

Efficacy of TCM therapy of tonifying lung–kidney's Qi-deficiency in a case of idiopathic pulmonary fibrosis

A case report

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Abstract

Rationale: Idiopathic pulmonary fibrosis (IPF) is a special form of spontaneous, chronic, progressive interstitial fibrotic pneumonia of unknown cause, and treatments for IPF have shown a poor prognosis. This study reports a new treatment, traditional Chinese medicine (TCM) therapy, for tonifying Qi-deficiency of lung–kidney in a 64-year-old patient with IPF.

Patient concerns: A 64-year-old man, who complained of cough and asthma, was diagnosed as IPF with mild impairment in lung function by thoracic high-resolution computed tomography and pulmonary function test. He received an 18-month N-acetylcysteine monotherapy but had no improvement in lung function.

Diagnoses: IPF with mild impairment in lung function was diagnosed.

Interventions: The Chinese herbal medicine composition was decocted in 300ml water for oral administration with 150ml decoction twice daily in June 2017.

Outcomes: The pulmonary function test showed that diffusing capacity for carbon monoxide had increased to 81% of predicted back to normal after 2-month TCM monotherapy. And diffusing capacity for carbon monoxide had increased to 89% of predicted, and forced expiratory volume in 1 s/forced vital capacity ratio increased to 92% at 14-month follow-up. No adverse events occurred during the 14 months of therapy and observation.

Lessons: The treatment by TCM therapy of tonifying lung–kidney's Qi-deficiency for IPF can improve the pulmonary function and reverse disease progression; it may be considered as a complementary treatment for IPF with mild-to-moderate impairment. However, the insights provided in this case report require further exploration and verification.

Abbreviations: CHM = Chinese herbal medicine, DLCO = diffusing capacity for carbon monoxide, ECM = extracellular matrix, FEV1 = forced expiratory volume in 1 s, FVC = forced vital capacity, IPF = idiopathic pulmonary fibrosis, TCM = traditional Chinese Medicine.

Keywords: Chinese herbal medicine, idiopathic pulmonary fibrosis, N-acetylcysteine monotherapy, traditional Chinese medicine

1. Introduction

Idiopathic pulmonary fibrosis (IPF) is a special form of spontaneous, chronic, progressive interstitial fibrotic pneumonia of unknown cause. It is reported that a conservative estimate of IPF prevalence rate is about three to nine cases per 100,000 people.^[1,2] Dyspnea is the main symptom of IPF, which is always

combined with a step-wise decline in pulmonary function test parameters.^[1] Several pharmacologic therapies are used in the treatment of IPF, including the N-acetylcysteine monotherapy that may benefit patients by altering the oxidative state but cannot reverse or slow down the progress of IPF through clinical trial data studies. Generally, no pharmacologic therapies have shown a dramatically enhanced survival in patients with IPF.^[3,4] Traditional Chinese medicine (TCM), a main part of medical treatments over the past 5000 years in China, has achieved certain curative effects on IPF. TCM therapy has shown antifibrotic benefit and lung-function improvement in recent years, and has been applied for the treatment of worsen dyspnea.^[5,6] Here, we report a case of a patient with IPF, who adopted N-acetylcysteine monotherapy with no effect, being successfully treated by TCM therapy.

2. Case report

We report the case of a 64-year-old Chinese male who had IPF with mild impairment in lung function. Before his IPF diagnosis, the patient complained no discomfort except cough and asthma. IPF diagnosis was confirmed by thoracic high-resolution computed tomography that showed intralobular interstitial

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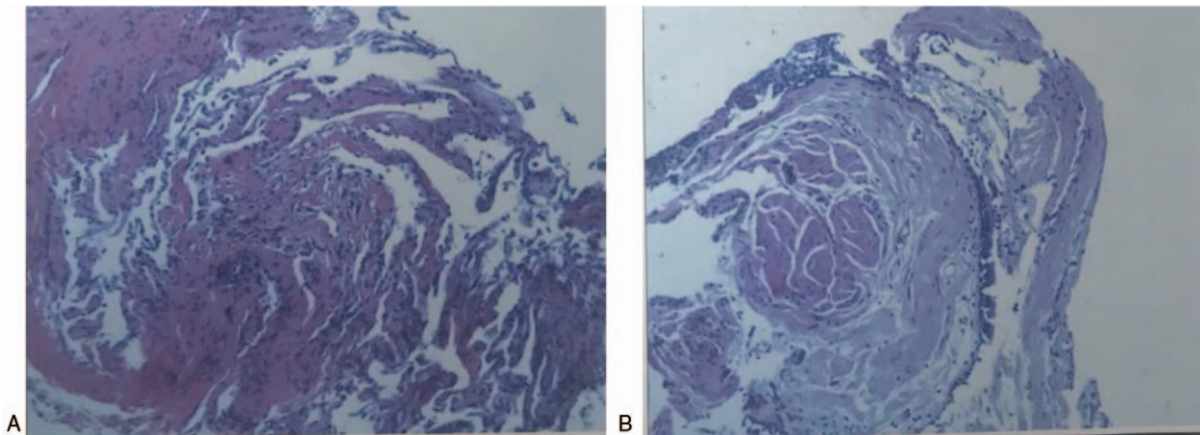


Figure 1. Endoscopic biopsy report. (A) Microscopy of right lower lobe segment. Mucosal and lung tissues covered with respiratory epithelium were visible in the examination materials. No abnormality was found in the epithelium. The alveolar interval was slightly widened, alveolar type II cells were slightly hyperplasia, and interstitial fibrous tissue hyperplasia was observed. (B) Clinical-radiologic-pathologic diagnosis of right lower lobe segment tissue; chronic nonspecific inflammation of the bronchial mucosa.

and septal thickening of both his lower lobes and subpleural regions. This patient exhibited a high burden of oxidative stress symptoms at the Department of Respiratory Medicine in Beijing, and received N-acetylcysteine monotherapy for 18 months. Diagnosis was confirmed as IPF with mild impairment in lung function at the respiratory department. But till June 2016, his pulmonary function test showed obstructive ventilation function disturbance and poor lung diffusing capacity for carbon monoxide (DLCO) that was 75% of predicted. Concurrent peripheral capillary oxygen saturation ($=77.1$ mm Hg) was diagnosed by arterial blood gas analysis. Further endoscopic biopsy at right lower lobe showed thickening basement membrane and interstitial fiber hyperplasia, and clinical-radiologic-pathologic diagnosis reported chronic nonspecific inflammation of the bronchial mucosa (Fig. 1). HIV combined detection of antigens and antibodies, syphilis, and rheumatic autoantibodies tests also come to negative meantime.

At the respiratory department, in December 2015, our patient had received N-acetylcysteine monotherapy that consisted of 600 mg acetylcysteine (Hainan Zambon Pharmaceutical Co., JX20060138) by oral administration twice daily. After 18 months of N-acetylcysteine monotherapy, the patient's lung function had not got improved, but concurred much frequent chest congestion and dyspnea symptoms. On June 17, 2017, the patient sought Chinese herbal medicine (CHM) treatment in TCM Department of Chinese People's Liberation Army general hospital.

On TCM observation, the patient had frequent chronic cough with asthma, which meant deficiency in the lungs; simultaneously, his cold intolerance, weakness in the waist and knees, and self-perspiration showed deficiency in the kidney. Pale red tongue covered by white coating together with deep pulse, which is diagnosed by tongue and pulse examination from TCM, exhibited lung-kidney's Qi-deficiency. Diagnosis of the TCM finally confirmed Qi-deficiency of lung-kidney internally. We prescribed traditional herbal medicine decoction to benefit the lung and kidney by tonifying Qi. CHM composition (Table 1), which was used for the patient, were Huangqi (*Astragalus membranaceus*), Baizhu (*Rhizoma atractylodis macrocephalae*), Fangfeng (*Saposhnikovia divaricata*), Shudi (*Radix rehmanniae*

preparata), Shanyao (Chinese yam), Shanyurou (*Fructus corni*), Ganjiang (*Rhizoma zingiberis*), Wuweizi (*Schisandra chinensis*), Banxia (*Pinellia ternata*), Zhimahuang (honey-fried *Ephedra sinica*), Kuxingren (*Semen armeniacae amarum*), Zhigancao (honey-fried *Glycyrrhiza uralensis*), Fuling (*Poria cocos*), and Guizhi (*Ramulus cinnamomi*). Buguzhi (*Fructus psoraleae*) and Baishao (*Radix paeoniae alba*) were later added at 8 weeks because the patient had gradually developed symptoms of self-sweating and intolerance of cold.

The CHM composition were decocted in 300 ml water for oral administration with 150 ml decoction twice daily. Previous N-acetylcysteine monotherapy prescribed in the respiratory department was halted concurrently in June 2017. Simultaneously, this patient received a TCM monotherapy for 14 months, with no other drug used during this period.

In August 2017, 2-month TCM monotherapy later, pulmonary function test showed that the DLCO had increased to 81% of predicted back to normal. In August 2018, after the 14-month TCM monotherapy, his pulmonary function test showed that DLCO had increased to 89% of predicted and forced expiratory volume in 1 s (FEV1)/forced vital capacity (FVC) ratio increased to 92%; thus, it was possible to enhance his pulmonary function with oral traditional herbal medicine decoction. No significant lung function and thoracic high-resolution computed tomography changes were observed. And relevant complaints of IPF got improved after the TCM monotherapy. This patient's adherence to the CHM decoction was good and no adverse events occurred during 14-month observation period. The changes in carbon monoxide and FEV1/FVC ratio are detailed in Table 2 and Figure 2.

3. Discussion

After the excessive accumulation of extracellular matrix (ECM) in affected lungs, which presents as dyspnea and asthma, the lung architecture disorders and diffuse inflammation led to a progressive, fibrosing, interstitial pneumonia.^[7,8] The superabundant inflammation is involved in ECM and results in imbalance between the synthesis and degradation of ECM. To date, treatments targeting these events, which include glucocorticoids, cytokine inhibitors, antifibrotic agents, and lung transplantation or else,

Table 1**Ingredient and function of Chinese herbal formulas.**

Classification	Traditional Chinese herb	Daily dose (g)	Function
Lung-Qi tonifying medicinal	Huangqi (<i>Astragalus membranaceus</i>)	30	Consolidates body-superficies and invigorates spleen-Qi
	Baizhu (<i>Rhizoma atractylodis macrocephalae</i>)	10	
Kidney-Qi tonifying medicinal	Fangfeng (<i>Saposhnikovia divaricata</i>)	10	Enhances kidney nourishment to improve respiratory function and lung-kidney concurrent treatment theory
	Shudi (<i>Radix rehmanniae preparata</i>)	30	
	Shanyao (Chinese yam)	15	
	Shanyurou (<i>Fructus corni</i>)	15	
Qi-descending and phlegm-resolving medicinal	Buguzhi (<i>Fructus psoraleae</i>)*	10	Directs lung-Qi download and dispels phlegm in bronchial to calm panting
	Ganjiang (<i>Rhizoma zingiberis</i>)	6	
	Wuweizi (<i>Schisandra chinensis</i>)	6	
	Banxia (<i>Pinellia ternata</i>)	10	
	Zhimahuang (honey-fried <i>Ephedra sinica</i>)	6	
	Fuling (<i>Poria cocos</i>)	10	
	Kuxingren (<i>Semen armeniacae amarum</i>)	6	
	Guizhi (<i>Ramulus cinnamomi</i>)	10	
Harmonizing medicinal	Baishao (<i>Radix paeoniae alba</i>)*	10	Harmonizes nutrition-Qi and defensive-Qi of body superficies
	Zhigancao (honey-fried <i>Glycyrrhiza uralensis</i>)	10	Harmonizes this prescription's various ingredients

The prescription was decocted in water for oral dose, one dose each day (300 ml) and two times a day.

* The herbals were later added at 8 wk for the patient presenting self-sweating and intolerance of cold.

may promote the effect of IPF. But few clinical therapies have shown a better prognosis, and 5-year survival for IPF remains to be 20% and 40%.^[9–11] N-acetylcysteine, a precursor of the antioxidant glutathione, was once reported that it may restore pulmonary glutathione levels and alter the oxidative state of the lung favorably, whereas recent studies have shown conflicting results that N-acetylcysteine monotherapy offered similar benefits, costs, and a worse effectiveness as compared to placebo, and could not improve IPF disease progression. It is also suggested that clinicians should not use N-acetylcysteine monotherapy in patients with IPF, detailed in an official ATS/ERS/JRS/ALAT Clinical Practice Guideline with respect to treatment of IPF issued in 2015.^[3,9,12] In this case, the Department of Respiratory Medicine used N-acetylcysteine monotherapy, but the improvements of discomfort symptom and pulmonary function test was not obvious.

TCM treatment of IPF has shown an effective and safe result reported during past 10 years.^[13–15] As one of the main parts of complementary medicine, reports showed that TCM in combination with Western medicine could improve FEV1 and DLCO and reduce incidence of adverse events.^[16] In comparison with N-acetylcysteine, the effectiveness of CHMs for the disease requires evaluation on mortality, the quality of life, 6-minute

walking test distance, lung function (DLCO and FVC), and safety in patients, which is detailed in a relevant systematic review protocol.^[17] Parameters of the pulmonary function could help predict and monitor the extent of IPF, of which carbon monoxide (DLCO) and FEV1/FVC ratio was reliably associated with decreased survival.^[18] Although CHMs appear beneficial in improving lung function, TCM therapy did not decrease the mortality significantly, which was mentioned by a meta-analysis that included 25 randomized controlled trials comparing TCM treatment with Western medicine on IPF.^[16] But this evidence was weak for limited quality and small sample size of the clinical trials. Meantime, few studies reported effectiveness of TCM monotherapy on IPF. According to this patient's desire and adherence for TCM, we used CHM decoction for 14 months and received a good result. According to TCM theory, we describe symptoms of chronic cough, dyspnea, fatigue, and cold intolerance or else as Qi-deficiency of lung-kidney. Regarding this patient's TCM syndrome, we prescribed CHM decoction to tonify the Qi-deficiency of lung-kidney.

In a 14-month TCM monotherapy, no serious complication happened; no serious asthma, ischemic heart disease, and reflux esophagitis occurred in this case. After TCM monotherapy, lung function significantly improved, as DLCO and FEV1/FVC ratio

Table 2**Results of respiratory functional tests before and after a TCM monotherapy in a patient with idiopathic pulmonary fibrosis.**

Test	June 2016	August 2017	August 2018	
Respiratory functional tests	FEV1/FVC	73.79%	88%	92%
Spirometry	FEV1	104.5% of predicted value	105% of predicted value	99% of predicted value
	FVC	114.3% of predicted value	118% of predicted value	107% of predicted value
	DLCO	DLCO (%)	75% of predicted value	81% of predicted value

June 2016 refers to the time before TCM monotherapy, August 2017 refers to the time after 2-mo TCM monotherapy, and August 2018 refers to the time after 14-mo TCM monotherapy.

DLCO=diffusing lung capacity for carbon monoxide, FEV1=forced expiratory volume in 1 s, FVC=forced vital capacity, TCM=traditional Chinese medicine.

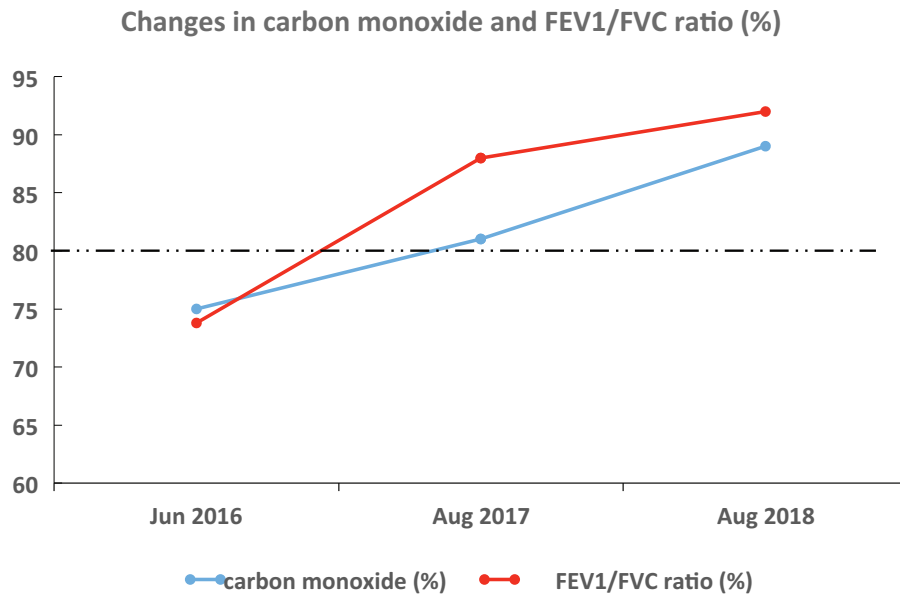


Figure 2. Changes in carbon monoxide and FEV1/FVC ratio (%). (A) Baseline represents the respiratory functional results before TCM monotherapy in December 2016, 1 refers to results in August 2017 after 8-wk TCM monotherapy, and 2 refers to results in August 2018 after 14-mo TCM monotherapy. DLCO = diffusing lung capacity for carbon monoxide, FEV1 = forced expiratory volume in 1 s, FVC = forced vital capacity, TCM = traditional Chinese medicine.

gradually increased. This case report demonstrates that tonifying lung–kidney’s Qi-deficiency CHM formula is effective and safe, and may be considered as a complementary and alternative treatment for IPF with mild impairment in lung function. Main components of Qi-tonifying medicinal herbs (*Astragalus membranaceus*, *Rhizoma atractylodis macrocephalae*, and *Saposhnikovia divaricata*) could improve lung function and exert protective role on IPF model rats by reducing the levels of cytokines in serum and downregulating TGF- β 1/Smad3 signaling pathway.^[19] Further series of case series are needed to determine the efficacy of the treatment of TCM monotherapy on IPF, as it is only a single case reported from our findings.

4. Conclusion

IPF with severe impairment is clinically difficult to treat for poor prognosis, so early interventions should be initiated for IPF with mild-to-moderate impairment. The TCM therapy of tonifying Qi-deficiency of lung–kidney can improve the pulmonary function and reverse disease progression; it may be considered as a complementary treatment for IPF with mild-to-moderate impairment. However, the insights provided in this case report require further exploration and verification.

5. Ethical approval

The patient has provided written informed consent for the publication of the case and any accompanying images.

Author contributions

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