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Clinical Efficacy of Xiaochaihu Decoction Combined with Guizhi Fuling Pill in Adjuvant Treatment of AECOPD and Its Influence on Inflammatory Factors in Patients

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Keywords

Xiaochaihu Decoction combined with Guizhi Fuling Pill, Acute exacerbation of chronic obstructive pulmonary disease, Inflammatory factors, Pulmonary function

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Abstract:

Background: We analyzed the clinical efficacy of Xiaochaihu Decoction combined with Guizhi Fuling Pill in adjuvant treatment of patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD).

Methods: 108 patients with AECOPD were randomly divided into control group and observation group. Patients in control group were treated with conventional therapy, while patients in observation group were treated with Xiaochaihu Decoction and Guizhi Fuling Pill on the basis of the control group. Clinical symptoms, pulmonary function, scores of modified British Medical Research Council Respiratory Questionnaire (mMRC), self-assessment test questionnaire (CAT), and the levels of inflammatory factors were compared between the two groups. **Results**: After treatment, total clinical effective rate of observation group was higher than that of control group (P<0.05). Compared with those before treatment, peak expiratory flow (PEF), forced expiratory volume in 1 second (FEV1), FEV1/forced vital capacity (FVC) ratio and FEV1 to predicted value ratio (FEV1% pred) in the two groups after treatment were increased (P<0.05), and those indicators in observation group were higher than those in control group (P<0.05). Compared with those before treatment, mMRC score, CAT score, procalcitonin (PCT), C-reactive protein (CRP), interleukine (IL)-18, and tumor necrosis factor (TNF)-α levels in the two groups after treatment were decreased (P<0.05), and those indicators in observation group were lower than those in control group (P<0.05).

Conclusion: Xiaochaihu Decoction combined with Guizhi Fuling Pill effectively improved the clinical symptoms and lung function of patients, and smoothly regulate the levels of inflammatory factors in patients with AECOPD.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a common chronic disease characterized by continuous airflow limitation, including the acute exacerbation of chronic obstructive pulmonary disease (AECOPD) and stable period (1). Patients with AECOPD often have following symptoms such as aggravated dyspnea or cough, increased sputum and/or purulent sputum, insomnia and mental disorders, and their lives are seriously threatened (1, 2). At present, the patients suffering from AECOPD are clinically treated through bronchodilators, glucocorticoids or respiratory support, but it is difficult to completely improve their lung function (3).

Traditional Chinese medicine therapy has a long history, and it has been reported that Xuanbai Chengqi Decoction could ameliorates pulmonary inflammation in a murine model of COPD (4). In addition, Traditional Chinese medicine classic herbal formula Xiaoqinglong decoction has shown effectiveness and safety in the treatment of AECOPD (5). Yunrun Ji et al have showed that Dachaihu Decoction combined with Guizhi Fuling Pill is effective in the treatment of folliculitis, which can effectively improve the irritability and mouth dryness of the patients (6). The main ingredients of Xiaochaihu Decoction combined with Guizhi Fuling Pill are *Scutellaria Baicalensis*, *Zingiberis Rhizoma*, White Ginseng, etc. Its main effects are to clear heat, regulate qi, benefit qi for activating blood circulation, and smooth activities of qi, which is mainly used for the treatment of following symptoms, including ragged breathing, chest swelling, congestion and oppression. At present, there are relatively few studies on clinical curative effect of Xiaochaihu Decoction combined with Guizhi Fuling Pill in adjuvant treatment of AECOPD. Therefore, this study investigated the clinical effects of Xiaochaihu Decoction combined with Guizhi Fuling Pill on the patients suffering from AECOPD and discussed the reliable methods to the treatment of AECOPD. Now, the results are reported as follows.

2. Data and methods

2.1 General data

Patients (n=108) with AECOPD admitted to our hospital from January 2019 to December 2021 were selected and randomly divided into the control group and the observation group, with 54 cases in each group. This study was approved by the ethics committee of our hospital, and all patients signed the written informed consents. The general data between the two groups were not significantly different and were comparable ($P > 0.05$), as shown in Table 1.

Table 1 Comparison of the general data between the two groups

Group	Care	Sex (care)		Age	Course of COPD (year)	BMI (kg/m^2)	Disease classification (care)	
		male	female				GOLD2	GOLD3
observation group	54	30	24	62.52±2.77	10.36±2.22	22.04±0.69	27	27
control group	54	28	26	62.60±2.85	10.38±2.32	22.05±0.89	25	29
χ^2/t		0.149		-0.148	-0.046	-0.065	0.148	
P		0.700		0.883	0.964	0.948	0.700	

2.2 Diagnostic criteria

Diagnostic criteria for western medicine: ① The diagnostic criteria for AECOPD in *Guidelines for the diagnosis and management of chronic obstructive pulmonary disease* (7) is followed.

Diagnostic criteria for Chinese traditional medicine: The diagnostic criteria of "lung distension" in *Chinese*

Traditional Medicine Guidelines for Diagnosis and Treatment of Chronic Obstructive Pulmonary Disease 2011 edition (8) is followed.

2.3 Inclusion criteria

① The diagnostic standards of traditional Chinese medicine and western medicine are followed; ② The clinical stages were consistent with the AECOPD.

2.4 Exclusion criteria

① Patients with severe primary diseases of brain, liver and kidney; ② Patients
who are allergic to the ingredients of Xiaochaihu Decoction combined with Guizhi Fuling Pill; ③ Patients with malignant tumors; ④ Patients with other respiratory diseases; ⑤ People with combined mental disorders.

2.5 Therapeutic methods

Routine treatments were given in both groups: a. Oxygen therapy (patients with hypoxemia can receive oxygen through the nasal catheter or through the side stove, with a general concentration of inhaled oxygen set to 28%-30%); b. Anti-infection treatment (amoxicillin, clavulanate potassium, cefaclor or cefuroxime was used for the treatment); c. Bronchodilator treatment (albuterol sulfate, ipratropium bromide); symptomatic treatment (treatment of expelling phlegm: Ambroxol Hydrochloride or Acetylcysteine). The control group received conventional treatment. The observation group was treated with Xiaochaihu Decoction combined with Guizhi Fuling Pill by the way of decoction based on conventional treatment, 3 times a day, 150 mL each time. The prescription included *Scutellaria baicalensis Georgi* (9 g), *Zingiberis Rhizoma* (6 g), *White Ginseng* (6 g), *Asarum heterotropoides Fr. Schmidt* (9 g), *Radix Bupleuri* (12 g), *Rhizoma Pinelliae* (12 g), *Glycyrrhizae*, *Schisandra chinensis (Turcz.) Baill* (9 g), *Cinnamomum cassia Presl* (9 g), *Poria*, *Persicae Semen* (9 g), *Moutan Cortex* (9 g), *Paeoniae Radix Rubra* (9 g). The treatment course of patients in both groups was 8 weeks.

2.6 Observational indicators

① Clinical efficacy: After treatment, the clinical effects of both groups were evaluated (9). Efficacy of the patients with AECOPD: clinical healing: the major clinical symptoms all disappeared, and pulmonary function index forced expiratory volume in 1 second (FEV1) increased by 35%; significant efficacy: FEV1 increased by 25%-35%; efficacious: FEV1 increased by 15%-24%; inefficacious: the measured value of FEV1 did not improve or even worsen. The clinical total effective rate = (number of clinical healing cases + number of cases with significant efficacy + number of efficacious cases)/total cases ×100%.

② Pulmonary function: Before and after treatment, pulmonary function detector (model: AS-507; registration number: CFDA (standard) 20162211982; manufacturer: Shanghai imu Medical Device Co., Ltd.) was used to detect the peak expiratory flow (PEF), FEV1, and FEV1/forced vital capacity (FVC).

③ The degree of dyspnea: Before and after treatment, modified British Medical Research Council Respiratory Questionnaire (mMRC) (9) was used to assess the degree of dyspnea in two groups. The lower mMRC score indicated that the dyspnea of the patients had relieved.

④ Daily quality of life: Before and after treatment, the self-assessment test questionnaire (CAT) (9) was used to evaluate the quality of life of both groups. CAT mainly evaluates clinical symptoms, mobility, psychology, sleep, social impact, with the score of 0 to 40. Lower scores indicated an improvement in patients' quality of life.

⑤ Inflammatory factor levels: Before and after treatment, 5 ml of fasting elbow venous blood was collected from the patients in both groups at morning and centrifuged at 3000 r/min for 10 min. The supernatant was taken and stored in -20℃ refrigerator. The levels of procalcitonin (PCT), C-reactive protein (CRP), interleukine (IL)-18, and tumor necrosis factor (TNF)-α in the serum were measured by an enzyme-linked immunosorbent assay.

2.7 Statistical methods

All data was analyzed using SPSS 20.0. Enumeration data were compared using χ^2-test. Measurement data are expressed as mean ± standard deviation ($\bar{x}\pm s$). Independent-sample *t*-test was used for the comparisons between two groups and paired-sample *t*-test was used for the comparison of the same group at the different time. $P < 0.05$ was considered as a statistically significant difference.

3. Results

3.1 Comparison of the clinical efficacy between the two groups

After treatment, the clinical effective rate was 96.30% in observation group and 83.33% in the control group. The total clinical effective rate of the observation group was visibly higher than that of the control group ($P<0.05$), seen in Table 2.

3.2 Comparison of pulmonary function before and after treatment between the two groups

Before treatment, there was no significant difference in the levels of PEF, FEV1, FEV1/FVC, and the FEV1 to predicted value ratio (FEV1% pred) between the two groups ($P>0.05$). The levels of PEF, FEV1, FEV1/FVC, and FEV1% pred were significantly increased in both groups compared with the levels in

the patients without treatment (P<0.05). The levels in observation group were significantly higher than that in the control group (P<0.05), as shown in Table 3.

Table 2 Comparison of the clinical efficacy between the two groups [case (%)]

Group	Case	Healing	Significant efficacy	Efficacious	Inefficacious	Total effective rate
observation group	54	2（3.70）	24（44.44）	26（48.15）	2（3.70）	52（96.30）
control group	54	0（0.00）	18（33.33）	27（50.00）	9（16.67）	45（83.33）
χ^2						4.960
P						0.026

Table 3 Comparison of pulmonary function before and after treatment between the two groups ($\bar{x}$±s)

Observational index		Observation group (n=54)	Control group (n=54)	t	P
PEF（L/min）	pretreatment	4.46±1.00	4.43±1.00	0.156	0.876
	post-treatment	7.24±1.25*	5.99±1.27*	5.155	0.000
FEV_1（L）	pretreatment	1.18±0.35	1.20±0.27	-0.332	0.740
	post-treatment	1.64±0.46*	1.46±0.44*	2.078	0.040
FEV_1/FVC（%）	pretreatment	48.17±4.83	47.80±4.46	0.414	0.680
	post-treatment	64.33±4.15*	57.18±5.31*	7.796	0.000
FEV1% pred（%）	pretreatment	43.14±4.50	43.24±2.97	-0.136	0.892
	post-treatment	58.18±5.37*	50.94±5.67*	6.813	0.000

Note: Comparison with the indexes before treatment: *P <0.05

3.3 Comparison of mMRC and CAT scores between the two groups

Before treatment, there was no significant difference in the levels of mMRC and CAT scores between the two groups (P>0.05). The scores of mMRC and CAT were significantly decreased in both groups compared with relative scores before the treatment (P<0.05). The scores of mMRC and CAT in observation group were significantly lower than that in the control group (P<0.05), as shown in Table 4.

3.4 Comparison of inflammatory factor levels before and after treatment between the two groups

Before treatment, there was no significant difference in the levels of PCT, CRP, IL-18, and TNF-α between the two groups (P>0.05). The levels of PCT, CRP, IL-18, and TNF-α were significantly decreased in both groups compared with relative levels before the treatment (P<0.05). The relative levels of these factors in observation group were significantly lower than that in the control group (P<0.05), as shown in Table 5.

Table 4 Comparison of mMRC and CAT scores between the two groups ($\bar{x}$±s)

Group	Case	mMRC score		CAT score	
		Pretreatment	Post-treatment	Pretreatment	Post-treatment
observation group	54	2.95±0.43	0.66±0.09*	31.96±3.75	11.49±1.43*
control group	54	2.94±0.43	0.93±0.11*	31.00±3.76	15.29±1.98*
t		0.121	-13.960	1.328	-11.433
P		0.904	0.000	0.187	0.000

Note: Comparison with the indexes before treatment: $^{*}P$ <0.05

Table 5 Comparison of inflammatory factor levels before and after treatment between the two groups ($\bar{x}$±s)

Observational index		Observation group （n=54）	Control group（n=54）	*t*	*P*
PCT（μg/L）	pretreatment	9.05±1.61	9.08±1.61	-0.097	0.923
	post-treatment	3.16±0.46*	4.51±0.58*	-13.401	0.000
CRP（mg/L）	pretreatment	17.34±2.41	17.28±2.29	0.133	0.895
	post-treatment	5.34±0.59*	7.99±0.81*	-19.433	0.000
IL-18（ng/L）	pretreatment	175.95±12.42	175.49±15.49	0.170	0.865
	post-treatment	151.96±10.02*	165.24±12.14*	-6.200	0.000
TNF-α（ng/L）	pretreatment	219.23±15.59	220.39±14.69	-0.398	0.691
	post-treatment	186.71±10.27*	199.21±21.18*	-3.902	0.000

Note: Comparison with the indexes before treatment: $^{*}P$ <0.05

4. Discussion

AECOPD is mainly caused by respiratory tract viruses and bacteria whose potential expression in alveolar epithelial cells strengthens the pulmonary inflammatory effect. In addition, smoking and air pollution will also increase the likelihood of AECOPD (1). Due to the significant decrease of partial pressure of oxygen in the patients with AECOPD, carbon dioxide is constantly retained and the respiratory function of the patients gradually decreases, leading to failure of respiration. Patients' lives will be threatened if there's no timely intervention (10). Traditional Chinese medicine believes that the pathogenesis of AECOPD is the deficiency of qi and blood, smooth moving state losing of liver, and pathogenic fire derived from stagnation of liver-qi. Liverzang-fire attacking lung causes dry cough and sputum with blood streaks. Splenasthenic fluid-retention and metabolic disturbance of body fluid causes sputum accumulation in patients. Thus, the basic principles for the treatment of this disease are spasmolysis and asthma-smoothing (11).

The mucus secreted by the bronchi of the patients with AECOPD are increased accompanied by the dysregulation of ciliary function, obstruction of the peripheral airway, limited expiratory airflow, and destruction of pulmonary parenchyma. The decrease of pulmonary gas exchange volume produces hypoxemia and chronic hypoxia leads to extensive constriction of pulmonary vessels, forming pulmonary hypertension, which seriously damages lung function of the patients. The common indicators of pulmonary function are PEF, FEV1, FEV1/FVC, and FEV1% pred (12). The results of this study showed that, after the treatment, the total clinical effective rate of the observation group was significantly higher than that of the control group. The levels of PEF, FEV1, FEV1/FVC, and FEV1% pred were significantly increased in both groups compared with those in the patients before treatment. Besides, the levels of these indicators in observation group were significantly higher than that in the control group. The scores of mMRC and CAT were significantly decreased in both groups compared with relative scores before the treatment, with the lower scores of mMRC and CAT in observation group compared with those in the control group. As for the prescription of Xiaochaihu Decoction, *Scutellaria baicalensis Georgi* has the effects of heat-clearing and damp-drying as well as miscarriage prevention (13). *Zingiberis Rhizoma* has the effects of wetness-depriving and sputum-eliminating as well as warming lung and promoting blood circulation (14). *White Ginseng* has the effects of reinforcing the spleen to benefit the lung, relieving uneasiness of mind and intelligence-enhancing (15). *Asarum heterotropoides Fr. Schmidt* has the effects of expelling wind and clearing away cold as well as warming lung to reduce

watery phlegm (16). *Radix Bupleuri* has the effects of bringing down a fever and nourishing qi and blood (17). *Rhizoma Pinelliae* has the effects of eliminating dampness and eliminating phlegm, as well as digesting the accumulation of food (18). *Glycyrrhizae* has the effects of Nourishing Yin and nourishing blood as well as calming down pulse and blood pressure of the patients (19). *Schisandra chinensis (Turcz.) Baill* has the effects of nourishing the kidney and calming down the mind of patients as well as nourishing yin and stemming essence (20). *Cinnamomum cassia Presl* has the effects of tonifying fire and helping yang as well as warming channel and relieving stagnation (21). *Poria* has the effects of inducing diuresis to alleviate edema as well as excreting dampness and tonifying spleen (22). *Moutan Cortex* has the effects of eliminating pathogenic heat from the blood as well as antibiosis and diminishing inflammation (23). The effects of removing blood stasis and reducing watery phlegm by the way of reconciling superficies and interior can be achieved by using the medicines mentioned above together (6). Furthermore, modern pharmacological research shows that cinnamomi cortex can not only accelerate the flow rate of pulmonary arteries, inhibit structural remodeling of the pulmonary arteries and improve the pulmonary function of the patients through expansion of pulmonary arterioles, but also improve the microcirculation and effectively relieve the clinical symptoms of patients by expanding the systemic blood vessels to increase the perfusion volume of tissues and organs. Through the production of nitric oxide (NO), extract of Schisandra Chinensis alleviates the infiltration of neutrophils and macrophages in the lung tissues, reduces lung histopathological changes, decreases sputum secretion, and improves lung function (24). Consistent with the above reports, our study found that Xiaochaihu Decoction combined with Guizhi Fuling Pill has an excellent clinical effect on patients with AECOPD, which can effectively improve the clinical symptoms and lung function of patients.

When patients with AECOPD are subjected to microbiological invasion or tissue injuries, inflammatory factors such as PCT, CRP, IL-18, and TNF-α are released in lung tissues, which induces the expressions of adhesion molecules in airway endothelial cells, thereby increasing mucus secretion and then leading to more severe airflow restriction in patients, further aggravating the condition of the patients with AECOPD. The results of this study showed that the levels of PCT, CRP, IL-18, and TNF-α were significantly decreased in both groups compared with relative levels before the treatment, with the lower relative levels of those indicators in observation group than those in the control group. Active ingredient of AsariRadix Et Rhizoma methyleugenol can act on the target cycloxidase-1 (COX-1), inhibit the catalytic lysis of the key enzyme (arachidonic acid) of prostaglandin, and alleviate the inflammatory reaction caused by prostaglandin E2. Active ingredient of AsariRadix Et Rhizoma Safrol can act on the target of LAT4H and inhibit the inflammatory process by reducing the content of leukotrienes B4 (25). By decreasing the expression of vascular cell adhesion molecule-1 (ICAM-1), baicalin inhibits the adhesion of white blood cells in endothelial cells, and can also suppress the chemotaxis and infiltration of neutrophils to lung tissues, thus reducing the lung inflammatory response of the body (26). Similar to the findings in these previous studies, we discovered that Xiaochaihu Decoction combined with Guizhi Fuling Pill can smoothly regulate the level of inflammatory factors in patients with AECOPD.

5. Conclusion

Xiaochaihu Decoction combined with Guizhi Fuling Pill has an excellent clinical effect on patients with AECOPD, which can effectively improve the clinical symptoms and lung function of patients, and can smoothly regulate the levels of inflammatory factors in patients.

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Not applicable.

Conflict of interest

The authors declare no conflict of interest.

Author contributions

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

Ethical Approval and Consent to Participate

The experiments were conducted in accordance with the principles approved by the ethics committee of our hospital, and all patients signed the written informed consents.

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Availability of Data and Materials

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

Supplementary material

Not applicable.

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