

Original Article

Concomitant acupoint therapy with hyperthermia and Chinese traditional herb improved lung function in patients with chronic obstructive pulmonary disease

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Abstract: Acupuncture, hyperthermia and traditional Chinese herb are used for control of many symptoms. In this study, we explored a novel therapeutic approach for achieving a long-term and potent therapeutic effect in patients with COPD at stable stage. A total of 120 patients with stable COPD were received concomitant acupoint sticking therapy with both hyperthermia and Chinese herb at BL13 (feishu) and BL20 (pishu) acupoints respectively. Patients were treated with acupoint alone and combined acupoint treatments with hyperthermia or Chinese herb were used as controls. After 6 and 12 weeks' post-initial treatment, lung function, 6 minute walk distance test (6MWT), the modified medical research council (mMRC) dyspnoea scale, COPD assessment test (CAT) were assessed. We observed moderately improved pulmonary function among all groups of patients, with increased percentage of forced expiratory volume in one second (FEV1) of predicted (FEV1% predicted) and percentage of forced vital capacity (FVC) of predicted (FVC% predicted). The improved pulmonary function in all treated groups were also associated with significantly increased 6-minute walk test score (6MWT) and symptom control ($P < 0.01$). In addition, lung function was more greatly improved in patients received concomitant acupoint therapy with both hyperthermia and Chinese herb than the patients received concomitant acupoint treatment with hyperthermia or Chinese herb ($P < 0.01$). In contrast, the patients received acupoint therapy alone achieved the lowest improvement in lung function compared to that of pre-treatment. Concomitant acupoint therapy with both hyperthermia and Chinese herb has additive and long-term therapeutic effects on COPD at stable stage.

Keywords: Chronic obstructive pulmonary disease, acupoint, hyperthermia therapy, traditional Chinese herb

Introduction

Chronic obstructive pulmonary disease (COPD) is a severe pulmonary disorder, characterized by shortness of breath, coughing and tachypnea, and ranks as the fourth leading cause of death in the United States and worldwide [1]. It is expected that COPD will become the leading cause of mortality in 2030 [2]. Cigarette smoke (CS) is a leading risk factor of COPD development, particularly in developing countries and rural area of China [3, 4]. It is reported that acrolein and other pollutants are major components of cigarette smoke, and critically involved in the pathogenesis of COPD [5]. However the underlying mechanisms are still unknown, it might be caused by CS-induced oxidative stress

to lung epithelial cells and immune cells that causes lung tissue damage and inflammation [6, 7]. Unfortunately, there is no effective cure for the irreversible disease. Current available therapeutics included bronchodilators and anti-inflammatory regimens, that can transiently control symptoms, such as long-acting β_2 agonist, phosphodiesterase (PDE) inhibitor and corticosteroid [8-10]. Long-term use of regimens can cause a series of side-effect such as osteoporosis, cardiovascular disease and infection [11-14]. Therefore, it is necessary to explore an effective, long-lasting and safe therapeutic approach in COPD therapeutics.

Traditional Chinese medicine (TCM) has been widely used for control of many symptoms in

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China. According to Chinese meridian theory, a sufficient qi and optimal balances between v Yang and Yin are important for health. Lack of qi and unbalanced Yang and Yin cause disease [15]. Based on modern medical science, lack of qi and unbalanced Yang and Yin are in association with disrupted immune function that causes a series of cellular and molecular changes under the pathological condition [15-17]. Therefore, a sufficient qi, in another words, “energy” and normal immune function are important for normal cell biological and physiological function. The therapeutic effects of traditional Chinese medicine may be caused by improving qi or “energy” throughout body. Recent studies using techniques of molecular biology and immunology showed that traditional Chinese medicine has anti-inflammatory and antipyretic function. Patients with COPD treated with acupuncture have significant improved lung function and associated with reduced lung inflammation after treatment [18-20]. The changes was also evidenced in COPD animal model, showing that acupuncture significantly improved lung function after 2 weeks treatment at Feishu (BL13) and Zusanli (ST36) acupoints [20].

In addition, many clinical trials also showed that hyperthermia and Chinese herb have similar therapeutic effects COPD patients [21, 22]. Due to anti-inflammatory property of Chinese herbs, patient treated with Chinese herb achieved significant relief of symptoms caused by lung infection, allergy and COPD [17, 23, 24]. Although little is known about the underlying mechanisms, recent studies revealed that there are significant attenuated pro-inflammatory cytokine such as TNF- α and IL-6 released by lung tissues after Chinese herb treatment from, the reduced cytokine release is correlated with suppressed activation of pro-inflammatory transcription factors such as NF-kB, p38 mitogen-activated protein kinase, JNK and PI3K/Akt/mTOR in lung tissues of treated patients [23-27]. The immune modulatory property of Chinese herb is also demonstrated by elevated CD4+CD25+ regulatory T cells and production of anti-inflammatory cytokine and mediators such as IL-10 in COPD animal models [23, 28].

Although traditional Chinese medicine has symptom control effects, the symptom relief

does not last long-enough and recurrence still occurs in most of treated COPD patients [17, 19, 29]. Combinational acupuncture treatment with rehabilitation also did not show better symptom control in COPD patients [17, 18]. Therefore we speculate that combinational acupuncture therapy with other Chinese medicine option may present better improvement than acupuncture therapy alone. To address this issue, we in this study for the first time explored a novel therapeutic approach in which COPD patients received concomitant acupuncture therapy with both hyperthermia and Chinese herb. Patients received acupoint therapy alone or in combination with hyperthermia or Chinese herb were used as controls. After 6 weeks of treatment on a total of 120 COPD patients, we observed a much better improved lung function and symptom control with the concomitant therapeutic approach than acupuncture therapy alone.

Methods

Patients

All patients were diagnosed with COPD in accordance with the updated guidelines “Global initiative for chronic obstructive lung disease (GOLD 2007): Global strategy for diagnosis, management and prevention of COPD” (<http://www.goldcopd.com>). All enrolled patients with COPD are at stable stage and at age of 40-75 years old. Patients complicated with other lung diseases such as bronchiectasis, tuberculosis, and pulmonary fibrosis were excluded from this study. Additional exclusion criteria include pregnant or lactating women, patients complicated with chronic asthma, infected with fungi and with history of taking anti-allergic medicine and immunosuppressant. Patients with tumors, psychiatric disorder, lack of verbal communication skills and unable to follow-up post-treatment were also excluded. Informed consent form was signed by all patients included in this study.

Treatment

A total of 120 COPD patients at stable stage were included in this study from March 2012 to June 2012, and treated with traditional Chinese medicine in the Traditional Chinese Medicine Hospital of Xinjiang Uygur Autonomous Region. Patients were divided into four groups with 30

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Table 1. Demographics of patients

Characteristics	Groups (Mean ± SD)				p value
	A	B	C	D	
Age (years)	63.83±14.16	64.30±11.66	64.63±10.05	65.90±12.13	0.922
Height (cm)	165.07±7.32	164.17±5.32	166.63±8.83	168.13±8.02	0.184
Weight (kg)	66.23±10.42	70.03±11.68	65.35±15.28	71.2±10.65	0.183
Cigarette Smoke (years)	24.26±10.04	22.59±9.98	24.95±10.04	24.87±10.16	0.884
FEV1 (L)	1.33±0.53	1.29±0.53	1.37±0.57	1.41±0.59	0.868
FVC (L)	2.29±0.77	2.30±0.67	2.29±0.74	2.46±0.79	0.759
FEV1/FVC	57.97±9.64	54.97±11.72	57.67±11.09	56.76±12.49	0.732

Table 2A. FEV1% predicted in patients with COPD

Groups	Weeks post-treatment	n	Mean ± SD
A	0	30	54.10±18.90
	6	28	57.39±19.51
	12	27	58.85±22.58
B	0	30	52.43±20.02
	6	28	53.64±22.62
	12	24	55.00±22.86
C	0	30	51.33±19.27
	6	30	55.43±19.98
	12	28	57.57±19.66
D	0	30	52.59±19.06
	6	24	57.25±20.35
	12	23	57.83±22.21

Table 2B. Increased in FEV1% predicted compared to the pre-treatment

Groups	Weeks post-treatment	Mean ± SD	p value
A	6	3.00±7.67	0.048
	12	4.37±8.59	0.014
B	6	1.17±10.33	0.551
	12	3.21±8.40	0.074
C	6	4.10±13.67	0.111
	12	6.11±12.90	0.019
D	6	5.62±12.91	0.044
	12	5.00±12.24	0.063

patients per group. Patients in all groups were received the indicated treatment for 6 hours per day, twice a week and a total of 6 weeks. In Group A (hyperthermia acupoint treatment), the patients received acupoint treatment with hyperthermia paste pad (13×10 cm) at BL13 acupoint (feishu). The hyperthermia paste pad was composed of iron powder, activated carbon, and salt. After applied to the indicated acupoint area, the past pad can keep warm for at least 6 hours. In Group B (herb acupoint treatment), the patients received acupoint treatment with Chinese herbal paste pad at BL20 acupoint (pishu). The traditional Chinese herb paste was a mixture of herbal powder, azone and glycerol (Pharmacy of the Hospital of Chinese Medicine of the Xinjiang Uygur Autonomous Region). The herbal powder was composed of sun-burnt ephedra, almond, radix astragali and saussurea involucrate. In Group C (Concomitant hyperthermia and herb acupoint treatment), the patients received acupoint

treatment with both hyperthermia and Chinese herb at BL13 (feishu) and BL20 (pishu) acupoints respectively. The patients in Group D received acupoint treatment at both BL13 (feishu) and BL20 (pishu) with placebo past pad. All patients were advised to avoid physical activity and spicy food during the treatment to prevent paste pad from falling off.

Pulmonary function test

All patients received pulmonary function tests (PFTs) at pre-treatment (day 0), 6 weeks and 12 weeks post-initial treatment by using KoKo Legend portable spirometer (Spire Health, Inc. Longmont, CO, USA). Forced expiratory volume in one second (FEV1), FEV1/predictive value percentage (FEV1%), forced vital capacity (FVC), FVC/predictive value percentage (FVC%) and ratio of FEV1/FVC were recorded and analyzed. Exercise tolerance capacity was assessed by standard 6-minute walk test (6MWT). Some patients were excluded during the 6MWT because of failing to perform 6MWT. Disease symptoms and potential risks were also assessed by the modified Medical Research Council (mMRC) dyspnoea scale and COPD

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Table 3A. FVC% predicted in patients with COPD

Groups	Weeks post-treatment	n	Mean ± SD
A	0	30	72.47±17.42
	6	28	72.71±18.60
	12	27	76.93±20.48
B	0	30	72.97±17.54
	6	28	72.79±19.47
	12	24	75.13±16.86
C	0	30	68.30±15.46
	6	30	71.40±20.07
	12	28	73.46±18.11
D	0	30	72.10±16.60
	6	24	75.67±18.74
	12	23	75.48±17.45

Table 3B. Increased in FVC% predicted compared to the pre-treatment

Groups	Weeks post-treatment	Mean ± SD	p value
A	6	-0.786±8.034	0.609
	12	3.778±8.890	0.036
B	6	0.071±10.729	0.972
	12	3.917±9.771	0.062
C	6	3.100±13.031	0.203
	12	5.500±12.787	0.031
D	6	2.417±11.850	0.328
	12	3.087±11.057	0.194

Table 4A. 6MWT test score in patients with COPD

Groups	Weeks post-treatment	n	Mean ± SD
A	0	30	351.76±75.65
	6	27	374.17±65.03
	12	27	385.14±94.52
B	0	30	375.74±107.59
	6	25	395.10±110.14
	12	21	389.90±107.28
C	0	30	374.51±78.93
	6	30	421.88±76.19
	12	28	391.32±62.39
D	0	30	349.94±80.73
	6	24	370.13±72.20
	12	23	360.17±68.06

Table 4B. Increased in 6MWT score compared to the pre-treatment

Groups	Weeks post-treatment	Mean ± SD	p value
A	6	16.089±46.587	0.084
	12	34.981±69.614	0.015
B	6	23.672±66.925	0.090
	12	31.810±79.927	0.083
C	6	47.367±45.238	0.001
	12	21.564±57.263	0.056
D	6	8.750±45.981	0.361
	12	3.487±45.120	0.714

assessment test (CAT) prior- and after treatment.

Statistical analysis

All data was presented as mean±SD as absolute value or subtracted value to the value of pre-treatment as indicated. Data with normal distribution was analyzed by student t-test by using SPSS 17.0 software. Data with non-normal distribution was analyzed by Wilcoxon rank-sum test. P value <0.05 was considered statistical significantly different.

Results

Patient demographics

A total of 120 patients including 73 males and 47 females were enrolled in the study. Average age, height and weight of patients were 64.67±11.96 year-old, 166.00±7.55 cen-

ter meters and 68.20±12.26 kilogram respectively. 80 cases were smokers with average smoking history of 24.26±9.91 years. There were no statistically significant differences in age and gender among pre-treated patients. Lung function, modified medical research council (mMRC) dyspnoea scale, 6 minutes walking distance (6MWT) and COPD assessment test (CAT) score were assessed before treatment (**Table 1**) and there was no significant differences among four groups. 18 patients were withdrawn from this study in which, 8 patients failed follow-up assessment after 6 weeks of initial treatment and 10 patients terminated the treatment.

Acupoint treatment with hyperthermia and Chinese herb improved pulmonary function

At 6 and 12 weeks post-treatment, lung function was tested for all patients. The patients in

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Table 5A. MMRC score in patients with COPD

Groups	Weeks post-treatment	n	Mean ± SD
A	0	30	2.17±1.15
	6	28	1.36±0.78
	12	27	1.37±0.96
B	0	30	2.00±1.08
	6	28	1.61±0.87
	12	24	1.38±0.97
C	0	30	2.17±1.09
	6	30	1.23±0.72
	12	28	1.50±0.92
D	0	30	2.17±1.07
	6	24	1.54±0.88
	12	23	1.43±1.19

Table 5B. Decreases in mMRC score compared to the pre-treatment

Groups	Weeks post-treatment	Mean ± SD	p value
A	6	-0.786±0.876	0.000
	12	-0.778±0.847	0.000
B	6	-0.321±0.612	0.010
	12	-0.625±0.711	0.000
C	6	-0.933±0.944	0.000
	12	-0.679±1.188	0.005
D	6	-0.667±0.963	0.003
	12	-0.783±1.313	0.009

four treated groups have increased FEV1% predicted value as compared to that of pre-treatment (Tables 1 and 2A). The highest increases were observed in Group C at 12 weeks post-treatment (6.11±12.90, P = 0.019) (Table 2B). Similar to FEV1%, the value of FVC% predicted was also moderately increased in the patients of 4 treated groups at 12-weeks post-treatment. The highest increases were also observed in the patients of Group C at 12 weeks post-treatment (5.50±12.79, P = 0.031) (Table 3A and 3B). However there were less increased FVC% in patients treated with acupoint alone (Group D) at 6 and 12 weeks post-treatment (P = 0.33 and P = 0.19). Thus the results indicated that concomitant acupoint therapy with both hyperthermia and Chinese herb achieved the best improvement in lung function test. In addition, FEV1% and FVC% values were further increased at 12 weeks than 6 weeks post-initial acupoint-treatment with

Table 6A. CAT score in patients with COPD

Groups	Weeks post-treatment	n	Mean ± SD
A	0	30	19.97±8.84
	6	28	11.36±5.16
	12	27	10.74±6.06
B	0	30	16.70±7.10
	6	28	13.00±7.48
	12	24	12.08±7.81
C	0	30	19.80±6.40
	6	30	10.67±3.92
	12	28	11.36±6.19
D	0	30	18.97±7.08
	6	24	15.79±6.52
	12	23	14.17±7.90

Table 6B. Decreases in CAT compared to the pre-treatment

Groups	Weeks post-treatment	Mean ± SD	p value
A	6	-8.536±7.255	0.000
	12	-9.000±7.248	0.000
B	6	-3.464±6.540	0.009
	12	-4.792±6.840	0.002
C	6	-9.133±4.337	0.000
	12	-8.500±7.476	0.000
D	6	-3.333±5.001	0.003
	12	-4.478±7.603	0.010

hyperthermia and/or Chinese herb. The results indicated that the therapeutic effects last for at least 12 weeks after initial treatment, demonstrated a long-term therapeutic effects. However the long-lasting effects was not achieved among patients received with acupoint treatment alone (Group D) because of no further increases in lung function after 12 weeks of initial treatment.

Acupoint treatment with hyperthermia and Chinese herb improved physiological activities

To further assess whether improved concomitant acupoint treatment with hyperthermia and Chinese herb was also correlated to improved exercise tolerance capability, 6MWT was performed for patients after treatment. As a result, we observed the significant increased 6MWT score in patients of four groups. The highest increases was observed at 6 weeks post-initial

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Table 7A. Decreases in CAT score at 6 weeks-post treatment compared to the groups

Groups	n	Mean ± SD	Compared groups	Mean differences	p value
A	28	-8.54±7.255	B	-5.071	0.002
			C	0.598	0.701
			D	-5.202	0.002
B	28	-3.46±6.540	C	5.669	0.001
			D	-0.131	0.937
C	30	-9.13±4.337	D	-5.800	0.001
D	24	-3.33±5.001			

Table 7B. Decreases in CAT score at 12 weeks-post treatment compared to the groups

Groups	n	Mean ± SD	Compared groups	Mean differences	p value
A	27	-9.00±7.248	B	-4.208	0.043
			C	-0.500	0.800
			D	-4.522	0.031
B	24	-4.79±6.840	C	3.708	0.071
			D	-0.313	0.883
C	28	-8.50±7.476	D	-4.022	0.053
D	23	-4.48±7.603			

treatment among patients received concomitant acupoint treatment with both hyperthermia and Chinese herb (Group C) (47.37 ± 45.24 , $P = 0.001$) (Table 4A and 4B). Patients received acupoint treatment with hyperthermia or Chinese herb achieved moderate increases in 6MWT. In contrast, there was less improvement in patients received acupoint alone (Group D) at 6 and 12 weeks post-treatment ($P = 0.36$ and $P = 0.71$). The results further indicated that combinational acupoint therapy with hyperthermia and Chinese herb additively increased lung function as well as exercise tolerance capacity for at least 12 weeks.

Acupoint treatment with hyperthermia and Chinese herb ameliorated symptoms of COPD

In addition to the lung function and 6MWT test, we also performed the mMRC and CAT test to assess the correlation of lung function with COPD symptom relief and risks. We observed significant decreased mMRC and CAT score in patients of four groups as compared to those of pre-treatment (Tables 5A and 6A). Patients received acupoint treatment with both hyperthermia and Chinese herb in Group C achieved

the greatest decreases in mMRC and CAT scores (-0.933 ± 0.944 and -9.133 ± 4.337) at 6 weeks post-treatment among four groups (Tables 5B and 6B); whereas the patients received acupoint treatment alone without treatment with hyperthermia and Chinese herb in Group D achieved the lowest decreases in CAT scores (-3.333 ± 5.001) at 6 weeks post-treatment among four groups (Tables 5B and 6B).

Because CAT scores were significantly decreased among four groups as compared to those of pre-treatment, we performed further statistical analysis to compare the differences among four treated groups. As a result, we observed that the patients in Group A and C have significant lower CAT scores than those of Group D at 6 and 12 weeks post-treatment. There was no significant difference between Group B and D. The results revealed that acupoint treatment with hyperthermia (Group A) and concomitant acupoint treatment with both hyperthermia and Chinese herb (Group C) have much better effects than acupoint treatment with Chinese herb (Group B) or acupoint treatment alone (Group D) (Table 7A and 7B).

There was no significant difference in CAT score between Group A and C. Thus acupoint treatment with hyperthermia (Group A) and concomitant acupoint treatment with both hyperthermia and Chinese herb (Group C) lead to comparable relief of COPD symptoms.

Discussion

Over 70,000 patients have been treated with traditional Chinese medicine for variable diseases in our hospital since 2003 and achieved significant recovery. To achieve better therapeutic effects with the approaches, we explored a novel therapeutic approach for patients with COPD at stable stage in the recent years. A total of 120 COPD patients were enrolled for our clinical trials. All patients were treated for a total of 6 weeks, two times per week. The lung function, 6MWT, mMRC and CAT scores were assessed at pre-treatment (day 0), 6 and 12 weeks post-initial treatment. Our clinical trials resulted in a great improvement in lung function and 6MWT among the patients received concomitant acupoint treatment with both hyperthermia and Chinese herb. The beneficial effects were correlated with significant

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decreased mMRC and CAT scores, and last for at least 12 weeks post-initial treatment. Our results indicated that concomitant acupoint treatment with both hyperthermia and Chinese herb has additive and long-lasting effects on lung function improvement, thus greatly improved quality of life of the treated patients. Similar to previous reports [30, 31], we also observed greater improvement in symptom relief than lung function in the treated patients, demonstrating highly reproducible for 6MWT, mMRC and CAT than lung function assay; combinational treatment with traditional medicine has immediate and long-term effects on COPD. Because COPD is a severe pulmonary inflammatory disorder with irreversible lung airway damage, suppression of inflammation become a major therapeutic option in controlling symptom. Concomitant acupoint treatment with both hyperthermia and Chinese herb may exert additive immediate anti-inflammatory effects in the treated patients. The immediately controlled symptoms may be caused by immediate suppression of lung inflammation. It warranted us for further analysis by histology analysis of lung biopsies and cellular analysis of sputum in the further. Previous studies in COPD animal models have confirmed that Chinese herb effectively controlled symptoms by attenuation of immune cell influx into airspace and suppressing release of some pro-inflammatory cytokines. However full recovery of lung function required repair of damaged lung tissues that is irreversible and difficult to repair during a short period of time after treatment, thus lung function assessment did not completely reflect actual symptoms in our study. We still observed gradually improved lung function and symptom relief even 6 weeks after stopping treatment. The results implied that concomitant treatment has more potent and long-lasting therapeutic effects than acupuncture treatment alone. We will perform a longer follow-up study in a larger scale of patient population to determine the long-term effects and possible effects on lung tissue remodeling.

It should be noted that there was a greater lung function improvement in the acupoint combined with hyperthermia treated patients as compared to acupuncture treatment alone, secondary to the patients treated in Group C. According to the meridian theory of Chinese medicine, the increased therapeutic effects

may be caused by increased blood circulation flow and qi through meridians, particularly in the acupoint area [15, 32], where immune cells were activated by acupuncture and hyperthermia stimulation and interplay each other through nervous and blood circulating system. According to the previous results [15], the activated anti-inflammatory immune cells may be recruited into the inflamed lung tissues where release anti-inflammatory cytokines and clear up irritants and dead cells. Studies in animal model have revealed that acupoint treatment and hyperthermia increased phagocytosis and clearance of dead cells [15, 19, 22]. Thus we speculate that hyperthermia increased blood vessel permeability, and subsequently allow efficient absorption of the applied Chinese herb components into blood circulation to achieve an efficient anti-inflammatory effect of Chinese herb. Without hyperthermia treatment, the applied Chinese herb was not efficiently absorbed into blood stream. That may explain the lower lung function improvement among the patients received concomitant acupoint treatment with Chinese herb than those received concomitant acupoint treatment with both hyperthermia and Chinese herb.

Concomitant acupoint therapy with hyperthermia and Chinese herb greatly improved lung function and exercise tolerance capacity, with more pronounced effects on symptom relief. The improved therapeutic effects last for at least 12 weeks post-treatment. We conclude that hyperthermia and Chinese herb are promising adjuvants of acupoint therapy for patients with COPD.

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Disclosure of conflict of interest

None.

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