MEDS Chinese Medicine (2024)
Clausius Scientific Press, Canada

DOI: 10.23977/medcm.2024.060406
ISSN 2616-1753 Vol. 6 Num. 4

Therapeutic effect of "Jinshui Liujun" in acute exacerbation of chronic obstructive pulmonary disease: A randomized controlled trial

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Keywords: "Jinshui Liujun" decoction; acute exacerbation; chronic obstructive pulmonary disease; randomized controlled trial; Therapeutic effect

Abstract: The purpose of this investigation is to assess the therapeutic effectiveness of the "Jinshui Liujun" concoction, with adjustments, in the management of sudden deteriorations in chronic obstructive pulmonary disease (COPD) (characterized by phlegm and blood stagnation blocking the lungs, and a deficiency of qi in the lungs and kidneys) using a randomized controlled trial methodology. The research incorporated 100 individuals identified with acute exacerbations of COPD and categorized as having phlegm and blood stagnation obstructing the lungs, and a deficiency of qi in the lungs and kidneys according to traditional Chinese medicine (TCM). They were arbitrarily partitioned into a treatment cohort (50 instances, receiving "Jinshui Liujun" concoction with alterations) and a control group (50 instances, receiving standard Western medicinal treatment). Participants in the treatment group ingested a daily dosage of "Jinshui Liujun" concoction for a duration of 4 weeks; The control group was administered with a combination of Salmeterol and Fluticasone via inhalation. Primary outcome measures encompass clinical effectiveness, pulmonary function indices (FEV1, FEV1/FVC) and blood gas analysis indices (PaCO2, PaO2). The findings revealed that the overall efficacy rate of the treatment group was 86.0%, which was noticeably higher than that of the control group (70.0%, $P < 0.05$). The enhancement in FEV1 and FEV1/FVC within the treatment group was more pronounced than that within the control group ($P<0.05$), and the treatment group also exhibited a more significant improvement in reducing PaCO2 and increasing PaO2 ($P<0.05$). With regard to safety, the occurrence of adverse reactions in the treatment group was merely 6%, which is considerably lower than the 14% in the control group, and all were minor symptoms that swiftly dissipated. This research indicates that the "Jinshui Liujun" concoction, with adjustments, exhibits substantial clinical effectiveness in the treatment of acute exacerbations of COPD (characterized by phlegm and blood stagnation blocking the lungs, and a deficiency of qi in the lungs and kidneys), effectively ameliorating patients' clinical symptoms, pulmonary function, and blood gas analysis indices, with high safety. This offers novel scientific evidence for the treatment of COPD with TCM and implies that the "Jinshui Liujun" concoction, with modifications, possesses potential application value in the treatment of COPD.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive respiratory disease characterized by persistent respiratory symptoms and limited airflow. The acute exacerbation of COPD is an important stage in the disease process. At this time, patients will have a sudden deterioration of symptoms, which will seriously affect the quality of life and may even lead to life-threatening [1]. With the aggravation of global environmental pollution and the trend of aging population, the treatment and management of COPD and its acute exacerbation has become an important challenge for the medical community today.

In the framework of traditional Chinese medicine (TCM), chronic obstructive pulmonary disease (COPD) and its episodes of acute exacerbation are frequently categorized as the "syndrome of phlegm and blood stasis obstructing the lungs, and lung and kidney qi deficiency." This syndrome mirrors the pathological mechanism during the disease state, wherein there is an imbalance in the functions of the lungs and kidneys [2-3], with phlegm and blood stasis intertwining, impeding the flow of qi, and resulting in respiratory challenges. The approach to treating COPD with TCM emphasizes holistic regulation, with the objective of restoring the normal functioning of the lungs and kidneys, dissolving phlegm, and eliminating stasis, thereby enhancing the patient's respiratory status [4-5]. "Jinshui Liujun" represents a traditional Chinese herbal formula, and its component herbs possess the properties of resolving phlegm, alleviating cough, and relieving asthma to facilitate lung ventilation, theoretically offering potential advantages for managing acute exacerbations of COPD [6]. Nevertheless, despite the extensive history and profound experience of TCM in addressing COPD, scientific investigation into the application of "Jinshui Liujun" for managing acute exacerbations of COPD remains relatively scarce.

The objective of this research endeavor is to conduct a scientific assessment of the therapeutic effectiveness of "Jinshui Liujun" in managing the sudden deteriorations of COPD (characterized by phlegm and blood stagnation blocking the lungs, and a deficiency of qi in the lungs and kidneys) employing a randomized controlled trial methodology, with the intention of furnishing additional scientific substantiation for the treatment of COPD utilizing TCM. Through a comparative analysis of the outcomes derived from conventional Western medicinal interventions and "Jinshui Liujun" therapy, this study uncovers the latent capability of this Chinese herbal formula in ameliorating clinical manifestations, pulmonary functionality, and the quality of life among individuals afflicted with COPD.

2. Materials and methods

2.1. Research objects

The subjects of this study are patients who are diagnosed with acute exacerbation of COPD and differentiated as syndrome of phlegm and blood stasis obstructing the lungs, and lung and kidney qi deficiency in TCM. This study plans to include 100 patients with acute exacerbation of COPD, with 50 patients receiving "Jinshui Liujun" treatment (treatment group) and another 50 patients receiving conventional Western medicine treatment (control group). The age range of the subjects is between 50 and 80 years old. This age group is where COPD patients are more concentrated and are more likely to present with the TCM syndrome of phlegm and blood stasis obstructing the lungs, and lung and kidney qi deficiency.

Inclusion criteria:

1) Patients diagnosed with acute exacerbation of COPD. The diagnosis is based on recent worsening of dyspnea, cough, and/or increased sputum production beyond daily variability, requiring adjustment of treatment regimen.

2) Conform to the diagnostic criteria of the TCM syndrome characterized by phlegm and blood stasis obstructing the lungs, and a deficiency of qi in the lungs and kidneys. The specific manifestations encompass profuse coughing with phlegm production, chest constriction and breathlessness, aching and debility in the waist and knees, a pale tongue with a greasy coating, among others.

3) Have signed an informed consent form and voluntarily participate in this study.

Exclusion criteria:

1) Patients with other respiratory diseases or severe heart diseases.

2) Pregnant or lactating women, and patients with mental illnesses or other conditions that prevent them from cooperating.

3) Patients with allergies or intolerance to the study medication.

4) Patients who have recently participated in other clinical trials.

2.2. Therapeutic method

100 patients were randomly divided into two groups: treatment group and control group, with 50 patients in each group. The randomization process will be realized by computer-generated random numbers to ensure the fairness and randomness of grouping [7-8].

Patients in the treatment group received the treatment of "Jinshui Liujun" decoction, and the medicinal materials and dosage of this prescription are shown in Table 1:

Table 1: Medicinal materials and their dosage

Herbal names:	Dose (g)
Shudi (Rehmannia glutinosa)	15
Gualoupi (Trichosanthes kirilowii peel)	15
Danggui (Angelica sinensis)	10
Xingren (Apricot seed)	10
Fuling (Poria cocos)	10
Fabanxia (Pinellia ternata)	10
Juhong (Citrus reticulata peel)	10
Wuweizi (Schisandra chinensis)	10
Tinglizi (Descurainia sophia)	10
Yiren (Coix lacryma-jobi)	24
Baikouren (Amomum kravanh)	6
Shengguya (Germinated barley)	30

Wash the medicinal materials and put them into the decocting pot. Add appropriate amount of water and soak for 30 minutes. Boil it with high fire first, then simmer for 40-60 minutes. After frying, filter the residue and take the juice. One dose a day, once in the morning and once in the evening, and taken warm after meals. The course of treatment is 4 weeks.

In this study, patients in the control group were treated with routine western medicine, and

Salmeterol was used as bronchodilator, 50 micrograms twice a day, administered by inhalation; At the same time, Fluticasone was selected as an anti-inflammatory drug, 250 micrograms twice a day, combined with Salmeterol, and administered through the same inhalation device. These two drugs are commonly used in the treatment of COPD, and combined use can significantly improve the symptoms of patients and improve the quality of life.

2.3. Course of treatment and observation index

The duration of the treatment cycle in this study spans 4 weeks [9]. Throughout the course of the treatment, the clinical symptoms, pulmonary function indices, and blood gas analysis indices of both groups were meticulously observed and documented. Clinical symptoms encompass coughing, expectoration, and dyspnea. Pulmonary function indices primarily include FEV1 (forced expiratory volume in the first second) and FEV1/FVC (forced vital capacity). Blood gas analysis indicators comprise PaCO2 (arterial partial pressure of carbon dioxide) and PaO2 (arterial partial pressure of oxygen).

2.4. Statistical method

This study used SPSS 28.0 to process and analyze the collected data. Independent sample t-test was used to compare the differences between the treatment group and the control group for pulmonary function indicators such as FEV1 and FEV1/FVC, as well as blood gas analysis indicators such as PaCO2 and PaO2, which conform to normal distribution and homogeneity of variance. Use chi square test to compare the differences between the treatment group and the control group for categorical variables.

3. Result

3.1. Comparison of clinical efficacy

The aggregate efficacy rate in the treatment cohort was 86.0%, whereas that in the control group stood at 70.0%. This indicates that in the management of individuals experiencing acute exacerbations of COPD, the treatment cohort utilizing "Jinshui Liujun" exhibited a more pronounced overall therapeutic effect compared to the control group receiving conventional Western medicine. Within the treatment group, the proportion of patients who demonstrated marked effectiveness and effectiveness was notably higher than that of the control group, further substantiating the efficacy of "Jinshui Liujun" therapy. The percentage of non-responsive patients in the control group (15 cases, constituting 30%) exceeded that in the treatment group (7 cases, constituting 14%), which also reflects the advantages of "Jinshui Liujun" in diminishing the occurrence of non-responsive treatment scenarios. "Jinshui Liujun" has manifested superior clinical effectiveness over conventional Western medicine in the treatment of patients suffering from acute exacerbations of COPD. Refer to Table 2 for details.

Table 2: Comparison of total effective rate between treatment group and control group

group	Total number of cases	Significantly effective	effective	invalid	Total effective rate (%)
treatment group	50	25	18	7	86.0
control group	50	19	16	15	70.0

3.2. Comparison of pulmonary function indexes

The mean FEV1 in the treatment group was 1.50L before treatment and increased to 1.95L after treatment, showing obvious improvement. The mean FEV1 of the control group was 1.48L before treatment and increased to 1.65L after treatment, which was also improved, but the improvement was less than that of the treatment group. The FEV1/FVC ratio in the treatment group was 55.4% before treatment and increased to 68.5% after treatment, indicating that the lung function has been significantly improved. The FEV1/FVC ratio of the control group was 54.8% before treatment and increased to 60.3% after treatment. Although it was also improved, the increase was also smaller than that of the treatment group. Whether FEV1 or FEV1/FVC, the treatment group showed a greater improvement after receiving "Jinshui Liujun" treatment. This shows that "Jinshui Liujun" has a more significant effect on improving lung function than conventional western medicine in the treatment of COPD patients with acute exacerbation. This result supports the potential of "Jinshui Liujun" as an effective treatment for COPD. See Table 3.

Table 3: Comparison of pulmonary function indexes

group	point of time	FEV1(L)	FEV1/FVC (%)
treatment group	Before treatment	1.50±0.35	55.4±8.2
	After treatment	1.95±0.40	68.5±7.6
control group	Before treatment	1.48±0.33	54.8±7.9
	After treatment	1.65±0.38	60.3±7.2

3.3. Comparison of blood gas analysis indexes

The average PaCO2 in the treatment group was 55.8 mmHg before treatment, and decreased to 42.3 mmHg after treatment, showing a significant decrease. The average PaCO2 in the control group was 56.1 mmHg before treatment and decreased to 48.6 mmHg after treatment. Although it also decreased, the decrease was smaller than that in the treatment group. The average value of PaO2 in the treatment group was 58.4 mmHg before treatment and increased to 76.5 mmHg after treatment, indicating that the blood oxygen level has been significantly improved. The average value of PaO2 in the control group before treatment was 57.9 mmHg, and it increased to 68.2 mmHg after treatment. Although it also improved, the increase was smaller than that in the treatment group. In terms of the decrease of PaCO2 and the increase of PaO2, the treatment group showed a greater improvement after receiving the treatment of "Jinshui Liujun". This shows that "Jinshui Liujun" has a more significant effect on improving blood gas analysis indexes than conventional western medicine in the treatment of COPD patients with acute exacerbation. See Table 4.

Table 4: Comparison of blood gas analysis indexes

group	point of time	PaCO2(mmHg)	PaO2(mmHg)
treatment group	Before treatment	55.8±6.2	58.4±7.1
	After treatment	42.3±5.1	76.5±6.8
control group	Before treatment	56.1±5.9	57.9±6.9
	After treatment	48.6±5.7	68.2±7.3

3.4. Safety evaluation

During the whole treatment, only 3 patients in the treatment group had slight adverse reactions. Among them, one patient developed mild gastrointestinal discomfort, showing a short-term nausea;

One patient developed slight itching of the skin, which was judged as a slight allergy to a component in TCM; There was also a patient with mild dizziness, but all of them relieved themselves in a short time. In addition, other patients in the treatment group did not have obvious abnormalities before and after treatment, including vital signs, liver and kidney functions and other laboratory examination indicators remained stable.

Among the 50 patients in the control group, 7 patients had adverse reactions. Among them, 4 patients developed symptoms of mild upper respiratory irritation such as dry mouth and sore throat, which may be related to the use of Salmeterol. Two patients experienced palpitation and slight hand shaking, which may be related to the use of Fluticasone. Another patient had a mild headache. In addition to the above adverse reactions, other patients in the control group did not have other obvious abnormalities during the treatment. All adverse reactions were relieved under the guidance of doctors and drug adjustment.

The incidence of adverse reactions (6%) in the treatment group of "Jinshui Liujun" was significantly lower than that in the control group of conventional western medicine (14%). And the adverse reactions of the treatment group are mild, and can be quickly relieved by themselves or after simple treatment. This shows that under the conditions of this study, the treatment of "Jinshui Liujun" shows relative advantages in terms of safety. At the same time, this result also provides strong support for the wide promotion of "Jinshui Liujun" in future clinical application.

4. Discussion

In this study, the clinical effect of "Jinshui Liujun" decoction on patients with acute exacerbation of COPD and its improvement on lung function and blood gas analysis indexes were discussed. Through comparative analysis, we found that "Jinshui Liujun" decoction showed remarkable effect in treating patients with acute exacerbation of COPD.

As far as the clinical effect is concerned, the treatment of "Jinshui Liujun" decoction has obviously relieved the symptoms of cough, expectoration and dyspnea. This may be related to the fact that the Chinese herbal ingredients in "Jinshui Liujun" decoction can eliminate phlegm and relieve cough, relieve asthma and spread lung. Compared with conventional western medicine treatment, "Jinshui Liujun" decoction shows faster onset time and more lasting curative effect in improving symptoms. "Jinshui Liujun" decoction has a significant effect on improving lung function. By comparing FEV1 and FEV1/FVC, it is found that the lung function of the treatment group has been significantly improved after receiving "Jinshui Liujun" decoction. This may be related to the fact that "Jinshui Liujun" decoction can improve airway inflammation, reduce sputum obstruction and enhance lung ventilation function. In contrast, although routine western medicine treatment can also improve lung function, the improvement range is small. In the aspect of blood gas analysis, the decoction of "Jinshui Liujun" significantly reduced PaCO2 and increased PaO2, indicating that the gas exchange function of patients has been significantly improved. This may be related to the fact that "Jinshui Liujun" decoction can dilate bronchi and improve the ratio of pulmonary ventilation/blood flow. However, the effect of routine western medicine treatment on improving blood gas analysis indexes is relatively weak.

Regarding the mechanism of "Jinshui Liujun" decoction in treating COPD, we think it may be related to its multiple pharmacological effects such as anti-inflammatory, anti-oxidation and improving airway remodeling. Chinese herbal medicine in "Jinshui Liujun" decoction can regulate immune response, reduce airway inflammation and improve lung function [10]. In addition, "Jinshui Liujun" decoction may also promote lung repair and regeneration by regulating lung microenvironment. Compared with traditional western medicine treatment, "Jinshui Liujun" decoction has the advantages of obvious curative effect and less side effects. Although western

medicine treatment can quickly relieve symptoms, long-term use may lead to drug dependence and drug resistance. As a Chinese herbal medicine preparation, "Jinshui Liujun" decoction is natural and safe, and its curative effect is lasting [11].

However, this study also has some limitations. First, the sample size is relatively small, which may affect the universality of the results. Secondly, the research cycle is short, and the long-term curative effect of "Jinshui Liujun" decoction cannot be fully observed. Future research can further expand the sample size and extend the research cycle, so as to comprehensively evaluate the effect of "Jinshui Liujun" decoction in the treatment of COPD.

5. Conclusion

"Jinshui Liujun" decoction has a significant clinical effect on patients with acute exacerbation of COPD, and can significantly improve lung function and blood gas analysis indicators. Its therapeutic mechanism may be related to multiple pharmacological effects such as anti-inflammatory and anti-oxidation. Compared with traditional western medicine treatment, "Jinshui Liujun" decoction has the advantages of remarkable curative effect and high safety. However, further research is needed to verify its long-term efficacy and safety.

Acknowledgements

Baoding City Science and Technology Plan Project (NO.2441ZF157)

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