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#### Review



# Progress in The Treatment of Chronic Obstructive Pulmonary Diseases with

# **Traditional Chinese Medicine**

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#### Abstract

Studies show that the prevalence rate of chronic obstructive pulmonary diseases (COPD) is 8.6% in Chinese adults over 20 year old and 13.7% over 40 year old. The total number of patients with COPD is about 100 million in China. Therefore, the prevention and treatment of COPD has become a severe challenge in China. According to clinical symptoms, COPD is divided into the acute exacerbation and stable stages. The urgent treatment is the principal one for the acute exacerbation of COPD, and the treatment for the stable stage is based on the origin of the disease. Here we review the progress in the treatment of COPD with traditional Chinese medicine (TCM).

**Key words:** Chronic Obstructive Pulmonary Disease (COPD); Traditional Chinese Medicine (TCM); Deficient Symptom.

#### Introduction

Chronic obstructive pulmonary disease (COPD) is a kind of obstructive pulmonary disease, mainly manifested as persistent airflow limitation with symptoms including shortness of breath, cough, and expectoration (1-2). In the past, COPD was divided into two types: Chronic bronchitis and emphysema. The term chronic bronchitis is now used to describe symptoms of "sputum and cough for more than three months for two consecutive years". COPD is a progressive disease, which will deteriorate over time (3). Finally, it is difficult for the patients to carry out daily activities such as walking and clothing.

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#### 1. Overview of COPD

# **1.1. Current epidemiological situation of COPD**

In 2010, COPDs caused a global economic loss of \$2.1 billion (4). According to Wang Chen's study (5), the prevalence of COPD in adults aged 20 and over in China is 8. 6% (95% CI: 7.5-9.9); it is estimated that in 2015, 99.9 (95% CI: 76.3-135. 7) million adults aged 20 and over in China suffered from COPD. The prevalence of COPD varies greatly among different regions, age groups and sexes. The prevalence of COPD in males (11.9%, 95% CI:10. 2-13. 8) was significantly higher than that in females (5.4%, 95% CI: 4.6-6.2; P<0.0001); the prevalence of COPD in people over 40 years old of age (13.7%, 95% CI: 12.1-15. 5) was higher than that in people aged 20-39 years (2.1%, 95% CI: 1.4-3.2; P<0.0001). In 2015, about 174 million people (2.4%) suffered from COPD worldwide, mainly affecting people over 40 years old of age with the same risk for men and women. In 1990, COPD caused about 2.4 million deaths; by 2015, the number had climbed to 3.2 million. About 90% of all deaths occur in developing countries, possibly due to high smoking rates. Smoking is the main cause of COPD. Other relatively minor factors include air pollution and heredity. In developing countries, the most common cause of air pollution is poor ventilation in cooking and heating stoves. Long-term exposure to such an environment can lead to inflammation in the lungs, narrowing airflow channels and impairment of lung function. The difference between COPD and asthma is that the former is not as effective as the latter after using bronchodilators.

Reducing exposure to risk factors can effectively prevent most COPD. This includes

reducing smoking frequency as much as possible and improving indoor and outdoor air quality. The treatment of COPD includes smoking cessation, lung rehabilitation, inhalation bronchodilators and corticosteroids. In addition, annual influenza vaccination can effectively prevent the occurrence of COPD. Some patients also need long-term oxygen supply or lung transplantation. When encountering patients with acute episodes, we can increase the dosage of drugs and hospitalization.

#### 1. 2 Pathogenesis and characteristics of COPD

The pathogenesis of COPD is not fully understood. It is generally believed that COPD is characterized by chronic inflammation of airway, pulmonary parenchyma, and pulmonary vessels. There are many inflammatory cells in different locations of the lung. Activated inflammatory cells release a variety of mediators, which can destroy the structure of the lung and promote inflammatory response. Inhalation of harmful particles or gases may lead to pulmonary inflammation. Smoking can induce pulmonary inflammation. Inflammation causes direct damage to the lungs. Various risk factors of COPD may produce similar inflammatory processes, leading to the occurrence of COPD.

The symptoms of COPD can be divided into two stages: one is acute attack stage, without acute attack, and the other is stable stage. During stable stage, there are also symptoms, such as cough and shortness of breath, especially shortness of breath, which can aggravate to be acute when it comes to infection, weather changes or strong abnormal gas stimulation. When acute exacerbation occurs, shortness of breath is obviously aggravated. Sometimes phlegm will increase, and most importantly, shortness of breath will increase. The increase of shortness of breath is an acute attack, which needs prompt treatment. Each acute attack will aggravate the

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deterioration of pulmonary function. The number of acute exacerbations in the previous year was an independent risk factor for death. If there are two or three acute exacerbations in a year, the mortality rate will be close to 30-40% within five years (6). Therefore, acute exacerbation is very important and need to be prevented. Chronic cough is often the earliest symptom of COPD. With the development of the disease, it does not heal for life. It is obvious in the morning and has paroxysmal cough or expectoration at night. When the airway is severely obstructed, it is usually difficult to breathe without coughing. Expectoration is usually white mucus or serous foam sputum. Occasionally, blood can be found. Sputum excretion is more frequent in the morning. During the acute attack, the amount of phlegm increased, and purulent phlegm could occur.

The main symptoms of COPD are shortness of breath or dyspnea, which occurs in the early stage of labor, and then increases gradually, resulting in shortness of breath in daily life and even during rest. Because of individual differences, some people can tolerate them. Breathing and chest tightness occur in some patients, especially in severe or acute exacerbations. Fatigue, emaciation, and anxiety often occur when the condition of COPD is serious, but they are not typical manifestations of COPD.

### **1.3 Evaluation of COPD**

Pulmonary function test is the main objective index for judging airflow limitation. The percentage of forced expiratory volume occupied by forced vital capacity in one second (FEV1/FVC) is a sensitive index for evaluating airflow limitation. The percentage of forced expiratory volume in one second (FEV 1%) is a good index for evaluating the severity of COPD. It has small variability and is easy to operate. When FEV1/FVC is less than 70% after inhalation of bronchodilator, it can be determined that airflow limitation cannot be completely reversible. Total lung volume (TLC), functional residual air volume (FRC) and residual air volume (RV) are increased, vital capacity (VC) is decreased, deep inspiration volume (IC) is decreased, IC/TLC is decreased, carbon monoxide diffusion volume (DLCO) and DLCO to alveolar ventilation volume (VA) ratio (DL-CO/VA) are decreased.

COPD pulmonary function is divided into four grades.

Grade I (mild): FEV1 (>80%) predicted value. Grade II (moderate): 50%<FEV1<80% predicted value.

Grade III (severe): 30%<FEV1<50% predicted value.

Grade IV (extremely severe): FEV1<30% predicted value or FEV1<50% predicted value with respiratory failure.

# 2. The application of traditional Chinese medicine in the treatment of COPD

# 2.1 Pathogenesis, classification, differentiation and treatment of acute exacerbation of COPD

Acute exacerbation of COPD (AECOPD) is a process of acute onset of COPD. The clinical manifestations of AECOPD are exacerbation of cough and asthma, shortness of breath, increased sputum volume. purulent or mucopurulent, accompanied by fever and other inflammatory symptoms. The treatment goal of AECOPD is to alleviate the clinical symptoms of acute exacerbation and prevent the occurrence of acute exacerbation later.

Traditional Chinese Medicine (TCM) believes that the pathogenesis of AECOPD is phlegm, heat, and blood stasis. Phlegm and heat can damage Qi and Yin for a long time, while Qi deficiency can weaken Qi and Jin fluid, which cannot be rectified and turned into phlegm and turbidity, resulting in insufficient biochemistry of Yin and Jin; phlegm can obstruct the lung system, inhibit Qi machine, damage the lungs facing hundreds of veins, which can cause blood stasis; Qi deficiency and blood weakness can also cause blood stasis; blood stasis can impede the operation of Jin fluid, promote

endogenous phlegm and Yin and blood stasis (7). If the phlegm obstructs the lung system seriously, it can disturb the Qi. It is manifested as phlegm heat and phlegm turbidity, which are the severe syndromes of acute aggravation. The clinical manifestations include wind-cold attack on lung, external cold and internal drinking, phlegm-heat obstruction of lung, phlegm-dampness obstruction of lung, phlegm-Meng-Shenqiao, etc.

AECOPD is an irreversible and progressive pulmonary dysfunction caused by many factors (8). TCM for the treatment of AECOPD is aimed for the emergency treatment of its target.

#### (1) Xuanfei Decreasing Cold and Phlegm

This method is suitable for external cold and internal drinking syndrome. Xiaoqinglong Decoction and Banxia Houpu Decoction are used in the prescription; Fenghan Cough Granule and Xiaoqinglong Granule can be used as Chinese patent medicine.

Guo Jianping selected 88 patients with Xuanmen obstructive pulmonary disease as the research object (9). Jianghuoxue Decoction started with Zongqi to treat COPD and used drugs of promoting blood circulation and removing blood stasis to eliminate congestion in lungs. Zouyuan (10) selected 70 patients with acute exacerbation of COPD as the research object. The control group was treated with Western medicine. The observation group was treated with Chinese medicine Pingchuan Zhike Decoction. The prescription composition was as follows: Platycodon grandiflorum 9 g, Moxibustion Ephedra 9 g, Scutellaria baicalensis 18 g, Roasted Aster 10 g, Ophiopogon japonicus 12 g, Fabanxia 9 g, Beisha ginseng 12 g, Fangfeng 12 g, Almond 9 g, Tianhua 30 g, Cinnamomum 6 g, Chen Pei 12 g, Poria 12 g, Hongjingtian 12 g, 18 g mulberry leaves, 12 g 100-flowers, 10 g tulipa, 12 g loquat leaves, 15 g Schisandra chinensis, 6 g woody incense and 3 g licorice. After soaking for half an hour, add water to decoct again. Take half of the medicinal juice in the morning and half in the evening, take one dose every day. Continuous treatment lasts for one

month. After treatment, the total effective rate of the observation group was 97.14%, higher than 77.14% of the control group, with statistical significance (P<0.05), indicating that the treatment of AECOPD with Pingchuan Zhike Decoction can help patients to improve symptoms more effectively, lung function and respiratory function can be significantly improved.

In addition, in the similar study of Duan Yanju et al (11), the total effective rates of clinical treatment of patients with acute exacerbation of asthma and cough relief Decoction were 94.3% (33/35, observation group) and 68.6% (24/35, control group), respectively, with significant difference (P<0.05). Yang Rongyuan et al (12) treated 52 patients with AECOPD with Xiaoqinglong Decoction based on routine treatment. Compared with the control group, it can effectively improve the clinical symptoms of cough, phlegm and asthma, and blood gas analysis has improved compared with pre-treatment data. It shows that the treatment of AECOPD with Xiaoqinglong Decoction is effective.

#### (2) Qingfei Huatan method:

This method is suitable for the syndrome of phlegm-heat obstructing the lungs. Patients have many coughs and phlegm (thick yellow), rough breathing; fever, red face, thirst, and cold drink preference; dry stool; red tongue and greasy fur, and smooth pulse. The prescriptions were composed of Qingqi Tan Pill and Fritillaria Melon Pine Powder. The Chinese patent medicine could be composed of Shedan Chuanbei Liquid, Qingqi Tan Pill, Qingfei Xiaoyan Pill and Tanreqing Injection.

Wang Aidong (13) randomly divided 142 patients with AECOPD into two groups. The control group were given anti-infection, spasmolysis, asthma relief and oxygen therapy. The observation group was given Tanreqing injection (scutellaria baicalensis, bear gallbladder powder, goat horn, honeysuckle, Forsythia suspensa) intravenously. The clinical efficacy and blood gas analysis of the observation group were better than those of the control group. It shows that Tanreqing

injection is effective in treating AECOPD in routine treatment.

Li Jiansheng (14) and others randomly divided 140 patients with AECOPD into two groups. Based on routine treatment, the experimental group was given prescriptions for clearing heat and resolving phlegm (trichosanthes. Pinellia ternata. Fritillaria chuanbei. Gardenia jasminoides, Scutellaria baicalensis, mulberry bark, bitter almond). The control group was given placebo for 2 weeks. The comprehensive clinical efficacy, single symptoms, laboratory indicators and quality of life of the patients were observed. Results showed that there was a significant difference in the comprehensive clinical efficacy between the experimental group and the control group (P<0.05). It shows that Qingre Huatan Prescription is superior to the control in improving the clinical symptoms of AECOPD, and can control and improve the symptoms of expectoration, wheezing, chest tightness, loss of appetite, etc. It has better effects of clearing heat. resolving phlegm and anti-inflammation. It alleviate can local inflammation reaction of airway and substantial damage of lung tissue, alleviate airway obstruction, thus improve pulmonary ventilation. It can improve the exercise, endurance, fatigue threshold, and the quality of life.

# (3) The method of drying dampness and resolving phlegm:

This method is suitable for the syndrome of phlegm dampness obstructing lung. The clinical manifestations are cough and asthma, phlegm sticky, or frothy), chest stuffiness, (white, abdominal fullness, less appetite, pale tongue (white and greasy), and smooth pulse. Banxia Houpu Decoction and Sanzi Yangxin Decoction were used in the prescription; Guilong Kechuanning Capsule, Kechuanshun Pill, Linggui Kechuanning Capsule and Suzi Jiangqi Pill could be used in Chinese patent medicine.

Zhang Lijun (15), based on routine treatment, 40 COPD patients were treated with Suzi Jiangqi Decoction and Sanzi Yangyan Decoction. The total effective rate was 82.5%. There was a significant difference between the observation group and the control group (P<0. 05). The results showed that it can improve the lung function (ventilation and hypoxia), and greatly improve the quality of life of patients. In the acute stage of COPD, based on the treatment of Western medicine, combined with the dialectical treatment of TCM, such as regulating qi and phlegm, resolving phlegm and improving qi, clearing heat and resolving phlegm, warming yang and diurging water, dispersing cold and drinking, the curative effect is obviously better than that of Western medicine alone, which can reduce the frequency of acute onset of patients and reduce the risk of disease deterioration.

# 2.2 Pathogenesis, classification, differentiation and treatment of stable stage of COPD

COPD at a mild or stable stage has manifestations of chronic cough, sputum, progressive dyspnea, and other symptoms. The theory of "treating both symptoms, preventing disease and seeking the root of disease" in TCM has irreplaceable advantages for COPD treatment in stable stage. Phlegm turbidity and blood stasis are both pathological consequence and pathogenic factors throughout the development of the disease. The therapy of resolving phlegm and removing blood stasis has also been widely used and clinically achieved good results. According to TCM theory, the main pathogenesis of COPD in stable stage is deficiency, which is the internal condition for the occurrence and development of COPD, and deficiency of lung, spleen and kidney is the root of the disease. The location of COPD is first in the lung, then in the spleen and kidney. Pathological changes in the lungs include that lungs suffer from long-term invasion of exogenous pathogens, lungs are not cleared for long time or no treatment, Lung Qi is damaged, Lung Qi is at deficiency, lung deficiency lasts for a long time or originates from motherhood stealing, lung and spleen are both at deficiency when the disease develops in-depth, then

consumption of kidney Qi eventually leads to lung, spleen and kidney deficiency and dysfunction (16).

#### (1) Bufei Yiqi method:

This method is suitable for lung-qi deficiency syndrome. Clinical manifestations are cough and asthma, or insufficient breath, aggravation of movement, thin sputum, fatigue, sweat, fear of wind, susceptibility to colds, tender tongue, sinking or weak pulse. The prescription can be modified from Ginseng Walnut Decoction and Ginseng Yangfei Pill. Yupingfeng Granule and Huangqi Granule can be used in Chinese patent medicine.

Fan Lingxiang (17) et al. used Huangqi granule to treat 40 COPD patients. The lung function of patients in the treatment group improved significantly (P<0. 05) than that of the long-acting theophylline control group, and more than that before treatment (P<0. 01), indicating that Huangqi granule can significantly improve the lung function and clinical symptoms of COPD patients.

Zhang Kui (18) et al. used Shenqi Bufei Decoction (Astragalus membranaceus, Codonopsis pilosula, Psoralea corylifolia, Salvia miltiorrhiza, Cortex Mori, Radix Baipi and Aster japonicus) in a randomized single-blind clinical trial. Sixty patients with lung-qi deficiency in stable stage of COPD were randomly divided into treatment group and control group and treated for 3 months. The results showed that the total effective rate was 89.66% in the treatment group and 66.67% in the control group. There was a significant difference between the two groups (P<0.05). It suggested that the treatment group could stabilize the pulmonary function of patients, and its effect was better than that of the control group. It the indicated that treatment group could significantly improve the symptoms of stable COPD by adding Shenqi Bufei Decoction based on routine treatment.

## (2) Bufei Jianpi method:

This method is suitable for the syndrome of deficiency of lung and spleen Qi. The clinical

manifestations are cough, asthma, shortness of breath, increased activity, fatigue or spontaneous sweating, bad wind, susceptibility to colds, inadequate diet, fullness of stomach or abdomen, fat tongue, pale coating of tongue, sinking or slow or weak pulse. Liujunzi Decoction and Huangqi Buzhong Decoction can be used with addition or subtraction in prescription medicine. Slow-Zhiguben Granule, Yupingfeng Granule and Jinkexi Capsule can be used in Chinese patent medicine.

He Yingchun (19) randomly divided 98 patients with stable COPD into treatment group and control group. Based on routine treatment, the treatment group was treated with Buzhong Yiqi Decoction plus or minus granules (ginseng, raw angelica, tangerine peel, fangfeng, astragalus, cimicifu. Atractylodes macrocephala, Poria cocos. angelica, yuzhu, sarseng). The control group was treated with placebo. Patients were treated for 6 months, and TCM clinical symptoms, lung function and the frequency of acute attacks were measured. The therapeutic effect of each index in the treatment group was significantly better than that in the control group. The difference was statistically significant. It showed that the method of cultivating soil and generating gold in TCM could reduce the number of acute episodes and improve the quality of life of patients.

# (3) Tonifying Kidney and Benefiting Lung Method:

This method is suitable for lung and kidney Qi deficiency syndrome. The clinical manifestations are pulmonary Qi deficiency accompanied by lumbar and knee weakness, dizziness and tinnitus, urine frequency increasing, or cough and enuresis, pale tongue, fine or weak pulse. Ginseng Bufei Decoction can be used with addition or subtraction in prescription medicine. Gushen Dingchuan Pill, Guben Kechuan Capsule and Bailing Capsule can be used in Chinese patent medicine.

Sun Zikai (19) and others randomly divided 38 patients with stable COPD into treatment group and

control group. They were given Yishen Guben Decoction (composed of Ziheche, Cancun, Gecko. Purple Quartz, Angelica sinensis, Dangshen, Radix Codonopsis, Radix Ophiopogonis, Radix Salviae Miltiorrhizae, Tulip, Flos Fagopyrum, Fructus Schisandrae, etc.) and Guben Kechuan Tablets, respectively. The results showed that the curative effect of treatment group was better than that of control group in clinical symptoms and lung function. It suggest that this prescription may improve lung function and immunity, and alleviating the development of COPD.

# (4) Activating blood circulation and removing blood stasis:

This method is suitable for blood stasis syndrome. Stagnation of phlegm and blood stasis is an important pathogenesis of pulmonary distention. The clinical manifestations of patients with long-term illness are purple and dark complexion, blue and purple tongue or ecchymosis, chest distress and painful pulse. Xuefu Zhuyu Capsule can be used in Chinese patent medicine.

Li Jisheng (21) et al. treated 100 patients with pulmonary distention with Xuefu Zhuyu Decoction (peach kernel, safflower, angelica, Rehmannia root, Ligusticum chuanxiong, red peony root, Achyranthes bidentata, Platycodon grandiflorum, bupleurum, Fructus aurantii, licorice). The results showed that the effective rate was 85.0% . This method could remove blood stasis in chest, smooth Qi and blood and improve lung function.

Liu Xin (22) used Mailuoning (Radix Scrophulariae, Achyranthes bidentata, Corydalis Yanhusuo) to treat 50 COPD patients with hyperviscosity. Results showed that the hemorheological parameters in the treatment group were significantly improved from those in the control group, which indicated that Mailuoning had a better therapeutic effect on COPD patients with hyperviscosity.

The treatment of COPD in stable stage should be based on the difference of disease location, deficiency and excess of pathogenic factors. After dialectical treatment, the methods of tonifying Qi and deficiency, tonifying lung, tonifying lung and spleen, tonifying lung and kidney, activating blood circulation and removing blood stasis can be used to improve the body's defensive function, dispel pathogenic factors and correct symptoms, reduce the frequency of acute attack, slow down the progressive decline of lung function, and improve the quality of life of patients.

#### 2. 3 Perennial Roots of COPD: Internal Phlegm

COPD recurrence for a long time will lead to lung, spleen and kidney deficiency, so that lung deficiency leads to abnormal application of fluid; spleen deficiency leads to abnormal transportation of water and dampness; kidney deficiency leads to abnormal warm water and dampness. Accumulation of dampness may be transformed into phlegm, which provides a pathological basis for the pr oduction of phlegm, so that the underlying phlegm becomes the "permanent root "of COPD.

Blood stasis may occur when blood circulation is not smooth, or even stagnates and coagulates; or the blood accumulates in the body after menopause. In the process of COPD recurrence, it will inevitably consume the human body's vital energy, causing the deficiency of vital energy, which leads to the weak blood movement, endogenous blood stasis. The heart governs blood, the lungs are facing hundreds of blood vessels and their joints, and the lungs can help the heart to regulate the blood movement.

Based on the above theory, some physicians have always considered COPD differentiation and treatment by removing blood stasis and resolving phlegm based on syndrome. For example, Wu Weiping (23), according to the pathogenesis of Qi deficiency, blood stasis and phlegm obstruction in COPD stable period, has achieved satisfactory curative effect by using Chinese herbal medicine of invigorating Qi, activating blood circulation and resolving phlegm. Hong Guangxiang (24) believed that COPD was based on Phlegm and yin, phlegm

and blood stasis, and phlegm and blood stasis were closely related to lung-yang deficiency. He proposed that the onset of COPD should be "expelling phlegm and blood stasis, supplemented by warming yang". In the remission period, deficiency and excess should be treated together, and warming yang and invigorating Qi should dissipate phlegm and blood stasis.

### 3. Prospect of TCM treatment of COPD

A large number of clinical studies have proved that TCM treatment of COPD can alleviate clinical symptoms, enhance the patient's physique, reduce AECOPD, and improve the quality of life. TCM treatment of COPD has unique advantages, extremely important clinical significance, and is very necessary and effective.

At present, there are still some problems in the treatment of COPD by TCM, such as the lack of standardized mechanism research or longitudinal and in-depth study of its mechanism due to the current technical means, and the lack of standardized and unified evaluation of its clinical effect. How to reasonably choose the appropriate treatment plan for patients based on syndrome differentiation is a problem that should be studied further. In the future, the direction of TCM treatment for COPD should be oriented to improving patients' quality of life, nutritional status and restoring lung function.

### **Declarations**

1) Consent to publication

We declare that all authors agreed to publish the manuscript at this journal based on the signed Copyright Transfer Agreement and followed publication ethics.

- 2) *Ethical approval and consent to participants* Not applicable.
- Disclosure of conflict of interests
  We declare that no conflict of interest exists.
- 4) Funding

None

#### 5) Availability of data and material

We declare that the data supporting the results reported in the article are available in the published article.

6) Authors' Contributions

Authors contributed to this paper with the design (CHP and ZQL), literature search (CHP and GX), drafting (CHP), revision (ZQL), editing (GX) and final approval (CHP).

- 7) *Acknowledgement* None
- 8) *Authors' biography* None

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