

# *Research Progress of Traditional Chinese Medicine Internal Treatment for Acute Phase COPD Disease*

Liu Miaoyu<sup>1,a</sup>, Ma Zhanping<sup>2,b,\*</sup>

<sup>1</sup>*Shaanxi University of Chinese Medicine, Xiayang, Shaanxi, 712046, China*

<sup>2</sup>*Pulmonary Disease Department, Shaanxi Provincial Hospital of Chinese Medicine, Xi'an, Shaanxi, 710003, China*

*<sup>a</sup>1601667943@qq.com, <sup>b</sup>2284976513@qq.com*

*\*Corresponding author*

**Keywords:** Chinese medicine internal treatment; acute phase; COPD disease

**Abstract:** Acute exacerbation of chronic obstructive pulmonary disease (COPD) is an important course of COPD and an important cause of death in COPD patients. In recent years, traditional Chinese medicine (TCM) has done a lot of explorations and researches in the treatment of acute exacerbation of COPD, and compared with the conventional treatments of Western medicine, the treatment of TCM has more significant efficacy in the improvement of patients' clinical symptoms, lung function and quality of life. In this paper, we searched the clinical studies on the treatment of acute exacerbation of chronic obstructive pulmonary disease (COPD) by traditional Chinese medicine (TCM) in the past 10 years, and elaborated on the etiology and pathogenesis of COPD, identification and typing of COPD, and therapeutic methods, and summed up the rules of TCM medication in the prevention and treatment of acute exacerbation of COPD, so that we can provide clinical ideas and theoretical guidance for the treatment of acute exacerbation of COPD by TCM in the future.

## **1. Introduction**

Chronic Obstructive Pulmonary Disease (COPD), abbreviated as chronic obstructive pulmonary disease (COPD), is characterised by airflow limitation and persistent respiratory symptoms, and is a common and frequent disease in respiratory medicine. Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) refers to an acute event characterised by a sharp worsening of respiratory symptoms, mainly worsening of cough and/or sputum, or even dyspnoea, occurring within a short period of time in patients with COPD, and patients need to be treated aggressively in order to reduce their mortality rate, improve their prognosis, and prevent complications [1]. The GOLD report states that the hospitalisation rate of AECOPD GOLD reports that the mortality rate of patients hospitalised with AECOPD is about 50% within 5 years, which is an important cause of death in COPD patients. At present, in clinical practice, Western medicine for AECOPD is still based on oxygen, anti-infection, hormone anti-inflammatory, bronchodilatation, phlegm and cough suppression as the main therapeutic measures, which can improve the symptoms of wheezing and coughing to a certain extent, but cannot effectively prevent the progression of the disease, and the

clinical effect is not good. In recent years, Chinese medicine has been widely used in the treatment of AECOPD, and has achieved more satisfactory therapeutic effects in improving lung function, reducing inflammatory response, and regulating body immunity; therefore, this paper now reviews the current research status of Chinese medicine internal treatment for AECOPD in recent years.

## **2. Research on the etiology and mechanism of AECOPD**

### **2.1. Ancient physicians' understanding of the etiology and mechanism of AECOPD**

Ancient texts describe "cough", "phlegm", "lung distension" and "wheezing" as similar to COPD, but the name "lung distension" was first mentioned in the "Ling Shu - The Treatise on Distension": "The lung distension is full of deficiency and wheezing", suggesting that the typical symptoms of lung distension are wheezing and coughing. COPD records, but the name of lung distension first appeared in the "Ling Shu - distension theory": "lung distension, fullness and wheezing cough", suggesting that the typical symptoms of lung distension is wheezing, coughing, the onset of lung deficiency due to long-term illness, phlegm stasis, obstructing lung qi, resulting in lung loss of ventilation and lowering, lung qi distension and fullness, compounded by the external evils, the evils lead to the evils, the recurrence of the disease, and the condition is gradually aggravated. It is pointed out that cold and heat are the causes of the disease. In the Treatise on Miscellaneous Diseases of Typhoid, there is a statement that "the person who is asthmatic and agitated in the upper air belongs to the lung distension, and he wants to be in the wind and water, and he will be cured if he sweats". Another "lung distension, coughing and gas, irritability and wheezing, floating pulse, water under the heart, small Qinglong plus gypsum soup main". They all believe that the wind-cold evil for its cause, drink stop in the internal, Yu long into heat, congestion of lung qi caused by lung distension. Origin and Criteria of Diseases" in "Typhoid Miscellaneous Diseases" on the basis of the proposed lung qi deficiency is the internal cause of lung distension, lung declination disorder, airway unfavorable to the upward reversal of gasping, such as "coughing disease caused by the lung deficiency and micro-cold. To the Yuan Dynasty, Zhu Danxi put forward the phlegm with blood stasis obstruction of qi for lung distension mechanism, such as "Danxi Xinfu" cloud: "lung distension and cough, or left or right, cannot sleep, this phlegm with blood stasis obstruction of qi and disease". Since then, it has been basically determined that the deficiency of lung qi is the internal factor, cold and heat evil is the causative factor, while retained fluid and phlegm stagnation are the pathological factors. Zhang Congzheng put forward "Heat evil exists in the body, leading to the onset of lung distension". Wu Kun also put forward that lung damage is caused by lung dryness, lung heat, autumn-dryness and so on, which can also be due to inadequate health care. Lung deficiency, cold and heat of the evil, positive and evil fight, between the wind and water stop, or phlegm and drink stagnation, or phlegm stasis obstruction, or wind and temperature and heat, gas gathered in the lungs, inverse in the upper, coughing and shortness of breath, chest fullness, stuffy, or even cyanosis of the lips and nails, palpitations and swelling and other symptoms.

### **2.2. Modern medical doctors' understanding of the etiology and mechanism of AECOPD**

Modern medical doctors generally believe that feeling external evil is the external cause of AECOPD attacks, exposure to harmful gases and overeating grease, seafood, etc. will affect the lung qi purging and lowering, internal and external correlation leads to acute attacks of cough and asthma. Hong Guangxiang, a master of national medicine, believes that the external evil that triggers AECOPD is cold, weak yang qi, wind and cold directly in the middle of the body, which attracts persistent phlegm, and internal and external combination of evils leads to the disease [2]. Professor Liu Xiaohong, a famous traditional Chinese medicine practitioner in Guangdong Province,

believes that patients mostly have phlegm first and then stasis, and phlegm and blood stasis breed each other and cause each other's problems, and stasis and blood stasis become heat after a long period of time, forming other variations of the disease [3]. Director Qin Dongfeng, a famous Chinese medicine practitioner in Shandong Province, believes that AECOPD manifests mostly as phlegm-heat embracing the lungs, which is due to the patient's phlegm and stasis obstruction, and the lung qi stagnation and closure of lung qi when he is exposed to wind-cold, and the stagnation of lung qi turns to heat, or the exposure to wind-heat, or his phlegm-heat physique [4]. Lv Hua, a famous veteran Chinese medicine practitioner, believes that the pathogenesis of AECOPD should be a mixture of deficiencies and realities, with external evils triggering phlegm, stagnation of lung qi, and insufficient excretion of lung qi, which in the long term will lead to the kidneys not receiving qi and the reversal of deficiency qi [5].

### **3. Identification and treatment study**

#### **3.1. Diagnosis and typing**

At present, there is no uniform standard for the distribution of AECOPD syndromes, but most researchers summarize them through statistical analysis: acute exacerbation: qi deficiency and blood stasis; phlegm-heat depressing the lungs, qi deficiency and blood stasis; phlegm turbid embedding in the lungs, qi deficiency and blood stasis; phlegm and turbid embedding in the lungs, yin deficiency and blood stasis; heat and phlegm attaching to the lungs, qi and yin; phlegm and blood stasis obstructing the lungs, spleen and kidney yang deficiency; water and dampness flooding the lungs, yin deficiency of liver and kidney; phlegm clouding the orifices of the heart. The diagnosis and treatment is the characteristic of TCM diagnosis and treatment, and the diagnosis and typing according to the patient's symptoms is more macroscopic and comprehensive. In the International Clinical Practice Guidelines for Chinese Medicine: Chronic Obstructive Pulmonary Disease [6], AECOPD is classified into five types: wind-cold attacking the lungs, external cold and internal drinking, phlegm-heat depressing the lungs, phlegm-dampness obstructing the lungs, and phlegm clouding the mind and orifices, and blood stasis is often included in these types. According to statistical analysis, phlegm congestion of the lungs, phlegm-heat in the lungs, phlegm-blood stasis and phlegm-kidney qi deficiency are the most common clinical types of AECOPD, especially in elderly patients and those with a long course of the disease, who are more likely to have lung-kidney qi deficiency and phlegm-blood stasis and lung obstruction. Phlegm, heat, stasis and deficiency are always the key factors running through each syndrome.

#### **3.2. Traditional Chinese Medicine (TCM)**

Chinese medicine treats both the symptoms and the root of the disease, and favors the relief of the symptoms and the root of the disease. If the symptoms are solid, the treatment should be to dissolve phlegm and calm asthma, activate blood circulation and remove blood stasis, warm yang and benefit water, dispel evil spirits and promote the lungs, or even to open up the orifices and extinguish the wind. For those who are deficient, they should nourish the heart and lungs, benefit the kidneys and strengthen the spleen, or regulate both qi and yin, or take care of both yin and yang; for those who want to lose their positive qi, they should support the positive and solidify the loss of yin and yang, and save the yin and return to the yang. In addition, some scholars put forward the idea of "lung and collaterals", they believe that the pathogenesis of COPD is mostly "lung deficiency and collaterals stasis" or "lung damage and collaterals injury", etc., and in the treatment of COPD, it is mostly taken as "treatment by collaterals". They believe that the pathogenesis of COPD is mostly "lung deficiency and collateral stasis" or "lung damage and collateral injury", etc.,

and that the treatment of COPD is mostly based on the treatment method of "treating by collateral". Generally speaking, whether from the perspective of the symptoms, or from the perspective of the pathogenesis of "lung collateral damage" and "upward reversal of lung qi", the so-called treatments are no more than two kinds of methods: conventional Chinese medicine, i. e., traditional Chinese medicinal tonics, but there are some medical practitioners who use acupoint compresses and other external Chinese medical treatments, such as acupuncture and cupping, and have achieved good results. But there are also doctors who use acupoints and other external treatments such as acupuncture and cupping, and have achieved good results.

### **3.3. Internal Treatment**

#### **3.3.1. Warming the Lungs and Resolving Drinks**

Zhang Zhongjing of the Eastern Han Dynasty and Gong Tingxian of the Ming Dynasty, respectively, in the "Essentials of the Golden Chamber", "Shou Shi Baoyuan - phlegm asthma", "the disease of phlegm, when the warm medicine and the", "lung distension and gasping fullness, diaphragm high gas, salivary congestion and cold, " are suggestive of the occurrence of this disease and the cold, phlegm, water, drink, the evil of the lung shot Since then, many generations of physicians have also believed that external cold and internal drinking is one of the important causes of acute exacerbation of chronic obstructive pulmonary disease (COPD). Zheng Jie et al. [7], through the study of ancient texts and clinical observation, believed that the acute exacerbation of COPD is mainly caused by "weak qi and yang, and phlegm and stasis in the lungs", and put forward the diagnostic and therapeutic point of view of "treating the lungs is not far from the warmth". Zhong Lianjiang et al. [8] concluded that Xiaoqinglong Tang combined with western medicine in the treatment of AECOPD can significantly lower calcitoninogen, increase the level of partial pressure of blood oxygen, and effectively improve respiratory function. Liu Hongxiang et al. [9] and Wang Lu et al. [10] clinically applied Xiaoqinglong Tang with additions and subtractions, which improved the Chinese medicine evidence, inflammatory factor levels, and lung function significantly, and hospitalisation time and cost were significantly reduced. Other formulas also have good efficacy in externally cold internal drinking evidence. Qu Leilei et al. [11] applied warming lung and dispersing cold to cleanse the drink soup combined with bladder meridian ginger therapy to treat patients, and its clinical effect was significant and more acceptable to patients.

#### **3.3.2. Method of drying dampness and resolving phlegm**

Phlegm and water retention is one of the pathological factors leading to AECOPD exacerbations. Chang Liang [12], Huang Xueyuan [13], Luo Zhaohu et al. [14] used random grouping method to treat patients with AECOPD phlegm turbidity and lung obstruction evidence by using the method of drying dampness and resolving phlegm in combination with Western medicine and Western medicine alone, respectively, and found that patients in the treatment group showed improvement in blood gas analysis, lung function, even distribution of intestinal flora, and the total effective rate was significantly improved. Huang Feifei et al. [15] self-prepared expectorant and lung-relieving soup had significant effects in improving patients' lung function, Chinese medicine signs and symptoms, and airway inflammation. Jiao Yazheng [16] applied Sizi Warm Lung Soup from warm discrimination, and the patient's symptoms of nausea, epigastric distension, shortness of breath, and mucus in the mouth were improved, and airway inflammation and mucus hypersecretion were improved by regulating the expression of serum interleukin-17A (IL-17A) and hypoxia-inducible factor-1 $\alpha$  (HIF-1 $\alpha$ ), and the patients were found to have significant improvement in the indexes of lipid metabolism after the treatment. Du Yibin et al. [17] treated AECOPD phlegm-heat-depleted

lung evidence with Jiawei Sangpi Tang combined with western medicines with remarkable effect, and the evidence efficacy and various symptom scores of the treatment group were better than those of the western medicine group after treatment, and the difference was statistically significant ( $P < 0.05$ ). Yang Cui et al. [18] studied the fish Baisang Cough Relieving Formula combined with western medicines to treat this evidence, compared with only western medicine treatment, can significantly reduce the number of days of fever, and the number of days of antibiotic use, and has a better clinical safety.

### 3.3.3. Method of clearing heat and resolving phlegm

In Danxi Xinfa, there is: "When qi is depressed, it generates dampness; when dampness is depressed, it becomes heat; when heat is depressed, it becomes phlegm; when phlegm is depressed, it does not work on blood; when blood is depressed, it does not transform food; the six are related because of the disease." This suggests that Qi stagnation leads to dampness, while prolonged dampness leads to heat. And heat fries body fluid to produce phlegm and dampness, which can produce phlegm and heat over time. It can ultimately affect the circulation of qi and blood, forming a vicious cycle. Early scholars Hua Wenshan [19] treated 60 cases of AECOPD phlegm-heat-depleted lung evidence with flavour-added Ma Xing Shi Gan Tang, and the results showed that the patients' symptoms such as wheezing, chest tightness and shortness of breath, coughing, sputum, croup, and rales improved significantly. It indicates that flavoured Ma Xing Shi Gan Tang can alleviate patients' symptoms, improve the amount of clear air entry, strengthen the effect of oxygen exchange in the lungs, increase the blood oxygen saturation, and improve patients' lung function. Chu Yahong et al. [20] pointed out through research that Sangbai Pi Tang has advantages in suppressing cough and calming asthma, especially in cough, cough and phlegm, wheezing control. The method of clearing heat and resolving phlegm is a common treatment for phlegm-phlegm-heat obstruction of the lungs in the symptomatic form, and the patient is characterised by coarse coughing and wheezing, fullness of the chest and fever, sticky and yellowish phlegm, distended and protruding eyes, and telangiectatic respiration. Subsequently, Liu Miao et al. [21] used a randomised grouping method to treat patients with AECOPD phlegm-heat-depleted lung type with Xuanbai Chengqi Tang, and found that lung function, partial pressure of oxygen, cytokine levels, and oxidative/antioxidant indices of patients in the treatment group improved significantly compared with those in the control group. Li Tan [22], Liu Xing [23], and Chen Ning et al. [24] demonstrated in clinical studies that combining the method of clearing heat and resolving phlegm on the basis of conventional Western medicine treatment for AECOPD had better efficacy in improving clinical symptoms and controlling infections. Zhong Xiujun et al. [25] applied Xiaoqinglong Tang plus flavour to reduce the expression of sputum mucin 5AC (MUC5AC) in patients, dilute sputum, reduce sputum volume, and alleviate the effect of mucus hypersecretion on patients. Jinfa et al. [26] applied Reed Stem Soup plus flavour to regulate the immune balance of the patient's body, the levels of immune factors CD4+, IFN- $\gamma$ , IFN- $\gamma$ /IL-4 increased, and the levels of CD8+, CD4+ CD25+ Treg, and IL-4 were reduced, so as to control inflammatory reactions of the body. Chen Wei et al. [27] demonstrated that Shufeng detoxification capsule attenuated airway inflammatory response by regulating the levels of serum inflammatory factors soluble myeloid triggering receptor- (sTREM-1), human chondrocyte glycoprotein-39 (YKL-40), alveolar surface-active protein (SP-D), and fibrinogen (Fib).

### 3.3.4. Methods for promoting blood circulation and removing blood stasis

Chinese medicine believes that the relationship between the lung and blood stasis is very close, Yuan - Zhu Danxi in the "Danxi Xinfa - Cough" expression that the onset of lung distension is



caused by phlegm and blood stasis condensation, obstructing the qi mechanism. The method of activating blood and removing blood stasis is one of the common treatments for the stasis and blood obstruction of the lungs syndrome, which is mostly seen in patients with a long course of chronic obstructive pulmonary disease and prolonged disease into the collaterals, which can be seen as cyanosis of the mouth and lips and stabbing pain in the chest, and is mainly composed of medicines for activating blood and removing blood stasis, such as peach kernel and dillon. Deng Jianying et al. [28] pointed out by analysing the data of 58 cases of AECOPD clinical patients that Yiqi activating blood and removing blood stasis soup has the effect of activating blood and removing blood stasis, relieving cough, calming asthma and removing phlegm, and the results of the blood gas analysis as well as the lung function indexes of patients with acute exacerbation of chronic obstructive pulmonary disease improved significantly, and the quality of life was improved significantly. Ni Haibin et al. [29] believed that by improving the microcirculation of alveoli, interstitium and fine bronchioles, blood-fu and blood-stasis-expelling soup can increase the local tissue concentration of anti-infective drugs, which can help to improve the local resistance of lung tissues, enhance the effectiveness of anti-infection, and make the window of control of lung infections appear in advance, which can effectively shorten the time of antibiotic use. Wang Wei et al. [30], by studying from the perspective of molecular pathology, concluded that micro-impediments in the lungs are the basic etiological mechanism of chronic obstructive pulmonary disease, and the causes of its formation mainly include the invasion of external evils that depletes the vital energy of the lungs, loss of nourishment in the veins and channels, condensation of fluid and phlegm, as well as stagnation of blood and stagnation of the toxin in the veins and channels. Li Changan [31] applied Haifu yuyu Tang and Er Chen Tang to significantly reduce serum fibrinogen (FBG) and D-dimer, and increase prothrombin time (TT) and prothrombin time (PT) in patients. Benefiting qi, resolving phlegm and eliminating blood stasis formula can also improve the fibrinolytic imbalance by regulating tissue plasminogen activator (t-PA)/plasminogen activator inhibitor-1 (PAI-1) balance. Wang Ailin [32] found that the combination of Western medicine and traditional Chinese medicine could improve the clinical symptoms, lung function and blood gas analysis values of patients with AECOPD by adding blood-activating drugs to Ling Gui San Zi Nourishing Relative Soup, and the safety of the treatment was high.

### **3.3.5. Lung tonifying and kidney benefiting method**

Liu Juan [33] applied the addition and subtraction of Pianpangguoben Tang and Lung Complementary Tang to treat patients with lung and kidney qi deficiency in AECOPD, and the lung function was further improved on the basis of the conventional western medical treatment. Liang Shiqin et al. [34] based on the Chinese medicine theory of "the lung and the large intestine are mutually exclusive", clinically applied Yu Nu Decoction enema to treat Yin deficiency and internal heat syndrome, and the patients' inflammatory factors, CCQ scores, and clinical efficacy were all significantly improved. Shen Mengyue et al. [35] applied Zhenwu Tang combined with Wu Ling San to treat Yang deficiency and water flooding syndrome, and the patients' quality of life mMRC scores, CAT scores, coughing phlegm, chest tightness, palpitations, and dysuria were all improved, and the rate of rehospitalisation was reduced within 1 year. Zhang Peng [36] applied Sang Bai Pi Tang to treat phlegm-heat and kidney deficiency syndrome, which significantly improved patients' pulmonary blood flow dynamics and reduced lung inflammation. The efficiency was as high as 94%. Hong Shihai et al. [37] used a poultice formula for tonifying the kidney, benefiting the lungs and strengthening the spleen (Huang Astragalus, Codonopsis, mealybugs, honey, maitong, perilla seeds, Atractylodes macrocephala, Schisandra chinensis, Chinese yam, Fagus sempervirens, bitter almonds, loquat leaves, yucca, fritillaria, tangerine peel, rock sugar, Cornus officinalis, Colla Cornu Cervi, Colla Corii Asini, Deer's horn gelatine) in treating this syndrome, which can effectively

regulate the activity of T-cell subpopulations and NK-cells as well as serum immunoglobulins, in order to enhance the immune function of the organism. Wu Longchuan et al. [38] treated this syndrome with an in-hospital preparation of Lung Replenishing and Kidney Benefiting Formula (Red Ginseng, Astragalus, Epimedium, Cornus officinalis, Radix et Rhizoma Dioscoreae) with remarkable effects, and based on network pharmacological analysis and molecular docking validation, concluded that its mechanism of action may be related to improving airway remodelling and airway mucus hypersecretion, modulating immune-inflammatory responses, inhibiting protease/antiprotease imbalance, and antioxidant.

### 3.3.6. Through the bowels and diarrhoea method

According to the theory that the lungs and the large intestine are mutually exclusive, the method of "through the bowels and diarrhoea" restores the purging and descending function of the lungs and achieves the effect of suppressing cough and calming asthma. Chen Xiaohui et al. [39] pointed out that by summarising the relevant literature in recent years, the method of Tongzhi diarrhoea can significantly improve the simultaneous function of patients with acute exacerbation of COPD, enhance gastrointestinal peristalsis, promote defecation or excretion, reduce abdominal pressure, increase the amplitude of the chest muscle movement, improve the respiratory function of the patient, improve the partial pressure of oxygen, increase pulmonary ventilation, improve the lung's ventilation, promote the metabolism of the organism, improve microcirculation, and stimulate the alveoli to increase the secretion of macrophages, thus improving the alveolar function. Macrophages to secrete more, thus improving the immunity of the lungs. Ye Siwen et al. [40] used peach kernel Chengqi enema liquid to treat patients with phlegm stasis and lung obstruction in the acute exacerbation of COPD, and the results of the study showed that peach kernel Chengqi enema liquid could significantly reduce PaCO<sub>2</sub>, increase PaO<sub>2</sub>, improve gastrointestinal function, and effectively improve the clinical symptoms of patients with phlegm stasis and lung obstruction in the acute exacerbation of COPD.

## 4. Summary

In summary, COPD is a respiratory disease with high prevalence and mortality. Because of its recurrent exacerbations, progressive aggravation, and its high hospitalisation costs, the prevention and treatment of COPD has become one of the main difficulties in clinical work. Currently, Western medicine has a single treatment method, which can temporarily relieve symptoms during acute exacerbation, but further aggravate the patient's condition after repeated use of antibiotics, hormones and other treatments. Chinese medicine treatment of AECOPD is rich and varied, with precise efficacy, which makes up for the shortcomings of conventional treatment in western medicine. In recent years, Chinese medicine has been effective in treating pulmonary distension under the guiding principles of holistic concept and evidence-based treatment, and side effects and adverse reactions are rare; it has played its unique advantages in improving patients' lung function and blood gas analysis indexes, lowering the frequency of acute exacerbations, prolonging the stable period of COPD, and improving the quality of life in many aspects. However, there are still some shortcomings in TCM treatment, firstly, due to its obvious individualised treatment characteristics, there are some differences in the identification and typing of AECOPD, which still cannot be completely unified and need to be further explored; secondly, most of the TCM treatments are based on the summary of experts' clinical experience and single-centre studies, and the level of experimental research should be further improved and the sample size should be increased for multi-centre clinical trial studies.

## References

- [1] López-Campos J L, et al. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease 2019 Report: Future Challenges [J]. *Archivos de Bronconeumología*, 2020, 56(2):65-67.
- [2] Chen Xuan, Gong Di, Huang Huai, et al. Expert consensus and operational guidelines on exercise rehabilitation of chronic obstructive pulmonary disease with integrating traditional Chinese medicine and Western medicine [J]. *Journal of thoracic disease*, 2021, 13(6):3323-3346.
- [3] Huang Aisi, Zhan Shaofeng, Zhang Tiange, et al. Introduction on clinical experience of professor Liu Xiaohong in the treatment of chronic obstructive pulmonary disease [J]. *China Medical Herald*, 2019, 16(27):151-154.
- [4] Ren Yuehong, Qin Dongfeng. The Experience of Qin Dongfeng in Treating Acute Exacerbation Chronic Obstructive Pulmonary Disease with Haibei Pingchuan Decoction [J]. *Guangming Journal of Chinese Medicine*, 2020, 35(14): 2143-2145.
- [5] Ma Jiarong, et al. Lv Hua's Experiences of Opening and Discharging Method in Treating Chronic Obstructive Pulmonary Disease [J]. *Journal of Shandong University of Traditional Chinese Medicine*, 2017, 41 (3):238-241.
- [6] Li Jiansheng, Yu Xueqing, Xie Yang. International Clinical Practice Guideline of Chinese Medicine Chronic Obstructive Pulmonary Disease [J]. *World Chinese Medicine*, 2020, 15(7):1084-1092.
- [7] Zheng Jie, et al. Clinical study of "treating lungs not far from warmth" in acute exacerbation of chronic obstructive pulmonary disease (COPD) [J]. *Jiangxi Journal of Traditional Chinese Medicine*, 2000, 31(6):20-22.
- [8] Zhong Lianjian, et al. Procalcitonin impact analysis, respiratory function and blood gas analysis on Xiaoqinglong decoction combined with non-invasive ventilation in treatment of AECOPD patients [J]. *Zhongguo Zhong yao za zhi = Zhongguo zhongyao zazhi = China journal of Chinese materia medica*, 2018, 43(14):3026-3030.
- [9] Liu Hongxiang, Zhao Yongchen, Wang Tao, et al. Sequential Therapy of Acute Exacerbation of Chronic Obstructive Pulmonary Disease with Syndrome of External Cold and Internal Fluid with Classical Prescriptions [J]. *Acta Chinese Medicine*, 2019, 34(7):1506-1510.
- [10] Wang Lu, Tian Rong, Zhou Wei. Clinical Study on Modified Xiao Qing Long Decoction and Cong Long Decoction for Acute Exacerbation of Chronic Obstructive Pulmonary Disease in Elderly Patients [J]. *World Journal of Integrated Traditional and Western Medicine*, 2020, 15(5):907-910.
- [11] Qu Leilei, Zhang Hengzhong, Yang Rui, et al. Clinical Study on Wenfei Sanhan Diyin Tang Combined with Ginger Therapy on the Bladder Meridian for Acute Exacerbation of Chronic Obstructive Pulmonary Disease [J]. *Journal of New Chinese Medicine*, 2019, 51(10):103-106.
- [12] Chang Liang. Clinical observation on treating COPD in TCM medicine [J]. *Clinical Journal of Chinese Medicine*, 2015, 7(23):75-76.
- [13] Huang Xueyuan, et al. The Effects of Kuanxiong Lifei Decoction Combined with Sanzi Yangqin Decoction on Pulmonary Function and serum Inflammatory Cytokines in Elderly Patients with Acute Exacerbation of Chronic Pulmonary Disease [J]. *Journal of Emergency in Traditional Chinese Medicine*, 2015, 24(12):2109-2112.
- [14] Luo Chaohu, Wu Zongjin, Hua Haihu, et al. Clinical observation of invasive mechanical ventilation in acute exacerbation of chronic obstructive pulmonary disease treated with Er Chen Tang combined with San Zi Nourishing Family Soup [J]. *Nei Mongol Journal of Traditional Chinese Medicine*, 2020, 39(5):20-21.
- [15] Huang Feifei, Zhang Ronggui. Effect of modified Qutan Lifei Decoction on cough, asthma and serum inflammatory factors in acute exacerbation of chronic obstructive pulmonary disease [J]. *World Journal of Integrated Traditional and Western Medicine*, 2020, 15(3):532-534+538.
- [16] Jiao Yazheng. Effect of Sizi Wenlong Tang on the expression of serum IL-17A and HIF-1 $\alpha$  in patients with acute exacerbation of chronic obstructive pulmonary disease [J]. *Yunnan Journal of Traditional Chinese Medicine and Materia Medica*, 2019, 40(2):52-53.
- [17] Du Yibin, et al. Clinical Observation of Modified Sangpi Tang Combined with Western Medicine for AECOPD with the Syndrome of Phlegm-Heat Obstructing Lung [J]. *Journal of New Chinese Medicine*, 2017, 49(4):25-28.
- [18] Yang Cui, Sun Liming, Jin Yang, et al. Evaluation on clinical efficacy of Yubaisang decoction on AECOPD with syndrome of stagnation of phlegmheat in lung and its influence on therapeutic time of antibiotic [J]. *International Journal of Respiration*, 2018, 38(16):1225-1230.
- [19] Hua Wenshan. The clinical observation of Modified Ephedra Apricot Gypsum and Licorice Decoction in treatment of AECOPD [D]. Nanjing University of Chinese Medicine, 2017.
- [20] Chu Yahong, Zhang Baoxia. Effects of Sangbaipi Decoction combined with western medicine in treatment of AECOPD in 39 patients [J]. *Medical Journal of National Defending Forces in Southwest China*, 2017, 27(8):882-884.
- [21] Liu Miao, Zhong Xianggen, Li Yuhang, et al. Xuan Bai Cheng Qi formula as an adjuvant treatment of acute exacerbation of chronic obstructive pulmonary disease of the syndrome type phlegm-heat obstructing the lungs: a multicenter, randomized, double-blind, placebo-controlled clinical trial [J]. *BMC complementary and alternative medicine*, 2014, 14(1):239.
- [22] Li Tan, Zhang Xiaoyue, Xu Min, et al. Effects of Qingjin Huatan Decoction in Treating acute Exacerbation of



- Chronic Obstructive Pulmonary Disease on the Clinical Efficacy, Inflammatory Response and Airway Mucus Hyper Secretion [J]. Clinical Journal of Traditional Chinese Medicine, 2020, 32(4):781-786.*
- [23] Liu Xing, Hou Yunxia, Zhang Hongyan. *Modern Journal of Integrated Traditional Chinese and Western Medicine [J]. Modern Journal of Integrated Traditional Chinese and Western Medicine, 2017, 26(34):3858-3860+3864, 3865.*
- [24] Chen Ning, Li Hui, Zhao Liyun, et al. *Therapy for clearing heat and resolving phlegm in treatment of systemic inflammatory response syndrome in acute deterioration stage of chronic obstructive pulmonary disease:a randomized controlled trial [J]. Journal of Chinese Integrative Medicine, 2009, 7(2):105-109.*
- [25] Zhong Xiujun, Xu Wei, Wang Zhen, et al. *The Effect of Juanyin Xiefei formula on Airway Mucus Hypersecretion in Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease [J]. World Journal of Integrated Traditional and Western Medicine, 2021, 16(3):410-414+421.*
- [26] Jin Fa, Zhang Xiaojuan, A liya, et al. *Study on Effect of Weijing Decoction on Inflammatory and Immune Factors in Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease [J]. Chinese Archives of Traditional Chinese Medicine, 2021, 39(9):204-207.*
- [27] Chen Wei, Zhang Nianzhi. *Effects of Shufeng Jiedu Capsule on sTREM-1, YKL-40, SP-D and Fib in patients with acute exacerbation of chronic obstructive pulmonary disease [J]. China Journal of Traditional Chinese Medicine and Pharmacy, 2021, 36(2):1171-1174.*
- [28] Deng Jianying, Zeng Yiju, Wang Taili. *Clinical Efficacy of Yiqi Huoxue Huayu Decoction for AECOPD [J]. Chinese Journal of Experimental Traditional Medical Formulae, 2014, 20(22):193-196.*
- [29] Ni Haibin, Liu Keqin, Zhang Xiaozhen. *Effect of Xuefu Zhuyu Decoction on Pulmonary Infection Control Window in Patients with AECOPD Complicated by Pulmonary Hypertension [J]. Journal of Emergency in Traditional Chinese Medicine, 2016, 25(3):405-407.*
- [30] Wang Wei, Wang Qi, Wu Haibin, et al. *The explanation of molecular pathology of micro-zhengjia in feiluo with COPD [J]. Global Traditional Chinese Medicine, 2016, 9(8):946-949.*
- [31] Li Chang'an. *Clinical Research of Using Xuefu Zhuyu Decoction Combined with Erchen Decoction in the Treatment of Acute Exacerbation of Chronic Obstructive Pulmonary Disease with Phlegm Stasis Blocking Lung Syndrome [J]. Journal of Sichuan of Traditional Chinese Medicine, 2021, 39(1):60-64.*
- [32] Wang Ailin, Wu Hongyan, Ma Chunlin. *Clinical Study of Ling Gui San Zi Decoction in Treating Acute Exacerbation of Chronic Obstructive Pulmonary Disease (Phlegm and Blood Stasis Type) [J]. Lishizhen Medicine and Materia Medica Research, 2019, 30(7):1651-1653.*
- [33] Liu Juan. *The Therapeutic Effect of Pingchuan Guben Decoction and Bufei Decoction on Patients with Chronic Obstructive Pulmonary Disease of Lung and Kidney Qi Deficiency Type [J]. Chinese and Foreign Medicine Research, 2020, 18(20):45-47.*
- [34] Liang Shiqin, Zhang Jilei, Ye Yan, et al. *Effects of Yunvjian retention enema combined with comprehensive intervention of Western medicine on inflammatory indices and CCQ scores of patients with acute exacerbation of chronic obstructive pulmonary disease [J]. Journal of Shanxi University of Chinese Medicine, 2021, 22(1):45-48.*
- [35] Shen Mengyue, Zhang Mi, Tang Zhiyu, et al. *Clinical observation of Zhenwu decoction combined with Wuling powder and routine western medicine therapy in treating acute exacerbation of chronic obstructive pulmonary disease with syndrome of water overflowing due to yang deficiency [J]. China's Naturopathy, 2020, 28(24):88-91.*
- [36] Zhang Peng. *Clinical Study of Syndrome Differentiation Addition and Subtraction of Sangbaipi Decoction for Phlegm-heat and Kidney Deficiency Type AECOPD [J]. Journal of Sichuan of Traditional Chinese Medicine, 2020, 38(11):78-81.*
- [37] Hong Shihai, Xia Qinghua, Huang Guanghui, et al. *Effect of Integrated Chinese and Western Medicine Therapy on Inflammatory Factor and Immune Function of Patients with AECOPD [J]. Journal of New Chinese Medicine, 2017, 49(7):40-43.*
- [38] Wu Longchuan, Chen Yu, Yi Jiao, et al. *Mechanism of Action of Bu-Fei-Yi-Shen Formula in Treating Chronic Obstructive Pulmonary Disease Based on Network Pharmacology Analysis and Molecular Docking Validation [J]. BioMed Research International, 2020, 2020:9105972-9105972.*
- [39] Chen Xiaohui, Ao Suhua, Yang Feng. *The use of the method of Tongzhi diarrhoea in the treatment of respiratory failure in chronic obstructive pulmonary disease [J]. Hunan Journal of Traditional Chinese Medicine, 2015, 31(3):164-166.*
- [40] Ye Siwen, Wu Songshan, Liu Huifen. *Clinical observation on 30 cases of acute exacerbation of COPD treated with peach kernel Chengqi enema [J]. Modern Traditional Chinese Medicine, 2013, 33(2):16-17.*