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Review

Analysis of modern and korean medicine treatments for chronic obstructive pulmonary disease

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ABSTRACT

The prevalence of respiratory diseases is increasing due to social and environmental factors such as increased environmental pollution and air pollution, and among them, chronic obstructive pulmonary disease (COPD) in particular has a high mortality and morbidity rate worldwide. As a result, medical expenses are rapidly increasing, creating a social and economic burden. In response to this, there is a need to discuss ways to reduce the risk from diseases and manage them appropriately, and the most basic starting point in this process is how these chronic lung disease patients are treated in actual clinical settings and how to improve the quality of treatment. There is a need to look into whether there are effective drugs.Western treatment for chronic obstructive pulmonary disease is basically a disease in which the airway narrows, so bronchodilators are used to widen the bronchi, and corticosteroids and antibiotics are mainly used to relieve the inflammatory response in the lungs. However, since the mainly used Western medicine does not serve as a fundamental therapeutic drug and contains many side effects, there is a need for drugs that improve the quality of life of patients and are more effective in managing symptoms as symptomatic prescriptions. Therefore, Western and Oriental medicine treatments are needed. The purpose is to suggest better treatments through comparative analysis.

Keywords korean medicine, modern medicine, chronic obstructive pulmonary disease

INTRODUCTION

Chronic Obstructive Pulmonic Disease (COPD) is a lung disease characterized by airflow limitation that does not fully recover. It is caused by damage to the airways and lung parenchyma caused by chronic inflammation and is accompanied by persistent respiratory symptoms such as shortness of breath, cough, and phlegm. COPD has a high mortality and morbidity rate worldwide, and is causing socioeconomic burden, including rapidly increasing medical costs due to COPD.[1] COPD, like hypertension, diabetes, and asthma, is a representative Ambulatory Care Sensitive Condition (CSC)[2] that can reduce symptom worsening and hospitalization if properly managed in primary care. It is so major that it is predicted to be the 4th cause of death by 2030. It is the cause of death. In Korea, the prevalence of COPD is 13.4% in the population over the age of 40 in 2008, and the number of deaths caused by COPD is 10.1 per 100,000 people, similar to the number of deaths caused by hypertension disease.[1] Irreversible airflow limitation, a characteristic of COPD, develops over a long period of time. Airflow limitation is caused by a combination of small airway disease and lung parenchymal destruction (emphysema). When chronic inflammation occurs in the small airways, structural changes such as airway fibrosis occur, narrowing the small airways. Destruction of the lung parenchyma also occurs due to chronic inflammation. Due to the destruction of the alveoli, which are the site of gas exchange, the connection between the alveoli and small airways is severed and the elastic recoil of the lung is reduced, causing the airway to narrow or not open during expiration, resulting in airflow limitation. Small airway abnormalities and lung parenchymal destruction are mostly accompanied, but depending on the patient, there are cases where small airway disease is the main abnormality (chronic bronchitis predominant type) and in other cases, emphysema, which is destruction of lung parenchyma, is the main abnormality (emphysema predominant type). Until now, emphysema and chronic bronchitis have been used as terms to represent COPD. However, these two terms are histologically or clinically defined, respectively, and represent only part of the characteristics of COPD. Emphysema or chronic bronchitis may be the main clinical phenotype depending on the patient's characteristics, but not everyone with emphysema or chronic bronchitis is a COPD patient. Spirometry is relatively easy to use anywhere in the world and is highly reproducible, making it the best method for measuring airflow limitation. The most important and well-known risk factor for COPD is smoking.[3] Other causes include occupational dust or chemicals, air pollution, low socioeconomic level, chronic bronchitis or respiratory infections, etc. Due to these various risk factors, chronic airflow obstruction can occur even in non-smokers.[4] The occurrence and clinical manifestations of the disease vary depending on each individual's susceptibility to the disease, and are influenced by external factors and Interactions between host factors also vary from individual to

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individual, so they can appear in various ways. For example, not everyone with the same smoking history develops COPD. Of course, compared to COPD patients who are smokers, non-smokers with chronic airflow obstruction.[5] There are fewer symptoms and less systemic inflammation. The risk of mortality and pneumonia due to respiratory failure increased in non-smokers with chronic airflow obstruction compared to non-smokers without chronic airflow obstruction, but the risk of lung cancer or cardiovascular disease did not increase.[6] This is because smoking history and exposure to environmental risk factors vary from person to person and may also vary depending on gender, and genetic factors may be involved in affecting the development of COPD. The time exposed to risk factors will increase as life expectancy increases, that is, as people age. The goals of COPD treatment are to relieve symptoms, improve exercise capacity, improve quality of life, reduce acute exacerbations, prevent disease progression, and reduce mortality. If there is a cause, it should be removed and regular hospital visits should be encouraged to evaluate and follow-up risk factors, disease progression, drug effects and side effects, acute exacerbations, and progression of concomitant diseases. In general, drugs that improve lung function, including FEV1, by changing the tone of airway smooth muscles are called bronchodilators. These include beta-2 agonists, anticholinergics, and methylxanthine drugs, and can be used alone or in combination. Bronchodilators are the mainstay of COPD treatment, and considering their effectiveness and side effects, it is recommended to use inhaled medications first and, in cases of persistent symptoms, use long-acting bronchodilators rather than short-acting ones. There is insufficient evidence and controversy regarding the effectiveness of inhaled steroids alone on local or systemic inflammation in COPD. In some studies, the use of inhaled steroids alone in COPD was effective in improving lung function or reducing acute exacerbations compared to the placebo group, but the effect was not superior to inhaled long-acting bronchodilators and did not show a significant effect in reducing mortality. It is very important to identify and eliminate risk factors that cause or progress COPD. Smoking is a very important risk factor that causes and progresses COPD, so patients who smoke are advised to quit smoking.[7] In addition to smoking, people should avoid dust, smoke, and gas in the workplace, and educate them to reduce or avoid outdoor and indoor air pollution. As COPD has been identified as an independent pathophysiological concept rather than a disease divided into emphysema and chronic bronchitis, oriental medicine has also suggested seven categories of 痰濁型, 肺熱型, 肺虛型, 脾虛型, 腎陽虛型, and 風寒型 as a new classification of variant types of COPD.[8] As a result of analyzing the frequency of oriental medical diagnosis names, 哮喘證s and 肺脹證s accounted for the majority. 喘 means 呼吸急促, and 哮 means 有聲響between 喉. All of them are symptoms of 哮喘證, which means asthma, bronchitis, emphysema, and cardiovascular asthma. The definition of 肺脹證 is 咳而. Pneumonia, asthma, bronchiectasis, emphysema, and combined infections of bronchitis are such diseases. COPD is mainly transformed into 虛證, and chronic bronchitis is divided into 脾虛痰濁, 肺腎陰虛, and 脾腎陽虛型, and emphysema is divided into 肺虛, 脾肺虛, and 腎虛型.Previous studies that evaluated the effectiveness of oriental medicine treatment on COPD include Socheongryongtang(風寒型), Macmundongtang and Saengmaekcheo ngwongeum(肺虛型), Cheongsangbohaetang(肺陰虛型),[9] Sagantang(痰濁型), and Guaruhongryeonhwan(肺熱型).[10] In one study using Socheongryong-tang, an inhalation agent was used.[11] Inhalation treatment can achieve pharmacokinetic characteristics such as high lung deposition, high bioavailability compared to oral administration, and maximum lung residence time, and can increase lung selectivity by increasing receptor selectivity. Pharmacodynamic properties were obtained.

Modern medicine treatments for the chronic obstructive pulmonary disease

1. Definition

Chronic Obstructive Pulmonary Disease (COPD) is a condition characterized by respiratory tract inflammation and excessive mucus production, leading to airflow obstruction. It primarily affects the elderly population, particularly those in middle age and beyond. COPD causes significant limitations in independent daily activities due to respiratory difficulties. In addition to physical issues such as weight loss and hormonal imbalance, it can also result in psychological problems such as anxiety, sleep disorders, and depression. The mortality rate associated with COPD is also reported to be increasing. This not only entails direct medical expenses for the diagnosis and treatment of COPD but also significant indirect medical costs, including disability caused by respiratory impairments, work absenteeism, and premature death. It indicates that the expenditure on healthcare for COPD, both in terms of direct medical costs and indirect costs, is likely to be substantial. In the future, it is expected that there will be an increase in healthcare and medication expenses for individual patients with COPD, and on a national level, it will be a major contributing factor to the rise in health insurance expenditure. Therefore, there is a significant need to monitor the prevalence of COPD and manage the disease systematically.

2. Diagnosis

Chronic obstructive pulmonary disease (COPD) is a chronic respiratory disease characterized by inflammation of the lungs due to the inhalation of harmful particles or gases, accompanied by progressive and irreversible airflow limitation. It encompasses symptoms of chronic bronchitis and emphysema, with smoking (including secondhand smoke) being the primary cause. The main symptoms include chronic cough, sputum production, and shortness of breath. The diagnosis and evaluation of the disease involve the use of pulmonary function tests to measure airflow limitation.[12]

In terms of pulmonary function tests, the diagnosis is made when the FEV1/FVC ratio is less than or equal to 70%. However, since the FEV1/FVC ratio naturally decreases with age, it is necessary to adjust for age to overcome the limitations of absolute values. Currently, the staging of the disease is based solely on FEV1, but considering the impact of "extrapulmonary symptoms" on prognosis in COPD patients, the "BODE index" that takes into account factors such as body weight, airway obstruction, severity of breathlessness, and exercise capacity is expected to become an important method for determining the stage of the disease.In the case of chronic respiratory diseases, asthma follows the GINA (Global Initiative for Asthma) guidelines, while chronic obstructive

pulmonary disease (COPD) follows the GOLD (Global Initiative for Chronic Obstructive Lung Disease) guidelines, which were jointly developed by the National Heart, Lung, and Blood Institute of the United States and the World Health Organization. According to the GOLD guidelines, the treatment goals for COPD are to prevent disease progression, improve symptoms, exercise capacity, and overall health status, prevent exacerbations and complications, reduce mortality, and minimize the side effects of treatment. These international guidelines, developed by the National Heart, Lung, and Blood Institute and the World Health Organization, provide standardized recommendations for the management of COPD.[13] The goals of COPD treatment include preventing disease progression, improving symptoms, exercise capacity, and overall health status, preventing exacerbations and complications, reducing mortality, and minimizing the side effects of treatment. While COPD guidelines like GOLD, developed based on evidence, are known to be useful, there is a problem of not reflecting the healthcare situation in South Korea. For example, in the case of asthma, it has been reported that the prescription rate of inhalers by primary care physicians in South Korea is low at 29.7%, while the prescription rate of oral medications is over 70%. Therefore, when developing asthma guidelines in South Korea, there is a need to supplement the establishment of evidence for the use of oral medications compared to the international asthma guidelines such as GINA (Global Initiative for Asthma). This can be achieved through setting key questions, conducting literature reviews, and establishing the level of evidence. Therefore, when developing guidelines for major diseases such as COPD or coronary artery disease, it is necessary to consider the healthcare priorities and financial issues of the country, as well as the practice patterns of primary care physicians. Without reflecting these factors, the guidelines may become disconnected from the reality faced by primary care physicians, making it difficult for them to follow. This can hinder the dissemination and utilization of the guidelines. To develop guidelines that reflect the situation in South Korea, it is necessary to investigate the practice patterns of primary care physicians in the country and evaluate them based on evidence. Additionally, establishing the level of evidence is crucial.

3. Treatment

The treatment of chronic obstructive pulmonary disease (COPD) can be broadly divided into smoking cessation, vaccination, pharmacological therapy, and non-pharmacological therapy. Smoking cessation is the only treatment that can effectively slow down the decline in lung function in patients with COPD, and it has been shown to reduce overall mortality from all causes by 27%. However, the success rate of smoking cessation is low, with only about 5% of patients achieving long-term success through physician advice alone. The success rate increases to about 25% when combined with counseling from specialists, smoking cessation education, nicotine replacement therapy, and medications like bupropion. Vaccination for influenza and pneumonia, among other preventive measures, is recommended for patients with COPD as it can reduce hospitalizations and mortality rates from all causes by 30-40% in the general elderly population. The pharmacological actions and characteristics of each drug class used in the treatment of chronic obstructive pulmonary disease (COPD) are as follows:

(1) Bronchodilators

Bronchodilators are the cornerstone of COPD treatment, as they help relieve symptoms such as chronic cough and breathlessness by expanding the airways. Beta2-agonists: They act on the smooth muscles surrounding the airways, relieving bronchial spasms and causing the expansion of narrowed airways. They come in short-acting and long-acting formulations, available in inhaler or oral forms. Anticholinergics: These medications block the effects of the parasympathetic nervous system that constrict the airways, thereby widening the bronchial passages. They are available in short-acting and long-acting formulations, administered via inhalation. They can also be used in combination with beta2-agonists. Methylxanthines: These drugs inhibit the enzyme phosphodiesterase in the airways, resulting in bronchial dilation. They are available in oral and injectable forms.

(2) Anti-inflammatory agents

These medications are used to alleviate inflammation. Inhaled corticosteroids: They are primarily used in inhaler form to minimize systemic side effects compared to oral formulations. They are usually used in combination with beta2-agonists or anticholinergics.PDE-4 inhibitors: These drugs inhibit the enzyme phosphodiesterase-4, preventing the breakdown of a substance called cAMP (cyclic adenosine monophosphate) in lung cells. By increasing the levels of cAMP, they enhance the anti-inflammatory effects within the lung tissue. Antibiotics: Quinolone antibiotics are commonly used. They exert their antimicrobial effects by inhibiting DNA synthesis, thus inhibiting bacterial growth. Antibiotic treatment may be required when symptoms worsen, such as increased sputum production, change in sputum color to yellow, or increased frequency of breathlessness. It can be differences in side effects, and the typical side effects for each type are as follows:

Beta2-agonists: They can potentially cause cardiovascular side effects. It is important to adhere to the prescribed dosage and not exceed the maximum daily limit.

Anticholinergics: They should not be administered to patients with narrow-angle glaucoma and should be used with caution in patients with prostate hypertrophy or bladder outlet obstruction. In the case of long-acting formulations, they should not be used as a primary treatment for acute symptoms. Additionally, dry mouth can occur, which may lead to dental caries, so it is important to maintain adequate hydration and not exceed the recommended daily dose.

Methylxanthines: Increased blood concentration of these drugs can lead to side effects. Close monitoring of blood concentration is necessary, and they should not be coadministered with central nervous system stimulants to avoid excessive stimulation of the central nervous system.

Inhaled corticosteroids: They are used regularly to prevent symptom exacerbation. After inhalation, rinsing the mouth with water or brushing teeth is recommended to prevent oral candidiasis.

PDE-4 inhibitors: They should not be administered to patients with severe liver disorders, immunological disorders, cancer, or severe infections. They can potentially induce anxiety, depression, or other psychiatric effects, so caution is required when prescribing to patients with a history of mood disorders or those taking medications that can cause psychiatric events.

Antibiotics: They should be administered for the minimum duration necessary to prevent antibiotic resistance. Their use is not established for children under 18 years of age.

According to the analysis of the pattern of dual medication use, it has been reported that oral medications are more commonly prescribed than inhalers for both asthma and chronic obstructive pulmonary disease (COPD) patients, despite inhalers being recognized as the cornerstone of treatment for chronic respiratory diseases. Inhalers have been shown to have significant benefits in improving pulmonary function, but there seems to be a gap between clinical guidelines and actual prescription practices.

Several factors contribute to this preference for oral medications. Firstly, it is a traditional belief in Korea that oral medications are more effective. Secondly, there may be difficulties and aversion associated with operating inhalation devices, concerns about the side effects of inhaled corticosteroids, underestimation of asthma conditions, economic constraints regarding the relatively high cost of inhalers, lack of knowledge or education among healthcare professionals regarding inhaler use, and other reasons.

It is crucial to examine how patients with chronic respiratory diseases are actually being treated in clinical practice, the extent to which cost-effective medications are being prescribed while maintaining the quality of care, and whether the prescribed medications are truly effective in terms of therapeutic outcomes.

In conclusion, both oral and inhaler medications are commonly used in the treatment of chronic obstructive pulmonary disease (COPD). Bronchodilators, which help to expand the airways, are primarily used in both treatment approaches. Adrenal corticosteroids and antibiotics are prescribed to alleviate pulmonary inflammation. Treatment is escalated gradually based on the severity of the condition, and it is recommended to maintain the same treatment stage for an extended period, assuming no significant side effects or worsening of symptoms. However, it should be noted that adrenal corticosteroids and antibiotics have significant drawbacks, including potentially serious side effects when used for a prolonged duration. Considering that COPD is a chronic condition that requires long-term treatment and overall health management, selecting medications that are associated with minimal side effects and safety even with long-term use should be a crucial consideration in the choice of therapeutic agents.

Korean medicine treatments for the chronic obstructive pulmonary disease

Drug treatment for COPD is centered on bronchodilators that improve lung function by changing the tension of airway smooth muscle, and beta 2 agonists, aminopillin, and anticholinergic drugs are included. There is no evidence yet that bronchodilators relieve symptoms, improve exercise performance and quality of life, help reduce acute exacerbation, suppress lung function, or improve mortality. In the case of adrenocorticotropic hormone drugs, systemic side effects such as skin bruises, adrenal suppression, and bone density reduction can increase the incidence of pneumonia, so inhalation steroid alone should be limited to special clinical situations accompanied by asthma. Accordingly, it is necessary to develop safe and effective treatments that can control the symptoms of COPD in the long term without side effects while preventing the prognosis of COPD patients from deteriorating.

1.Inhibitory Effects of GGX on Lung Injury of Chronic Obstructive Lung Disease

(COPD) Mice Model

It is difficult to expect a sufficient effect with monotherapy in COPD patients, but it is reported that the combination of herbal medicine according to the existing herbal medicine treatment is effective in preventing stable symptoms and quality of life in COPD patients and preventing the change from stable to acute exacerbation. Furthermore, it is reported that herbal medicine treatment in acute exacerbation can also help prevent recurrence after acute exacerbation and improve symptoms and quality of life afterwards.

2. Korean herbal therapy for chronic obstructive pulmonary disease (COPD)

Chinese herbal medicine treatment by stable phase dialectic

Until now, studies related to the effectiveness of various herbal medicine prescriptions on COPD have been conducted. This study was mainly conducted for the purpose of preventing acute exacerbation by adjusting the response to inflammation in the human body (confirmed by CRP and TNF-α) by administering herbal medicine in the stable phase, and studies on Bojungikgitang are dominated. However, in actual clinical practice, there are many cases where the herbal medicine prescription according to the type is selected through dialectic (辨證). If dialectic herbal medicine treatment is performed, COPD symptoms and QOL can be improved, and when administered in a stable phase, the incidence of acute exacerbation can be improved as well as effectively used to alleviate symptoms in case of acute exacerbation.

1) Chinese herbal medicine treatment by stable phase dialectic

It met the COPD diagnostic criteria, corresponds to 肺脾虛, 肺腎 虛, or 肺腎 陰虛 according to the dialectic criteria. As a result of applying the dialectic prescription to 352 COPD patients in GOLD 1 to 3, the dialectic treatment group showed statistically significant differences ($p<0.05$) in cough, phlegm, gasp, chest tightness, shortness of breath, lethargy score, and symptoms score, and the dialectic treatment group showed effective results. In WHO QOL-BREF, there was also a statistically significant difference ($p<0.05$) in physical, mental, and social environmental areas compared to the control group, and in COPD-QOL, the test group showed more effective results in daily living ability, social activity, depression and anxiety areas than the control group ($p<0.05$).

A randomized comparative study was conducted on 352 COPD patients in a review of the incidence of acute exacerbation during stable administration, and the control group (176 patients) continued the existing herbal medicine treatment for 6 months, and the treatment group (176 patients) administered one of the preservative medicine granules, the preservative medicine granules, and the ripening self granules according to the existing herbal medicine treatment and followed up for 12 months. As a result, the incidence and duration of acute exacerbation were significantly reduced in the symptomatic drug treatment group, and lung function

(FEV1, walking distance for 6 minutes, clinical symptom index, and QOL were significantly improved.

2) Korean herbal therapy for chronic obstructive pulmonary disease (COPD)

3) Korean Medicine Medical Examination and Treatment Guide for KCD Oriental Medicine Clinical Trials

Thirty COPD patients (21 male and 9 female) with emphysema were administered either Bojungikgitang or Socihotang. As a result, the frequency of secondary infection was 6.3±2.8 times in the control group, 3.4±1.5 times in the Bojungikkitang group, and 3.7±1.2 times in the Sohoekkitang group, which was significantly less in the Bojungikkitang group and the Sohoekkitang group. NK cells also showed a significant increase in activity in the Bojungikgitang group and the Socihotang group.

McMundongtang has been known to improve cough scores in COPD patients at 8 weeks after administration in clinical studies. However, no significant improvement was found in terms of improving quality of life or lung function.

Among COPD patients who are quitting smoking, a study of 31 patients who did not lose respiratory symptoms such as coughing, phlegm, and shortness of breath even after quitting smoking for a month showed a significant improvement over 1-6 months in the group using the clean and waste bath compared to the group who only quit smoking.

As a result of a meta-analysis of a total of 1,112 patients in 16 clinical studies using various types of additional and subtraction catapult in the acute attack phase of COPD, the additional catapult was effective in alleviating the symptoms of the acute attack phase of COPD. However, it was also concluded that better designed research results were needed.

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CONFLICT OF INTEREST

The authors declare no conflicting financial interests.

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