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A New Anti-inflammatory Therapy for COPD

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Abstract

COPD is a chronic progressive inflammatory lung disease. The key in treating COPD is to treat the inflammation. Current treatments of COPD are LABA, LAMA, and ICS. LABA and LAMA only treat the symptoms of COPD by dilating the small airway; they do not target the underlying mechanism of COPD (the inflammation). ICS only temporarily suppress the inflammation in COPD, cannot terminate the inflammatory reaction and therefore it cannot stop the progression of COPD. Corticosteroid resistant is a big issue in treating COPD. In order to effectively treat COPD, we must find new anti-inflammatory therapies or developing new anti-inflammatory drugs. The author is a clinician and found that the smoke (or the tar) of burning *Artemisia argyi* (an herb, also called moxa) had special anti-inflammatory effect, which is different to corticosteroid. It not only can effectively treat corticosteroid resistant chronic inflammation, but also can terminate chronic self-perpetuating inflammation. Treatment done for 25 COPD patients with inhalation of moxa smoke, 3/25 patients had no improvement in breathlessness and 22/25 patients became symptoms free after 1-2 months treatment and kept symptoms free without any further treatment.

Keywords: Moxa; Anti-inflammatory; Corticosteroid

Abbreviations: LABA: Long-Acting Beta-adrenoceptor Agonist; LAMA: Long-Acting Muscarinic Antagonists; ICS: Inhaled Corticosteroid; COPD: Chronic Obstructive Pulmonary Disease;

Introduction

COPD is a chronic progressive inflammatory lung disease. It is caused by various stimuli, like cigarette smoking, air pollutants, exposing to noxious agents and recurrent infection. All these stimuli can cause small airway and lung tissue injury, which induces an inflammatory reaction. Prolonged inflammation further damages small airway and lung tissue, subsequently the inflammation becomes self-perpetuating, i.e., the inflammation will last for ever even when the initial stimuli are eliminated. The activated neutrophils and alveolar macrophages produce neutrophil elastase and macrophage elastase, these two proteolytic enzymes and some other enzymes cause disruption of the wall of alveoli and fusion of alveoli, resulting in decreased gas-exchanging airspaces. Activated inflammatory cells also produce various inflammatory factors, which stimulate secretion of mucus in the lining of airway and cause fibrosis and thickening of the wall of small airway. All these increase the obstruction of small airway, reduce the air flow. The on-going inflammation in small airway and lung tissue will continue to cause tissue damaging, as a result, the lung function in COPD patients will progressively deteriorate.

Current Treatments of COPD

The key in treating COPD is to treat the inflammation. Current treatments of COPD are SABA, LABA, LAMA, oral theophylline and ICS. SABA, LABA, LAMA and theophylline only treat the symptoms of COPD by dilating the small air way, they do not target the underlying mechanism of COPD i.e., the inflammation. ICS can only temporarily supress the inflammation in COPD, cannot terminate the inflammatory reaction and therefore it cannot stop the progression of COPD, though it is the mainstay of current treatment of COPD.

Corticosteroid Resistant Chronic Inflammation

The inflammation in COPD is partially resistant to corticosteroid. The underlying mechanism that sustains the chronic inflammation in COPD is due to bidirectional intercellular reactions between T cells and alveolar macrophages and/or neutrophils. The activated macrophages and neutrophils produce interleukin 12 and other cytokines to activate T cells, in turn, activated T cells produce interferon-gamma and interleukin 8 to activate macrophages and neutrophils. Once these vicious intercellular reactions are established, they cannot be terminated by corticosteroid and will last for ever. This is the common basic mechanism of the self-perpetuating chronic inflammations, regardless of the initial stimuli or in what tissue or organ the inflammatory reaction occurs. There may be more destructive positive feedback loops in COPD that involved in the fuelling and sustaining the inflammation.

Corticosteroid resistance is a big issue in treating COPD (especially in neutrophil infiltrates predominant panlobular emphysema) and other chronic inflammatory lung diseases, like asthma, pulmonary fibrosis, radiation pneumonitis and other interstitial inflammatory lung diseases. In order to effectively treat COPD, we must find new anti-inflammatory therapies or develop new anti-inflammatory drugs.

Looking for New Anti-inflammatory Therapy

The author is a clinician, and suffered from severe chronic laryngitis in 2000. The inflammation in chronic laryngitis is completely resistant to corticosteroid, not treatable by any medication. The author tried to look for new anti-inflammatory therapies for fighting against his severe chronic laryngitis. He has tried 15 different therapies, most of them were herbal therapies, eventually found that the smoke (or the tar) of burning *Artemisia argyi* (an herb, also called Chinese mugwort or moxa) had special anti-inflammatory effect, which is different to corticosteroid. It not only can treat corticosteroid resistant chronic inflammations, but also can terminate chronic self-perpetuating inflammation.

Introduction to moxibustion

A. argyi, also called moxa or Chinese mugwort, is an herbaceous

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perennial plant with a creeping rhizome. It is native to China, Korea, Mongolia, Japan, and the Russian Far East. Its leaves have been used to treat various diseases by Chinese people for more than two thousand years.

One traditional Chinese therapy is called moxibustion. It is to grind dried moxa (*A. argyi*) up to fluff and further process it into a cigar-shaped stick or cone. Practitioners burn this moxa stick to heat certain points (acupuncture points) on the patient's skin or put the moxa cones on the acupuncture points and burn them to treat various diseases.

This therapy has two thousand and five hundred years history in China and it is highly regarded by traditional Chinese herbalists, claiming it can treat hundreds different diseases, including many intractable cases. But it is little known to Western medical world.

The mechanisms of moxibustion based on the theory of traditional Chinese medicine

Moxibustion therapy is based on the theory of traditional Chinese medicine and Chinese herbalists always use this theory to explain the mechanisms of moxibustion. They think moxibustion can give the body extra energy, warm the blood and open the body's meridian lines to improve the blood flow to treat diseases. It is very difficult for western doctors to understand these theories. A few western people make comments on moxibustion on internet, saying there are no scientific evidence to support that moxibustion can effectively treat any diseases.

The author's explanation of the mechanisms of moxibustion

The author has carefully studied moxibustion for many years and proved that the major therapeutic effect of moxibustion was due to the strong and special anti-inflammatory effect of the moxa tar (or moxa smoke) produced by the burning moxa. The role of the heat in moxibustion is to improve the local blood circulation, dilating blood vessels and hair follicles to facilitate absorption of the moxa tar on the skin. The heat produced by burning moxa per se, does not have anti-inflammatory effect or special therapeutic effect compared to heat produced by other methods. Without the moxa tar (or moxa smoke), moxibustion does not have any therapeutic effect.

The author has done experiments, using foil to cover the acupuncture points on the skin of patients, then heated these covered acupuncture points with burning moxa stick. The heat produced by burning moxa stick could penetrate the foil to heat the skin of the patients, but the moxa smoke (or moxa tar) could not reach to the skin of the patients. After many treatments with moxibustion, these patients did not have any improvement in the diseases they were treated for. The other experiment was to collect the moxa smoke with water. The moxa smoke becomes moxa tar and dissolved in the water when it reaches to the water. To apply this moxa tar dissolved water to eczematous lesions on the skin of patients, patients' eczema has been cured. This experiment proves that without the heat, moxa tar still has anti-inflammatory effect.

Inhalation Therapy of Moxa Smoke

The author treated his chronic laryngitis with the smoke of burning moxa, he had five to ten inhalations of moxa smoke once a day, or alternatively applied the smoke of burning moxa to the skin above the larynx for fifteen to twenty minutes a day, consecutive 15 days as a course, there were a 3-5 day interval between two courses. Both methods alleviated the pain, dryness and tightness in the larynx due to the chronic laryngitis. After seven courses of treatment with the above-mentioned therapies, the author's chronic laryngitis has been successfully cured (chronic laryngitis is an incurable chronic inflammatory disease, it is completely resistant to any treatment, including corticosteroid). The author's treatment experience proves the moxa smoke or tar is the key element of the therapeutic effect of moxibustion.

The author used chronic laryngitis as a chronic inflammatory model to test the anti-inflammatory effect of the moxa smoke (or moxa tar), treated more than twenty chronic laryngitis patients with inhalation of moxa smoke. They had two to eight inhalations of moxa smoke once a day for consecutive 15 days as a course, there was a three-day interval between two courses. All of these chronic laryngitis patients have been cured after one to four courses of treatment. It proves the anti-inflammatory effect of moxa smoke can be reproduced on different patients.

Assessment of the risk of inhalation of moxa smoke

The therapy of inhalation of moxa smoke only shows slightly increased risk of developing flu if patients contacted flu patients during their inhalation treatment. The author has discussed the risk of inhalation of moxa smoke with other moxibustion practitioners and patients who received the inhalation therapy of moxa smoke for chronic laryngitis. Two of the twenty two patients and a half of moxibustion practitioners reported that they had had more frequent episodes of flu if they contacted flu patients during their treatment or practicing moxibustion. These moxibustion practitioners inhaled a lot of moxa smoke during their practicing. A few patients also reported it was difficult to fall asleep at night after the inhalation of moxa smoke, but the problem has been solved by shifting inhalation therapy of moxa smoke to the morning. An article about the study of the safety of moxa smoke by an America company was published on internet, it concluded that moxa smoke was no more harmful than tobacco smoke.

Considering the small quantity of inhaled moxa smoke (the daily inhaled moxa smoke is equivalent to one half to one cigarette a day) during treatment, the author thinks the risk of inhalation therapy of moxa smoke is low or minimal for normal people.

Treatment of COPD patients with inhalation of moxa smoke

As the basic mechanisms of all chronic self-perpetuating inflammation in different chronic inflammatory diseases are the same or similar i.e., there are one or more positive feedback loops between T cells and other inflammatory cells and/or tissue cells, the author believes theoretically moxa smoke (or tar) could treat other chronic inflammatory diseases if it can treat chronic laryngitis. The author decided to generalize the application of the anti-inflammatory therapy of inhalation of moxa smoke to other chronic inflammatory diseases. The author treated twenty-five COPD patients with inhalation of moxa smoke (Tables 1-4).

Pre-conditions for receiving treatment

1. No evidence of active respiratory tract infection (no fever, no yellow or green colour sputum)

2. If patients do have active respiratory tract infection, they must be treated with antibiotics to clear the infection before starting the inhalation treatment.

3. Stop smoking

Treatment

Normally when patients start a new therapy, they should

Patients	Gender		Age	Location	History of smoking
	M	F			
Total: 25	20	5	50-88	1/25 in Australia 24/25 in China	
22/25					>10 years (All had stopped smoking for at least 1 year before receiving the inhalation therapy of moxa smoke).
3/25					None

Table 1: Patients information.

Patients number	Spirometry value before treatment of inhalation of moxa smoke	Degree of severity of COPD
All 25	FEV_1/FVC <70%	
3/25	FEV_1<30% predicted	Very severe (had severe dyspnoea and cyanotic lips at rest, no productive cough)
10/25	30% predicted < FEV_1 <40% predicted	Severe (had dyspnoea on minimal exertion with or without chronic productive cough)
12/25	FEV_1=40% to 59% predicted	Moderate severe (had dyspnoea on moderate exertion with or without cough and/or sputum)

Table 2: Spirometry value of patients.

Emphysema	Chronic obstructive bronchitis
22/25 patients diagnosed as emphysema by CT scan	3/25 patients: had dyspnoea and productive cough for more than three consecutive months in more than two consecutive years without imaging evidence of emphysema, diagnosed as chronic obstructive bronchitis. These 3 patients: 40% predicted <FEV_1 <59% predicted (moderate severe chronic obstructive bronchitis patients).

Table 3: Classification of COPD patients.

Symptoms	Treated with SABA, LABA, LAMA and or ICS before receiving inhalation therapy	One or two days after discontinuation of SABA, LABA, LAMA and/or ICS before receiving inhalation therapy
	All still had mild to severe COPD symptoms (shortness of breath on exertion)	All had moderate to severe COPD symptoms (from breathless walking on level ground to dyspnoea at rest)

Table 4: COPD symptoms of patients with or without previous treatment of SABA, LABA, LAMA and/or ICS.

Methods of treatment	Dose	Duration	Number of patients
Inhalation	3-8 inhalations per session a day	15 days as a course Total treatments: 2-4 courses (there is a 3-5 day break between courses)	23/25
Alternative (for those who cannot cope with smoke inhalation). It is to apply the moxa smoke to the front and back chest except the precordial area by waving a burning moxa stick to each side of the chest.	7-10 minutes, one session a day.	15 days as a course Total treatments: 2-4 courses (there is a 3-5 day break between courses)	2/25

Table 5: Dose and duration of inhalation treatment and the alternative treatment.

Modes of treatment	Number of patients	Severity of patients
Co-treatment	3	Very severe
	10	severe
	7	Moderate severe
Mono-therapy	5	Moderate severe

Table 6: Modes of treatment.

discontinue with the previous therapy, but COPD patients would have severe shortness of breath if they suddenly stop inhaled bronchodilators and or ICS, therefore these patients were allowed to keep their previous treatment with inhaled bronchodilators and or ICS when they started the inhalation therapy of moxa smoke or the alternative therapy (Table 5) if they had severe shortness of breath without inhalation of bronchodilators and or ICS. They continued with this co-treatment until the inhalation therapy or alternative therapy started to take effect i.e., they had less shortness of breath, compared with when only using bronchodilators and or ICS. Then they stopped bronchodilators/ICS completely, but continued with inhalation therapy of moxa smoke until their COPD symptoms completely disappeared.

As per the Table 6, all 3 very severe patients and 10 severe patients had co-treatment initially. Seven of twelve moderate patients also had co-treatment until the inhalation therapy started to take effect. Five of twelve moderate patients stopped previous treatment with inhaled bronchodilators and or ICS when they started inhalation therapy of moxa smoke. They managed to cope with shortness of breath after discontinuation of inhaled bronchodilators and or ICS by reducing physical activity.

Evaluation of the Therapeutic Effects of Inhalation of Moxa Smoke

Clinical therapeutic effects were evaluated according to COPD symptoms and values of spirometry. Three out of twenty five patients (1 chronic obstructive bronchitis patient, 2 moderate emphysema patients) had no improvement in their COPD symptoms or spirometry values after having one course (15 days) treatment with the inhalation of moxa smoke and refused to continue treatment with this therapy and remaining twenty two patients showed improvement in breathlessness and or cough with or without sputum after one or two courses of treatment with the inhalation of moxa smoke or the alternative therapy.

Among all, 18 patients with co-treatment stopped treatment with bronchodilators or ICS but continued treatment with the inhalation therapy of moxa smoke or the alternative therapy until symptoms free. Four patients with mono-therapy (only inhalation of moxa smoke) continued inhalation therapy until symptoms free. The lips cyanosis of 3 very severe emphysema patients has disappeared after treatment with inhalation therapy.

The definition of symptoms free:

1. No breathlessness on moderate exertion for moderate severe and severe patients

2. No breathlessness on walking level ground for very severe patients

3. No productive cough

4. Do normal daily life activities without limitation

Comparison of spirometry values of 22 symptoms free patients before and after treatment with inhalation therapy or alternative therapy are given below:

1. Three very severe and 10 severe emphysema patients: No change in spirometry value before and after treatment with inhalation of moxa smoke or alternative therapy.

2. Seven moderate severe emphysema patients: Before treatment with inhalation of moxa smoke: FEV_1/FVC <70%; FEV_1=40% to 59% predicted. After treatment with inhalation of moxa smoke: FEV_1/FVC <70%; FEV_1= 50% to 70% predicted.

3. Two moderate severe chronic obstructive bronchitis patients: Before treatment with inhalation of moxa smoke: FEV_1/FVC<70%; FEV_1=40% to 59% predicted. After treatment with inhalation of moxa smoke: FEV_1/FVC <70%; FEV_1>80% predicted.

All these 22 patients became symptoms free after 2 to 4 courses of treatment with inhalation of moxa smoke or the alternative method. They could do their normal daily life activities without limitation and did not need any further treatment with SABA, LABA, LAMA and or ICS. These patients were followed up from 6 months to 2 years, no relapse and all 22 patients kept symptoms free.

Spirometry tests were repeated for these 22 symptoms free patients 6 months to 2 years after inhalation therapy of moxa smoke or alternative therapy, the spirometry values of all 22 patients were the same as that when they had just finished inhalation therapy of moxa smoke or alternative therapy.

At clinical level, inhalation therapy of moxa smoke or alternative therapy show some curative effect for COPD patients, i.e., after a period of treatment with inhalation therapy of moxa smoke or alternative therapy, 22 of 25 COPD patients kept symptoms free without any further treatment. While the successful rate is 88%, 3 patients had no improvement in their COPD symptoms or spirometry values after one course (15 days) treatment with inhalation of moxa smoke thus the failure rate is 12%.

Self-comparison of these 25 patients showed big difference in COPD symptoms before and after treatment with inhalation therapy of moxa smoke or alternative therapy. Before treatment with the inhalation of moxa smoke or alternative therapy, all 25 patients needed daily treatment with inhaled bronchodilators and or ICS, but they still had mild to severe shortness of breath and or cough with or without sputum; without treatment with inhaled bronchodilators and or ICS, all these 25 patients had moderate to severe dyspnoea and or cough with or without sputum, their daily life activities were severely affected by COPD. After treatment with the inhalation of moxa smoke or the alternative therapy, 22 of 25 patients kept symptoms free without any further treatment.

The difference of COPD symptoms of these 22 of 25 patients before and after treatment with the inhalation of moxa smoke or the alternative method is significant. As moxa tar or smoke has been proved it can cure chronic inflammation in many other different chronic inflammatory diseases (chronic laryngitis, chronic muscle injury, chronic pelvic inflammatory disease, chronic atrophic gastritis, thrombophlebitis obliteran), the author presumes that the disappearance of COPD symptoms for these 22 of 25 patients who received inhalation therapy or alternative therapy could be due to curing of the inflammation in the lungs and respiratory tract, this would markedly improve the efficiency of gas-exchanging in the lung. But this presumption needs to be confirmed by more objective tests, like diffusing capacity for carbon monoxide, bronchoalveolar lavage for counting inflammatory cells before and after treatment, or bronchoscopic biopsy. Unfortunately, these tests are beyond the author's capability. Though the inhalation therapy or alternative therapy show curative effect in COPD symptoms for 22 of 25 COPD patients, the spirometry values of 3 very severe and 10 severe emphysema patients have not changed after treatment with inhalation therapy or alternative therapy. The spirometry values of 7 moderate severe emphysema patients have slightly improved after treatment with inhalation therapy. The spirometry values of 2 moderate chronic obstructive bronchitis patients have moderately improved after treatment with inhalation therapy.

The author believes the reason there had been no change or no significant improvement in spirometry values for these 22 symptoms free COPD patients after treatment with inhalation therapy or alternative therapy is that the tissue damage in COPD cannot be reversed. Curing the inflammation in COPD could stop progression of tissue damage, but cannot reverse the tissue damage.

The side-effects of the inhalation therapy of moxa smoke

Inhalation of moxa smoke can slightly increase the risk of chest infection for COPD patients. One of 23 patients who received the treatment of inhalation of moxa smoke developed mild chest infection (symptoms and signs include wheezing, increased shortness of breath and fever 37.5°C) after twenty days treatment with 8 inhalations of moxa smoke one session a day. The author immediately stopped this patient's treatment with inhalation of moxa smoke and treated her with cephalexin 500 mg tablet, one six hourly for five days. This patient's wheezing, increased shortness of breath and fever settled after one-day treatment with cephalexin 500 mg tablet, one six hourly. She continued the antibiotic treatment for another four days and completely recovered.

The author restarted the inhalation therapy of moxa smoke for this patient but reduced the dose from 8 inhalations a day to 4 inhalations a day. This patient continued her treatment with this dose for another two courses (30 days) until her COPD symptoms completely disappeared. She did not have chest infection again after her inhaled dose of moxa smoke had been reduced.

The other side-effect of the inhalation therapy of moxa smoke is that a few patients felt difficult to fall asleep at night after receiving the inhalation therapy. This problem was solved by giving the treatment in the morning.

Two of the twenty five patients felt the smoke of burning moxa irritable and could not tolerate it. They were treated with the alternative treatment.

Discussion of the Possible Anti-inflammatory Mechanisms of Moxa Tar

Chronic self-perpetuating inflammation is very common in many chronic inflammatory diseases, like COPD, chronic pelvic inflammatory disease, chronic laryngitis, chronic muscle injury, chronic gastritis and so on. T cell plays an important role in sustaining the chronic self-perpetrating inflammation.

The author has noticed that moxa tar was only effective in treating chronic inflammatory conditions in which there were T cells involved. For example, moxa tar is not effective for hay fever, there are no T cells involved in the pathogenesis of hay fever. Moxa tar is also not effective in treating diseases of type III immune reaction. The author hypothesizes that the active components of moxa tar can inhibit T cell activity or molecules related to T cell activity, leading to block or terminate the chronic inflammatory reaction.

Discussion of Potential of Moxa Tar Treating Other Chronic Inflammatory Diseases

As many chronic inflammatory diseases have the same or similar mechanisms that sustain the inflammation i.e., positive intercellular reactions between T cells and other inflammatory cells. Theoretically, if moxa tar can treat one of these chronic inflammatory diseases it is possible to treat other chronic inflammatory diseases.

At clinical practicing, the author and other Chinese herbalist have used moxa tar to successfully treat and cure many chronic inflammatory diseases which have the same or similar mechanisms that sustain the inflammation, including COPD, chronic laryngitis, chronic pelvic inflammatory disease, radiation colitis, asthma, diabetic foot, pulmonary fibrosis, sarcoidosis, Buerger's disease, angina, psoriasis, corticosteroid resistant eczema, crohns disease, refractory migraine, chronic gastritis, chronic muscle injury, irritable bowel syndrome and so on, all these diseases are resistant to corticosteroid.

The author believes that moxa tar has potential to treat any T cells involved chronic inflammatory diseases, especially atherosclerosis. Atherosclerosis is considered as a chronic inflammatory response of the vascular wall to a variety of insults. The mechanisms that sustain the inflammation in atherosclerosis could be the same as in many other chronic inflammatory diseases, i.e., due to bidirectional intercellular reactions between macrophages and T cells and or T cells and smooth muscle cells. Theoretically it is highly possible that moxa tar can effectively treat the inflammation in atherosclerosis, if it can treat and cure other chronic inflammations that may have the same sustaining mechanisms as the inflammation in atherosclerosis has.

Clinically, there is evidence to support the author's belief. Moxa tar can effectively treat angina, diabetic foot and chronic renal failure in aged people who do not have other chronic kidney diseases (chronic renal failure in aged people is due to renal artery atherosclerosis). All these three conditions are related to atherosclerosis.

As inflammatory cells and factors are involved in the initiation, progression and complications of atherosclerotic lesions, if the inflammatory process in atherosclerosis can be controlled or terminated by moxa tar, it would lead to stopping or reversing the growth of atheroma.

The purpose of this paper is to introduce a new anti-inflammatory therapy for treatment of COPD and other chronic inflammatory lung diseases, including asthma, pulmonary fibrosis, other interstitial lung diseases, radiation pneumonitis, and open up a whole new field for developing novel anti-inflammatory drugs [1,2].

Conclusion

1. Inhalation of moxa smoke can cure the inflammation in COPD. Moxa tar is a cure for chronic non-specific inflammation.

2. Moxa tar has strong and special anti-inflammatory property; its anti-inflammatory mechanisms are different from that of corticosteroid. It can treat and cure a wide range of corticosteroid resistant chronic inflammatory conditions.

3. Moxa tar is a very important source for developing novel anti-inflammatory drugs.

If the active anti-inflammatory components in moxa tar are identified and isolated, they can be used to make a new anti-inflammatory drug and used systemically to treat and cure many chronic inflammatory diseases which are not curable by current medications.

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