phlegm and the stagnation of Qi in the lung [3]. Besides, the recurrence and prolongation of pulmonary disease can result in the deficiency of the lung and the injury to the spleen, causing the obstruction of Qi and blood flow within the body, the blockage of the meridians and the diffusion of the disease. As such, the main principle for the treatment of COPD using TCM is based on eliminating the blood stasis, clearing the collaterals, warming the lung, resolving the phlegm, strengthening the spleen, removing the stagnation and benefiting the Qi [4]. TCMs are commonly applied in the treatment of COPD, such as antipyretic drugs, anticough medications, and asthma drugs. [5]. For example, lianhua-qingwen capsule, flavonoids and Bufei granule are used for COPD treatment [6-8].

Here, it's the aim of our study to investigate the clinical efficacy of the Jianpi Xiaoyu recipe in the treatment on patients with moderate COPD and to

analyze its effects on the clinical symptoms score, pulmonary function and oxidative stress in order to provide a reference for the adjuvant treatment of COPD using TCM.

2. Material and methods

2.1 Ethics statement

The conduction of our study has been approved by the Ethics Committee of our hospital, and all enrolled patients have also signed the written informed consent as well.

2.2 Subjects

80 patients with stable COPD diagnosed and treated in our hospital from January 2017 to January 2019 were selected and divided into study and control groups according to the random number table method, with 40 cases in each group. Study group included 26 males and 14 females with age of 57-80 (mean age: 67.53 ± 8.46) and course of disease of 6-23 years (mean course of disease: 12.40 ± 5.23 years), whereas the control group consisted of 24 males and 16 females, with age of 60-80 (mean age: 68.54 ± 9.21) and course of disease of 5-25 years (mean course of disease: 11.95 ± 6.03 years). There was no statistically significant difference between the two groups in terms of gender, age, and disease duration ($P > 0.05$) yet the data were comparable.

All patients were conformed with the following inclusion criteria: 1) the criteria for Western medicine corresponded with those in the "Guideline for primary care of chronic obstructive pulmonary disease (2018)" [9] designated by the Respiratory Disease Branch of Chinese Medical Association, including the symptoms of cough, sputum, and chest distress, with a duration > 2 weeks, score for the questionnaire of Modified Medical Research Council (mMRC) ≥ 2 , grade 2 or 3 of the pulmonary function grading test, and forced expiratory volume in the first second (FEV1) accounts for 30%-50% of the predicted value; 2) the criteria for TCM were in accordance with those diagnostic criteria for COPD in the "Guiding Principles for Clinical Study of New Chinese Medicines" [10], including the primary symptoms

(cough, sputum, dyspnea, sulking chest, shorted breath, chest pain and palpitations) and the secondary symptoms (easy to catch cold, chills, sweat at night, insomnia, less food-intake, fatigue, dry mouth, yellow face and dullness). COPD was diagnosed when patients met all the primary symptoms and two or more secondary symptoms. 3) those in the stable stage of COPD with duration of disease ≥ 5 years. 4) those with no previous history of mental disability and could communicate normally. 5) those with complete clinical data.

Exclusion criteria: 1) those with severe insufficiency of heart, liver, kidney and other organs. 2) those with pulmonary diseases, like tuberculosis and pulmonary fibrosis. 3) those with deficiency of immune system. 4) those with allergy to the drugs used in our study. 5) those with pregnancy or in lactating period. 6) those who have no capability to look after themselves.

2.3 Treatment regimens

The patients in the control group were given salmeteroticasone aerosol (50 μg /100 μg / press, Glaxo Wellcome Production, France, approval number for National Medical Products Administration (NMPA): H20150324) twice sprays a day for bronchodilation therapy, and were administrated with acetylcysteine tablets (Hainan Zambon Pharmaceutical Co., Ltd., specification: 0.6 g \times 12 tablets, approval number for NMPA: H20080325) for expectorant and anti-asthmatic treatment with one tablet once a day. Corresponding anti-inflammatory and oxygen inhalation measures were given for 21 consecutive days at the same time.

In addition to the control group, the patients in the study group were given Jianpi Xiaoyu recipe once dose per day on the basis of the control group, including 20 g Dang Shen (*Radix Codonopsis*), 15 g Fulin (*Sclerotum Poriae Cocos*), 10 g Bai Zhu (*Rhizoma Atractylodis Macrocephalae*), 10 g Chen Pi (*Pericarpium Citri Reticulatae*), 15 g Chuan Bei Mu (*Bulbus Fritillariae Cirrhosae*), 10 g Fa Ban Xia (*Rhizoma Pinelliae Preparatum*), 10 g Dan Shen (*Radix Salviae Miltiorrhizae*), 20 g Huang Qi (*Radix Astragali*), 6 g Sha Ren (*Fructus Amomi*), 30 g Bai

Hua She She Cao (*Herba Hedyotis Diffusae*), and 6 g Zhi Gan Cao (fried *Radix Glycyrrhizae*). The components were decocted with water every day and the volume of the decoction was adjusted to 400 ml. One dose of decoction was administrated twice in a day and patients received the recipe for 21 days (d) in total.

2.4 Observational index

(1) Clinical efficacy: (a) Before and after treatment, the COPD assessment test (CAT) was introduced to evaluate the severity of COPD, including coughing, the volume of sputum, chest distress and other 8 items, with 0-5 points indicated the severity from mild to severe [11]. Higher total score suggested the higher severity of COPD. (b) St. George's Respiratory Questionnaire (SGRQ) was used for the evaluation of the life quality of patients, which was divided into 50 items, with a total score of 100 [12]. Lower score indicated the fewer influence of COPD on patients and the better life quality. (c) 6-minute walking test: patients were told to walk back and forth in a 30-meter corridor, and stop when there were obvious symptoms of chest distress or dyspnea, with the measurement of the walking distance in 6 minutes.

(2) Clinical symptoms: The clinical symptoms, including cough, sputum, dyspnea, and suffocation, were scored as 0 (no symptoms), 1 (mild symptoms), 2 (moderate symptoms) and 3 (severe symptoms), respectively. Lower score indicated the milder symptoms.

(3) Pulmonary function indices: A pulmonary function detector (Masterscreen PFT System, Jaeger, Germany) was introduced to the detection and calculation of forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), one second rate (FEV1 / FVC).

(4) Serum Lipid peroxide (LPO) and superoxide dismutase (SOD) activities: 5 ml fasting venous blood was isolated from the patients in both group prior to and after the treatment, followed by the harvest of the supernatant via centrifuging at 3000 rpm for 15 minutes. Serum LPO activity was determined using thiobarbituric acid, whereas that of SOD was measured via xanthine oxidase. All detection kits were

ordered from Nanjing Jiancheng Bioengineering Institute and all procedures were repeated strictly following the instructions provided with the kits.

2.5 Statistical analysis

All data were analyzed using SPSS 20.0 (IBM Corporation, Endicott, NY, USA) and expressed as mean ± standard deviation (SD). Statistical significance was determined with Chi-square and compared with *t* test, which was defined when *p*<0.05.

3. Results

3.1. Jianpi Xiaoyu recipe improved clinical

efficacy in patients with COPD

Before treatment, there were no significant differences in the score of both CAT and SGRQ and 6-minute walking distance (*p*>0.05). After treatment, both CAT and SGRQ indices in all patients were significantly decreased in the two groups (*p*<0.05), and those in the study group was significantly lower than the control group (*p*<0.05), according to Table 1. After treatment, 6-minute walking distance in all patients were significantly increased in the two groups (*p*<0.05), and that in the study group was significantly higher than the control group (*p*<0.05), according to Table 1.

Table 1. Comparison on clinical efficacy

Group	Case	CAT score (point)		SGRQ score (point)	
		Before treatment	After treatment	Before treatment	After treatment
Study group	40	28.43±6.41	14.95±4.26*	55.65±12.38	29.12±11.33*
Control group	40	27.95±5.63	18.23±4.85*	56.21±11.85	42.62±13.23*
<i>t</i>		0.356	-3.214	-0.207	-4.902
<i>P</i>		0.723	0.002	0.837	0.000

Group	Case	6-minute walking distance (m)	
		Before treatment	After treatment
Study group	40	382.48±86.27	652.84±76.52*
Control group	40	388.55±90.62	482.61±80.41*
<i>t</i>		-0.306	9.699
<i>P</i>		0.760	0.000

Note: **P*<0.05, vs. Before treatment.

3.2. Jianpi Xiaoyu recipe reduced clinical symptoms in patients with COPD

Based on Table 2, before treatment, there was no significant difference in the scores of clinical symptoms (cough, sputum, dyspnea, and suffocation) between the two groups of patients (*P*>0.05). After treatment, lower scores were evidenced in patients of both group, and those in study group was additionally confirmed to be lower than the control group (*P*<0.05)

3.3. Jianpi Xiaoyu recipe alleviated lung dysfunction in patients with COPD

In Table 3, there was no significant difference concerning the levels of FVC, FEV1 and FEV1/FVC in patients of both groups before treatment. However, after treatment, these levels were increased in the two groups, and these of study group were evidently higher than the control group (*P*<0.05).

3.4. Jianpi Xiaoyu recipe alleviated oxidative stress response in patients with COPD

In Table 4, there was no significant difference concerning the activities of LPO and SOD in the serum patients of both groups. However, after

treatment, the level of LPO was decreased yet that of SOD was increased in the two groups of patients ($P<0.05$), and in study group, the level of LPO was lower yet that of SOD was higher than the control group ($P<0.05$).

Table 2. Comparison on clinical symptoms

Group	Case	Cough		Sputum		Dyspnea	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Study group	40	2.64±0.31	0.94±0.22*	2.71±0.24	1.13±0.27*	2.53±0.43	0.92±0.29*
Control group	40	2.57±0.40	1.74±0.35*	2.68±0.31	1.86±0.31*	2.56±0.38	1.67±0.33*
<i>t</i>		0.875	-12.24	0.484	-11.231	-0.331	-10.797
<i>P</i>		0.384	0.000	0.630	0.000	0.742	0.000

Group	Case	Suffocation	
		Before treatment	After treatment
Study group	40	2.73±0.25	1.05±0.34*
Control group	40	2.70±0.26	1.72±0.43*
<i>t</i>		0.526	-7.730
<i>P</i>		0.600	0.000

Note: * $P<0.05$, vs. Before treatment.

Table 3. Comparison on pulmonary function indices

Group	Case	FVC (L)		FEV1 (L)		FEV1/FVC (%)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Study group	40	2.27±0.34	3.42±0.48*	1.42±0.28	3.02±0.43*	45.25±7.62	72.52±9.12*
Control group	40	2.22±0.41	2.75±0.39*	1.39±0.26	2.25±0.35*	46.23±8.04	60.52±8.64*
<i>t</i>		0.594	6.922	0.497	8.784	-0.560	6.041
<i>P</i>		0.554	0.000	0.621	0.000	0.577	0.000

Note: * $P<0.05$, vs. Before treatment.

Table 4. Comparison on serum LPO and SOD activities

Group	Case	LPO (μmol/L)		SOD (μg/L)	
		Before treatment	After treatment	Before treatment	After treatment
Study group	40	5.52±0.71	2.15±0.45*	148.46±25.84	205.21±20.88*
Control group	40	5.64±0.82	4.42±0.43*	150.25±27.16	172.52±18.63*
<i>t</i>		0.700	-23.066	-0.302	7.388
<i>P</i>		0.486	0.000	0.763	0.000

Note: * $P<0.05$, vs. Before treatment.

4. Discussion

Jianpi Xiaoyu recipe effectively reduces clinical symptoms, improves the exercise endurance and life quality of patients, and alleviates lung dysfunction and oxidative stress response in patients with COPD.

The cause of chronic pulmonary diseases lies in the pulmonary infiltration of those exogenous pathogenic factors like wind, cold, heat and dampness, which results in the shortness of breath, cough and sputum, shallow and short breathing [13, 14]. If left prolonged and uncured, these factors may induce the impediment of the lung by the sputum or dampness [15]. In addition, the lung plays a role in the regulating the circulation and excretion of body fluid, whereas the chronic wheezing or coughing can lead to the lung failure, where the rise of pulmonary Qi indicates the diminished circulation function, and the upward reverse accumulation of moisture thus becomes the sputum, which in turn blocks the breathing and gives rise to the lung distension and chest distress [16]. The five elements and the five organs are related to each other, and therefore, the filling of phlegm within the lung may injure other internal organs. According to the suggestion of the relation between the five elements and the five organs, the lung is related to the element of Gold, the spleen is associated with the Earth, whereas the kidney is concerned with the Water. Thus, the spleens can generate and grain the water into the lungs, which then purges the water back into the kidneys [17]. In accordance with the beliefs on the relations of phase generation and transformation, the deficiency of kidney function can be traced back to the pulmonary stagnation, which is caused by the pulmonary Qi loss and kidney deficiency. Therefore, the recurrence and persistence of chronic pulmonary diseases is associated with the deficiency of these three viscera, which is attributed to the distention and phlegm in the lung. Based on this, the focus of TCM on stable COPD is to strengthen the body, invigorate the spleen, benefit the lung, dispel the phlegm and alleviate the asthma.

In lights of these discoveries, in addition to the conventional therapy, we also applied Jianpi Xiaoyu

recipe to invigorate the spleen, tonify the kidney, remove blood stasis, and resolving the phlegm. 11 prescriptions have been included in the recipe, including *Radix Codonopsis* (which replenishes Qi and spleen and eliminates the phlegm), *Sclerotum Poriae Cocos* (which tranquilizes mind and promotes diuresis and detumescence), *Rhizoma Atractylodis Macrocephalae* (which replenishes Qi and spleen and invigorates the body), *Pericarpium Citri Reticulatae* (which removes the phlegm to smoothen the breath), *Bulbus Fritillariae Cirrhosae* (which moistens the lung, reduces the phlegm, disperse clot and dissolves carbuncle), *Rhizoma Pinelliae Preparatum* (which removes the dampness to dissolve phlegm, invigorate the spleen and eliminate the distension) [18], *Radix Salviae Miltiorrhizae* (which promotes blood circulation, removes blood stasis, cleans the heart and rids of the irritability), *Radix Astragali* (which tonifies lung, invigorates spleen, solidifies the body and replenishes Qi), *Fructus Amomi* (which can moisten Qi, warm the spleen and regulate the spleen), *Herba Hedyotis Diffusae* (which is capable to relieve pain, disperse the clot, and promotes the dehumidification and diuretics), and fried *Radix Glycyrrhizae* (the effects of which are to replenish the Qi in the spleen, dissolve the phlegm, and stop the coughing). The combination of these prescriptions is contributory to activating blood circulation, removing blood stasis, regulating Qi, invigorating the spleen and tonifying the lung, which reflects the concept of “holistic treatment” in TCM [19]. Based on the results in our study, the scores of both CAT and SGRQ and 6-minute walking distance as well as the clinical symptoms in patients of the study group were evidently better than those in the control group, indicating that the adjuvant treatment of Jianpi Xiaoyu recipe has an obvious advantage in the improvement of clinical symptoms and exercise endurance in patients.

FVC, FEV1 and FEV1/FVC% are the gold standard for the evaluation of pulmonary functions in patients with pulmonary diseases [20]. In accordance with the results in our study, these indices of patients in the

study group were evidently increased than those in the control group following the treatment, suggesting that the adjuvant treatment of Jianpi Xiaoyu recipe can help to improve the pulmonary capacities, relieve ventilation obstacles and promote pulmonary functions in patients with stable COPD. These effects can be attributed to the discovery that the components of Jianpi Xiaoyu recipe, including *Radix Codonopsis*, *Pericarpium Citri Reticulatae*, *Rhizoma Pinelliae Preparatum*, and *Bulbus Fritillariae Cirrhosae*, have the effects of reducing phlegm, relieving cough, and attenuate asthma, resulting the relieved bronchial inflammation, dilated bronchus, and removed accumulation of sputum in the lung so as to reduce the occurrence of the symptoms, enhance the pulmonary ventilation function and exercise endurance, improve the immunity of the body. Besides, it has been shown in modern pharmacological studies that the poria acid in *Sclerotum Poriae Cocos* and the Atractylenolide in *Rhizoma Atractylodis Macrocephalae* exert satisfying anti-inflammatory and detumescent effects, in addition to the repairment of damage cells, the enhancement of the phagocytosis and bactericidal effects in the macrophages, the inhibition of inflammation in the alveolar cells, and the reduction of sputum [21]. *Fructus Amomi* and *Radix Astragali* can mediate the spleen and the stomach, promote the gastrointestinal peristalsis and increase the absorption of the nutrients, which thus enhances the hydration function of the spleen [22]. The application of multiple prescriptions can comprehensively take the requirement of treatment into account in order to improve the function of body, ameliorate the physical disorders, and promote the better life quality of patients.

The harmful particles inhaled by patients with COPD may produce oxide, which affects the anti-inflammatory activities of cells within the pulmonary tissues and leads to the increase of oxidative stress-related markers in the blood yet the decreased activity of antioxidant, in addition to the stimulation on the secretion of airway mucus and sputum and the inactivation of antiprotease, aggravating the bronchial stenosis and causing cough,

dyspnea, and other symptoms [23]. Therefore, the inhibition of oxidative stress plays a pivotal role in the improvement of the airflow restriction, the reduction of inflammation and the secretion of mucus in patients with COPD. Based on the results in our study, the level of LPO was decreased yet that of SOD was increased in patients of the study group, which may be possibly associated with the active ingredients of TCM. The saponins in *Radix Salviae Miltiorrhizae* and *Radix Codonopsis* can enhance the anti-coagulation function of blood, promote the blood circulation, accelerate the metabolism in the body, reduce free radical-induced cell damage, nourish cells in the tissues, and improve the activity of SOD in the body. The alcohol extract of *Herba Hedyotis Diffusae* and *Radix Glycyrrhizae* can scavenging the oxygen radicals in a way and reduce the reaction between oxygen radicals and polyunsaturated fatty acids to the production of LPO, which therefore further enhances the activity of SOD and improve the anti-oxidant capability of the body.

5. Conclusion

Jianpi Xiaoyu recipe has a significant clinical efficacy in the adjuvant treatment of patients with stable COPD, which can be of help to alleviate the clinical symptoms, ameliorate the oxidative stress, and improve the exercise endurance effectively, in addition to the positive significance in enhancing pulmonary function and promoting the better life quality in patients with COPD.

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Conflict-of-Interest

The authors declare no conflicts of interest.

Authors' contributions

Conceptualization: J.L and H.C.Z; Data curation: F.J.Z and X.L.L; Formal analysis: C.W.S; Methodology: Z.R; Writing – original draft: J.L and H.C.Z; Writing – review and editing: J.L and H.C.Z; All authors have read and agreed to the published

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Ethics approval and consent to participate

The conduction of our study has been approved by the Ethics Committee of our hospital, and all enrolled patients have also signed the written informed consent as well.

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Availability of Data and Materials

The analyzed data sets generated during the study are available from the corresponding author on reasonable request.

Supplementary Material

Not applicable

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