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Overview of TCM Etiology, Pathogenesis and TCM Treatment of Chronic Obstructive Pulmonary Disease

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Abstract: ***The number of patients with Chronic Obstructive Pulmonary Disease (COPD) in China is nearly 100 million, and it has become the fourth leading cause of death in the country. At present, Western medicine has a variety of treatment methods for COPD, including oxygen therapy, antibiotics, glucocorticoids, and smoking cessation. However, due to the long course of the disease, long-term use of drugs may lead to drug resistance and adverse reactions, resulting in limitations in application, which still cannot meet the needs of solving clinical problems of COPD. Traditional Chinese Medicine (TCM) has unique advantages in the treatment of COPD, and has formed a series of prevention and treatment measures including "preventing disease before its onset", "holistic concept", and "treating the symptoms in acute phase and the root cause in stable phase". This article reviews the etiology, TCM pathogenesis, and TCM treatment of COPD to further improve the management of such patients.***

Keywords: Chronic Obstructive Pulmonary Disease, Etiology and Pathogenesis, Traditional Chinese Medicine Treatment**.**

1. Introduction

Chronic Obstructive Pulmonary Disease (COPD) is one of the major causes of disability and death worldwide, and a major global public health issue. The 2017 Global Burden of Disease Study estimated that the point prevalence of COPD worldwide was 3.92%, and the mortality rate caused by COPD was approximately 42 per 100,000 population (accounting for 4.72% of all-cause deaths) [1]. COPD is currently ranked as the fourth most common specific cause of death globally, and is expected to become the third leading cause of disability-adjusted life years (DALYs) by 2030 [2]. In 2017, the mortality rate of COPD in China was 683.8 per 100,000 population, with 965,900 deaths [3]. The prevalence of COPD has been increasing year by year, rising from 30.9 million in 1990 to 51.52 million in 2010. The latest national epidemiological survey results show [4]: the prevalence of COPD among adults aged 20 years and above in China is 8.6%, and the prevalence among patients aged 40 years and above is as high as 13.7%. Moreover, the mortality rate of COPD is high, with deaths in China accounting for 31.1% of the global total deaths in 2013 [5]. In China, the burden of COPD is high in terms of both economic and life burdens; the direct medical costs of COPD account for 33.33% to 118.09% of the local average annual income [6].

COPD is highly correlated with "Fei Zhang" (Lung Distention) in TCM [7]. Lung Distention is a common syndrome in TCM, referring to chronic lung diseases such as chronic bronchitis and emphysema. After long-term recurrent attacks and protracted course, it leads to distention of the lung and dysfunction of dispersion, descent, and purification of lung qi. The term "Lung Distention" was first recorded in Huangdi Neijing (Huangdi's Internal Classic), and the description of its related symptoms laid the foundation for the understanding of this disease in later generations. According to TCM theory, the etiology of Lung Distention is complex, and its core is closely related to deficiency of healthy qi and invasion of external pathogens. Deficiency of innate endowment, consumption of healthy qi due to prolonged cough and asthma, or improper diet and overwork in the acquired stage leading to dysfunction of the spleen and stomach can all weaken the defensive function of the body, making it vulnerable to repeated invasion of external pathogens. The lingering external pathogens cause disturbance in water metabolism of the body, dysfunction of the lung, spleen, and kidney, leading to accumulation of water and fluid, and production of pathological products such as phlegm turbidity and fluid retention. At the same time, qi deficiency failing to promote blood circulation or obstruction of collaterals by phlegm turbidity can also lead to blood stasis. Phlegm turbidity, fluid retention, and blood stasis interact with each other, further blocking the lung collaterals and qi movement, aggravating the symptoms of Lung Distention, and making the disease protracted and difficult to heal. During the progression of COPD, TCM syndromes are affected by multiple factors and show regular progression and evolution. Exploring these rules is of great significance for improving the prevention and treatment of COPD and further exerting the advantages of TCM in treating COPD [8].

2. Etiology and Pathogenesis

Western medicine holds that COPD is mostly evolved from the long-term progression of chronic bronchitis and emphysema, and is a progressive airway disease. Its core pathological mechanism involves the interaction of multiple factors: stimuli such as tobacco smoke and air pollution trigger oxidative stress and persistent inflammatory response; the imbalance between proteases and antiproteases destroys the metabolic balance of lung tissue; long-term damage further leads to airway remodeling, and finally results in airway stenosis and ventilation dysfunction. Cardiovascular diseases, long-term smoking, excessive dependence on glucocorticoids, abnormal increase of BNP, infection with Pseudomonas aeruginosa, and advanced age are important risk factors for acute exacerbation of COPD [9].

According to TCM theory, the core internal cause for the recurrent and protracted course of COPD lies in the impaired

functions of the lung, spleen, and kidney [10]. These three organs interact and affect each other, eventually leading to qi stagnation, blood stasis, and phlegm turbidity retention, which cause recurrent symptoms such as cough, expectoration, and wheezing. The lung, as the "canopy" of the body, governs qi and controls respiration. COPD patients, due to long-term invasion of external pathogens or consumption by chronic diseases, first have their lungs affected, resulting in deficiency of lung qi and dysfunction of dispersion and descent. Insufficient lung qi weakens the body's resistance to external pathogens, making it prone to repeated invasion by pathogenic cold, phlegm, and dampness. Prolonged unhealed cough further consumes lung yin and damages lung collaterals, forming a vicious cycle. The spleen is the "acquired foundation" and governs the transportation and transformation of water-dampness. If patients have improper diet, overwork, or the disease involves the spleen and stomach in the chronic stage, it will lead to spleen deficiency and dysfunction in transportation. The internal retention of water-dampness generates phlegm turbidity, which ascends and obstructs the lung, aggravating airway blockage and making cough and expectoration protracted. The kidney is the "innate foundation" and governs the reception of qi. When the disease involves the kidney in the chronic stage, it leads to kidney qi deficiency and decreased qi-receiving function, resulting in wheezing, shortness of breath, and worsening symptoms with activity. At the same time, the kidney's inability to warm and transform water-dampness further aggravates the pathological state of phlegm turbidity retention. The coordinated dysfunction of the three organs leads to lung qi stagnation and unsmooth qi movement (qi stagnation); qi deficiency failing to promote blood circulation or obstruction of collaterals by phlegm turbidity leads to blood stasis. Phlegm turbidity, qi stagnation, and blood stasis interact and interweave, blocking lung collaterals and airways, and finally resulting in the protracted and recurrent course of COPD. The team of Li Xiuyuan [11] believes that the main pathological factor of COPD is phlegm turbidity, and the root cause is deficiency of healthy qi. The body's defensive function is weakened, damaging lung collaterals; prolonged lung deficiency involves the spleen and stomach; spleen deficiency leading to dysfunction in transportation affects kidney qi; and finally kidney fails to receive qi.

3. Research on TCM Treatment

3.1 Syndrome Differentiation and Treatment

In the TCM syndrome differentiation system, COPD is divided into two major stages: stable phase and acute exacerbation phase. The acute exacerbation phase is characterized by sudden onset and obvious symptoms, with common syndrome types being excess syndromes or mixed excess-deficiency syndromes, mainly including syndrome of external cold with internal fluid retention, syndrome of phlegm-heat obstructing the lung, syndrome of phlegm-turbidity blocking the lung, and syndrome of intermingled phlegm and blood stasis. These syndromes are mostly caused by external pathogen invasion and obstruction of airways by phlegm turbidity and blood stasis, manifested as aggravated cough, increased sputum volume, and obvious wheezing. The stable phase is relatively mild, mainly presenting with deficiency syndromes or deficiency syndromes complicated with excess syndromes. The core syndrome types include syndrome of lung qi deficiency, syndrome of lung-spleen qi deficiency, syndrome of lung-kidney qi deficiency, and syndrome of qi-yin dual deficiency. These syndromes are mostly caused by consumption of healthy qi due to chronic disease and decline of organ functions, clinically manifested as shortness of breath, fatigue, worsening symptoms after activity, and protracted cough and expectoration.

In view of the complexity of COPD syndrome distribution and clinical diagnosis and treatment needs, modern TCM practitioners have carried out a large number of clinical studies on the rules of its syndromes, accumulating rich evidence-based basis. Yu Xueqing et al. [12] conducted a systematic investigation on the syndrome distribution characteristics of 266 COPD patients. The results showed that the core syndrome types of the included patients were syndrome of lung qi deficiency, syndrome of lung-spleen qi deficiency, syndrome of lung-kidney yin deficiency, syndrome of intermingled phlegm and qi, syndrome of phlegm-heat obstructing the lung, and syndrome of cold fluid retaining the lung. Fang Linxia et al. [13] classified and summarized the syndrome types of a large sample of COPD patients, and found that the most common syndrome types in the acute exacerbation phase were syndrome of phlegm-turbidity blocking the lung, syndrome of phlegm-heat obstructing the lung, and syndrome of intermingled phlegm and blood stasis, reflecting that the core pathogenesis of the acute exacerbation phase is the obstruction of excess pathogens such as phlegm, heat, and blood stasis. In the stable phase, the main syndrome types are syndrome of lung qi deficiency, syndrome of lung-spleen qi deficiency, syndrome of lung-kidney qi deficiency, syndrome of lung-kidney yin deficiency, and syndrome of qi deficiency with blood stasis, indicating that the deficiency of healthy qi in the lung, spleen, and kidney is the main pathological basis, and some patients are complicated with excess pathogens such as blood stasis, reflecting the pathogenesis characteristic of "deficiency complicated with excess". In addition, the impact of geographical environment on the distribution of COPD syndromes has also attracted attention. Tan Ye's team [14] conducted a special study on patients with acute exacerbation of COPD (AECOPD) in the high-altitude area of Qinghai, and found that the main syndrome types of patients in this area included syndrome of phlegm-turbidity blocking the lung, syndrome of phlegm-blood stasis blocking the lung, syndrome of phlegm-heat blocking the lung, syndrome of phlegm-fluid blocking the lung, and syndrome of intermingled phlegm, dampness, blood stasis, and heat. The high-altitude area is characterized by cold climate, thin oxygen, and large temperature difference between day and night. The special environment is prone to invasion of pathogenic cold and obstruction of qi movement, and long-term hypoxia may affect blood circulation and water metabolism. Therefore, the syndrome types of patients in this area are more characterized by the interweaving of excess pathogens such as phlegm, blood stasis, dampness, and heat, which is different from the syndrome distribution of patients in plain areas.

3.2 TCM Internal Treatment

The treatment of COPD should follow the core principle of "treating the symptoms in acute phase and the root cause in stable phase", taking into account the disease stage and the balance between healthy qi and pathogenic factors. The acute exacerbation phase is mostly induced by external pathogens, with airway obstruction and internal accumulation of phlegm-heat. The treatment focuses on diffusing the lung to dispel pathogens, supplemented by clearing heat and resolving phlegm, descending qi and relieving asthma, so as to quickly relieve acute symptoms such as cough, wheezing, and excessive sputum. In cases of critical conditions with symptoms such as coma and convulsions, it is necessary to promptly resolve phlegm to open the orifices and calm wind to stop convulsions, so as to save the critical state. The pathogenesis of the stable phase is mainly deficiency of the lung, spleen, and kidney, imbalance of yin and yang, and deficiency of qi and yin. The treatment focuses on nourishing the heart and lung, regulating the spleen and kidney, harmonizing yin and yang, and balancing qi and yin, so as to strengthen the body's healthy qi through consolidating the root and cultivating the source, and reduce the frequency of acute exacerbations. If there is a sign of healthy qi collapse during the disease course (such as profuse sweating and faint pulse), emergency measures of strengthening healthy qi to secure the collapse and rescuing yin to restore yang should be taken to protect the primordial qi and prevent danger. The whole course of treatment requires syndrome differentiation and treatment, giving consideration to both the symptoms and the root cause, so as to achieve the balance of dispelling pathogens without damaging healthy qi and strengthening healthy qi without assisting pathogens.

3.2.1 Acute Exacerbation Phase

The main syndrome types in the acute exacerbation phase are as follows: (1) Syndrome of external cold with internal fluid retention: The main manifestations are cough, wheezing with inability to lie flat, shortness of breath, excessive thin and white sputum, thin white tongue coating, and floating and tight pulse. The treatment focuses on warming the lung to dispel cold and resolving fluid retention to descend counterflow, with the selected prescription being Xiaoqinglong Decoction. Xiaoqinglong Decoction [15] has the effects of alleviating clinical symptoms of patients with asthma-COPD overlap syndrome, improving lung function, and reducing the level of inflammatory factors. (2) Syndrome of phlegm-turbidity blocking the lung: The main manifestations are chest fullness, cough with excessive sputum (white, sticky, or frothy), short-term wheezing, and thin and greasy tongue coating. The treatment focuses on resolving phlegm to descend counterflow, with the selected prescription being the combination of Erchen Decoction and Sanzi Yangqin Decoction. Geng Min's study [16] found that Sanzi Yangqin Decoction combined with budesonide and formoterol fumarate powder for inhalation in the treatment of COPD can significantly improve clinical efficacy, achieve more obvious improvement in lung function indicators, and more significantly reduce the levels of SuPAR and HNP1-3. (3) Syndrome of phlegm-heat obstructing the lung: The main manifestations are cough with reversed qi, rapid and rough breathing, chest fullness, yellow or white sticky sputum (difficult to expectorate), red tongue, and yellow and greasy tongue coating. The treatment focuses on clearing the lung to resolve phlegm and descending qi to relieve asthma, with the selected prescription being Qingjin Huatan Decoction. Basic research [17] has found that Qingjin Huatan Decoction can treat AECOPD by maintaining iron homeostasis, inhibiting autophagy, regulating various signaling pathways, improving intestinal flora, etc., so as to reduce inflammatory response and lung damage.

3.2.2 Stable Phase

The main syndrome types in the stable phase are as follows:(1) Syndrome of yang deficiency with water overflow: The main manifestations are cough and wheezing with inability to lie flat, clear and thin sputum, chest fullness and shortness of breath, white and slippery tongue coating, and deep, deficient, rapid or irregular pulse. The treatment focuses on warming the kidney and invigorating the spleen, resolving fluid retention and promoting diuresis, with the selected prescription being the combination of Zhenwu Decoction and Wuling Powder. Guan Zhuquan's study [18] found that Zhenwu Decoction combined with Wuling Powder in the treatment of COPD patients with syndrome of yang deficiency with water overflow can reduce the level of inflammatory factors and improve oxidative stress indicators.(2) Syndrome of lung-kidney qi deficiency: The main manifestations are short and discontinuous breathing (even opening the mouth and raising the shoulders, unable to lie flat), cough with white frothy sputum (difficult to expectorate), pale tongue, and deep, thin, and weak pulse. The treatment focuses on tonifying the lung and astringing the kidney, descending qi to relieve asthma, with the selected prescription being Bufei Decoction. Bufei Decoction has the effects of tonifying both the lung and kidney, relieving cough and resolving phlegm, relieving asthma, regulating qi and blood, and enhancing the functions of the lung and kidney. He Peng's team [19] found that Bufei Decoction can inhibit the apoptosis of lung tissue cells in COPD model mice, improve lung function and inflammatory level, and its mechanism may be related to the activation of endoplasmic reticulum-related protein GRP78.

3.3 TCM External Treatment

Traditional TCM external treatment also has significant efficacy in COPD, such as common acupuncture, du moxibustion, auricular point pressing, and point injection. At present, the research on the anti-inflammatory mechanism of acupuncture [20] mainly focuses on inflammatory mediators, kinase-related pathways, cholinergic-related pathways, and autophagy. It achieves the goal of inhibiting inflammatory response through the overall regulation of multiple mechanisms, and the commonly selected acupoints include Dingchuan (EX-B1), Fenglong (ST40), Taiyuan (LU9), and Kongzui (LU6). As a traditional TCM external treatment integrating the comprehensive advantages of meridians, acupoints, drugs, and moxibustion, du moxibustion has the advantages of simplicity, convenience, low cost, and effectiveness. It has been confirmed [21] to have a definite effect in improving the lung function of COPD patients in the stable phase. At the same time, Chen Hongxin's team [22] found through research that du moxibustion treatment can effectively improve the motor function of patients and the

fatigue tolerance threshold during exercise, enhance the cardiopulmonary endurance of COPD patients with syndrome of lung-kidney qi deficiency in the stable phase, alleviate clinical symptoms, and thus improve the quality of life. Auricular point therapy, as a non-pharmacological TCM external treatment, has the advantages of simple operation, long-lasting effect, and good efficacy. Li Jibo [23] conducted data mining on clinical studies of auricular point therapy for COPD, and found that the main method of auricular point therapy for COPD is auricular point pressing, with the Lung point (CO14) being the most frequently selected. The Lung point, Shenmen point (TF4), and Trachea point (CO16) are the main intervention auricular points. Association rules show that the core combination of auricular points is Lung-Trachea-Subcortex (AT4)-Shenmen, and the main point selection rules of auricular point therapy for COPD are "selecting points according to corresponding parts" and "selecting points based on zang-fu theory".

4. Limitations and Prospects

Although TCM has made considerable progress in explaining the etiology and pathogenesis of COPD and constructing the syndrome differentiation and treatment system, providing rich ideas for clinical diagnosis and treatment, there are still many aspects to be improved in current research. At the theoretical research level, there is no unified consensus on the definition of the scope of TCM syndrome factors and syndromes. Different TCM practitioners have different understandings of the core pathogenesis of COPD, leading to inconsistent criteria for syndrome classification, which affects the comparability and repeatability of research results. Clinical studies are mostly single-center and small-sample, lacking high-quality evidence-based medical evidence supported by multi-center, large-sample, and long-term follow-up studies. In particular, there is insufficient special research on special populations (such as elderly patients and patients with comorbidities) and special regions (such as high-altitude and cold-humid areas), making it difficult to fully reflect the rules of syndrome evolution in patients with different environments and constitutions. In addition, the research on the mechanism of TCM treatment mostly stays at the level of superficial observation. The molecular mechanism of TCM compound prescriptions and external treatments in regulating the core pathological links of COPD (such as inflammatory response, oxidative stress, and airway remodeling) is not deeply explained, and there is a lack of systematic exploration on the correlation between syndrome types and objective indicators, which limits the precise development of TCM treatment. At the clinical application level, the optimal plan for integrated TCM-Western medicine treatment has not been clarified. How to scientifically integrate TCM internal treatment, external treatment, and conventional Western medicine treatment according to the disease stage and syndrome characteristics to achieve synergistic efficacy still needs further exploration. Although external treatments have shown unique advantages, there is a lack of unified standards for the selection of indications, operation specifications, and efficacy evaluation criteria of different treatments (such as acupuncture, du moxibustion, and auricular point pressing), and the data on their long-term efficacy and safety are insufficient. At the same time, there are problems such as inaccurate syndrome differentiation and homogenization of medication schemes in the clinical application of Chinese patent medicines, and the individualized medication guidance system for different syndrome types has not been improved.

Therefore, in the future, we should promote the in-depth development of TCM research on COPD from multiple dimensions. First, multi-center and large-sample clinical epidemiological investigations should be carried out, combined with modern detection technologies, to establish a standardized syndrome factor differentiation system, clarify the syndrome distribution characteristics and evolution rules of different populations and regions, and provide a basis for standardized diagnosis and treatment. Second, strengthen the research on the mechanism of TCM treatment, use modern biological technologies to deeply explain the molecular mechanisms of TCM compound prescriptions and external treatments in regulating inflammatory pathways, improving lung function, and inhibiting airway remodeling, and construct a "syndrome type-index-efficacy" correlation model. At the same time, it is necessary to optimize the integrated TCM-Western medicine treatment plan, verify the clinical efficacy of different treatment models through randomized controlled trials, and clarify the optimal timing and dosage of TCM intervention. In addition, standardize the operation procedures and efficacy evaluation criteria of external treatments, and conduct long-term follow-up studies to evaluate their safety and long-term efficacy. With the help of modern technologies such as big data and artificial intelligence, develop a TCM syndrome differentiation auxiliary system to realize the accurate identification of syndrome types and intelligent matching of individualized treatment plans. Finally, promote the continuous update and popularization of TCM diagnosis and treatment guidelines, strengthen the training of syndrome differentiation thinking for clinical physicians, promote the in-depth integration of TCM theory and clinical practice, and provide more high-quality and efficient prevention and treatment services for COPD patients.

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