Acupuncture treatment of lung-spleen Qi deficiency in stable chronic obstructive pulmonary disease: a randomized, open-label, controlled trial

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Supported by the Science Projects of Administration of Traditional Chinese Medicine of Sichuan (No. 2016C067)
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Accepted: September 9, 2019

Abstract

OBJECTIVE: To evaluate the effectiveness and safety of acupuncture that reinforces the spleen to strengthen the lung in patients with stable chronic obstructive pulmonary disease (COPD).

METHODS: This was a randomized, open-controlled trial in which the acupuncturist and the participants were not blinded, but the outcome evaluators and data analysts were blinded. One-hundred-and-two patients with stable COPD were randomly divided into two groups in a 1:1 ratio. The acupuncture group received 30-minute sessions of acupuncture therapy at the same acupoints three times weekly for 6 weeks in addition to routine conventional Western Medicine treatment; the control group received routine conventional Western Medicine treatment alone. The primary outcome was the Borg scale score, which was assessed immediately after the 6-minute walk test. The secondary outcomes were the 6-minute walk distance, lung function, and oxygen saturation. Measurements were obtained at baseline and after 6 weeks of treatment.

RESULTS: After 6 weeks of treatment, the Borg scale score in the acupuncture group was significantly better than that in the control group (2.02 ± 0.71 versus 5.01 ± 0.34, P < 0.05). Furthermore, the post-treatment improvements in the 6-minute walk distance, lung function, and oxygen saturation were significantly greater in the acupuncture group than in the control group, showing that the acupuncture group had better exercise tolerance.

CONCLUSION: The findings suggest that acupuncture that aims to reinforce the spleen to strengthen the lung is a safe and effective adjuvant therapy that effectively improves the exercise capacity of patients with stable COPD.

Keywords: Acupuncture; Pulmonary disease, chronic obstructive; Randomized controlled trial; Symptoms and signs
INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common respiratory disease characterized by incomplete reversible airflow limitation, which can be treated and prevented. The airflow limitation in COPD develops continuously and is related to the chronic inflammatory response of airway and lung tissue to harmful particles or harmful gases such as tobacco smoke. The global incidence, disability, and mortality of COPD have increased in recent years. The data collected by the Global Burden of Disease in 2016 indicate that COPD will be the third leading cause of death worldwide by 2020, and a recent study reported that there are approximately 100 million patients with COPD in China, bringing huge social and economic burdens.

The Global Initiative for COPD indicated that the main therapeutic goal of stable COPD is to relieve symptoms and prevent acute exacerbation. Acute exacerbation of COPD leads to a faster decline in lung function and an exponential increase in the risk of death. Therefore, it is crucial to treat patients in the stable stage of COPD to improve the prognosis of COPD. In the treatment of COPD, the first task is for the patient to quit smoking, followed by pharmacologic intervention. Despite the use of inhaled bronchodilators (beta-2 agonists and anticholinergic agents) and glucocorticoids recommended by the clinical guidelines of Western Medicine, patients with COPD still frequently have symptoms such as cough, sputum production, dyspnea, and acute exacerbation. Furthermore, these drugs cause adverse effects such as osteoporosis, arrhythmia, or cognitive function impairment, which independently influence mortality and hospitalization. Thus, there is a need for the identification of more effective and safer therapies to treat the symptoms of stable COPD.

Traditional Chinese medicine (TCM) provides alternative treatment options for COPD. In TCM theory, COPD is summarized as lung distention (Fei Zhang). "Qi" is a unique concept in TCM. In TCM, the lung governs Qi and controls breathing. Therefore, when the lung is attacked by evil Qi, the rise and fall of the lung Qi will be disturbed and the lung Qi will become deficient without timely treatment. The lung belongs to the "metal" element, while the spleen belongs to the "earth" element. In TCM theory, "earth can transform into metal". In other words, "earth (spleen)" is the mother of "metal (lung)". Spleen Qi can digest, obtain and transfer energy (Qi) from food, thus strengthening the lung Qi, just as the land can provide nutrients to plants. If the "son organ (lung)" is becoming weak, the energy (Qi) provided by the "mother organ (spleen)" will be overused. However, in trying to meet the needs of the "son organs (lungs)", the "mother organ (spleen)" will eventually become weak. Therefore, lung-spleen Qi deficiency is one of the most common TCM symptom patterns identified in patients with stable COPD, and the main therapeutic method is to reinforce the spleen to strengthen the lung.

Acupuncture is a part of TCM that is used in China to treat various diseases such as stroke, migraine, Alzheimer’s disease, and COPD. Several clinical trials have shown that the use of Chinese herbal medicine to reinforce the spleen to strengthen the lung in patients with COPD significantly reduces the frequency of exacerbation, relieves the symptoms, and improves the lung function and quality of life. However, little research has evaluated the treatment of COPD by performing acupuncture to reinforce the spleen to strengthen the lung. Thus, the aim of the present study was to evaluate the efficacy of acupuncture therapy to reinforce the spleen to strengthen the lung in the treatment of stable COPD.

METHODS

Patients

The present study was conducted from October 2016 to March 2018, and included patients with stable COPD who were treated in the Chengdu Pidu District Hospital of TCM. The study was approved by the medical ethics committee of the Chengdu Pidu District Hospital of TCM (approval No. 2016KY-001). Each patient provided written informed consent for treatment and study inclusion.

Randomization and blinding

The study was conducted as a randomized, single-blind, controlled trial. Patients who met all the inclusion criteria and did not meet the exclusion criteria were randomly allocated to the acupuncture group or the control group in a 1:1 ratio. A computerized random number table was used to generate a random code for each participant. Acupuncturists and patients were not blinded to the group assignments. However, the efficacy evaluators and data analysts were blinded to the grouping of the patients.

Sample size

The sample size calculation was based on the primary outcome, which was the pre- to post-treatment change in the Borg scale score at the end of the 6-min walk test (6MWST). According to Suzuki et al., the minimal clinically important difference in the Borg scale score in patients with COPD is 2 units. Therefore, a sample size of 88 patients (36 per group) was required under the conditions of \( \alpha = 0.5 \) (two-sided) and \( \beta = 0.8 \). Considering a dropout rate of 20\%, a total of 102 patients (51 per group) were recruited.

Diagnostic criteria

COPD was diagnosed using the criteria of the Global Initiative for Chronic Obstructive Pulmonary Disease. The key diagnostic criteria were: (a) dyspnea, chronic cough or sputum production, and/or a history of expo-
sure to risk factors for COPD; (b) lung function testing after bronchodilator inhalation indicated that the forced expiratory volume in 1 s (FEV₁) to forced vital capacity (FVC) ratio (FEV₁/FVC) was < 0.7; (c) no other diseases.

TCM symptom pattern identification was based on the guiding principles of new TCM clinical research (2002 edition). The key diagnostic criteria for the lung-spleen Qi deficiency pattern included: (a) cough or wheezing and shortness of breath, especially during movement; (b) latissitude and spontaneous perspiration that worsen during physical activity; (c) frequent infection with the common cold virus; (d) inappetence or decreased appetite; (e) stomach turgor, abdominal distension or loose stools; (f) an enlarged tongue with white or greasy fur and a pulse that is deep and thready, deep and slow, or weak and thready. The diagnosis of the lung-spleen Qi deficiency pattern were made based on the patient having two of the items listed as (a), (b), and (c), and two of the items listed as (d), (e), and (f).

**Inclusion criteria**
The included patients met all three of the following criteria: (a) met the diagnostic criteria for stable COPD and the lung-spleen Qi deficiency pattern; (b) aged between 40 and 80 years, regardless of sex, race, education, or economic status; (c) volunteered to participate in this study and provided written informed consent.

**Exclusion criteria**
Patients with the following conditions were excluded: (a) age ≤ 40 years or ≥ 80 years; (b) pneumothorax, asthma, bronchiectasis, pleural effusion, lung cancer, pulmonary tuberculosis, tuberculosis and diffuse bronchiolitis, or other severe pulmonary disease; (c) mental disorders, serious neurological dysfunction, or other diseases leading to difficulties in understanding and communication; (d) serious cardiovascular disease, endocrine disease, hematopoietic disease, liver or kidney disease, or severe complications of other organs; (e) bleeding tendency; (f) pregnancy or lactation; (g) participation in a clinical trial within the past 3 months.

**Intervention**
Acupuncture group: in addition to routine Western Medicine treatment, the acupuncture group received 30-minute sessions of acupuncture therapy to reinforce the spleen to strengthen the lung, three times weekly for 6 weeks. The patient took the sitting position and fully exposed the following acupoints: Zusanli (ST 36), Pishu (BL 20), Feishu (BL 13), and Dingchuan (EX B1). After disinfection of the acupoints, the acupuncturist inserted a disposable acupuncture needle (0.25 mm diameter, 25 mm length) into each acupoint. The needle insertion depth ranged from 5 to 20 mm, and the needles were manually rotated clockwise and counter-clockwise at each point until the De Qi sensation occurred; the De Qi sensation comprises numbness, tingling, heaviness, and other feelings that occur after acupuncture needle insertion. The needles were retained and manually manipulated every 5 min for a total of 30 min per treatment. All patients in the acupuncture group were treated at the same acupoints.

Control group: the control group received only routine conventional treatment for 6 weeks.

**Outcome measurement**
All outcomes were measured at baseline and after 6 weeks of treatment, and the original data were recorded in case report forms. All adverse events that occurred during the study were recorded.

The primary outcome was the severity of dyspnea on exertion, which was assessed using the 6MWT. The severity of dyspnea before and immediately after the 6MWT was measured using a modified 10-point Borg category ratio scale, where 0 signified "breathing very well, barely breathless" and 10 signified "severely breathless". The Borg scale score after the 6MWT was used in the analysis.

The secondary outcome measures were: (a) 6-min walk distance (6MWD); (b) lung function based on the FVC, FEV₁, and FEV₁ as a percentage of the predicted value (FEV₁% pre); (c) oxygen saturation (SaO₂) assessed via arterial blood gas analysis.

**Statistical analysis**
Analysts who were blinded to the grouping of patients conducted the statistical analysis using SPSS 21.0 software (IBM Corp., Armonk, NY, USA). Continuous data are expressed as the mean ± standard deviation and were tested with the independent t-test for quantitative variables that were normally distributed, or with the Kruskal-Wallis test for quantitative variables that were non-normally distributed. Discrete data were tested with the χ² test. The significance level was set at P < 0.05.

**RESULTS**
A total of 102 patients were enrolled. Ten patients withdrew from the trial, giving a dropout rate of 9.8%; six patients withdrew from the acupuncture group due to loss to follow-up (n = 4) and voluntary withdrawal from the study without explanation (n = 2), while five withdrew from the control group due to loss to follow-up (n = 3), voluntary withdrawal from the study without explanation (n = 1), and death (n = 1). The final numbers of patients were 45 in the acupuncture group and 46 in the control group (Figure 1).

**Baseline data of the two groups**
There were no significant differences between the two groups in baseline characteristics such as sex, age, and course of disease (P > 0.05) (Table 1).
The mean pre- to post-treatment decrease in the Borg scale score was significantly greater in the acupuncture group than in the control group ($P < 0.05$) (Table 2).

**6MWD**

After 6 weeks of treatment, the 6MWD of the acupuncture group had significantly increased, and the increase in the 6MWD was significantly greater in the acupuncture group than in the control group ($P < 0.05$) (Table 2).

**Lung function**

Compared with the pre-treatment values, there was a significant improvement in lung function (FVC, FEV1, FEV1% pre) after treatment in the acupuncture group ($P < 0.05$). Furthermore, the lung function of the acupuncture group was significantly better than that of the control group after 6 weeks of treatment ($P < 0.05$) (Table 2).

**Arterial blood gas analysis**

The $\text{SaO}_2$ in the acupuncture group significantly increased from 87.12% ± 0.31% before treatment to 94.26% ± 0.10% after 6 weeks of treatment ($P < 0.05$). Furthermore, the acupuncture group showed a significantly greater post-treatment improvement in the $\text{SaO}_2$ than the control group ($P < 0.05$) (Table 2).

**Safety evaluation**

No adverse events occurred in either group during the study period.

**DISCUSSION**

The present results suggest that acupuncture therapy that aimed to reinforce the spleen to strengthen the lung was effective in treating COPD. In TCM theory, the pathogenesis of COPD belongs to the pattern of deficiency of Ben and excessive Biao. Within this TCM deficiency pattern, the main internal causes of stable COPD are deficiencies of the lung, spleen, and kidney. In particular, lung-spleen $\text{Qi}$ deficiency is the most common TCM symptom pattern of patients with stable COPD.28 The lung belongs to the "metal" element, while the spleen and stomach belong to the "earth" element. In accordance with the theory of the five elements,
COPD with the lung-spleen Qi produce the effects of reinforcing the spleen to strengthen the lung. Three times weekly for 6 weeks; the control group was treated with only routine conventional treatment for 6 weeks. (Individualized standard treatment according to the Global Initiative for Chronic Obstructive Pulmonary Disease 2016). Data are expressed as the mean ± standard deviation and were analyzed with the independent t-test unless stated otherwise. *Data were analyzed using the χ2 test; †Compared with the control group, P < 0.05.

Table 1 Baseline characteristics of the patients

<table>
<thead>
<tr>
<th>Factor</th>
<th>Acupuncture group (n = 45)</th>
<th>Control group (n = 46)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (%)*</td>
<td>Male</td>
<td>28 (62.22)†</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>17 (37.78)†</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td>65.9 ± 1.11†</td>
</tr>
<tr>
<td>Course of disease (years)</td>
<td></td>
<td>14.2 ± 12.5†</td>
</tr>
</tbody>
</table>

Notes: the acupuncture group was treated with routine western medicine treatment (individualized standard treatment according to the Global Initiative for Chronic Obstructive Pulmonary Disease 2016), and 30-minute sessions of acupuncture therapy to reinforce the spleen to strengthen the lung, three times weekly for 6 weeks; the control group was treated with only routine conventional treatment for 6 weeks (individualized standard treatment according to the Global Initiative for Chronic Obstructive Pulmonary Disease 2016). Data are expressed as the mean ± standard deviation and were analyzed with the independent t-test unless stated otherwise. *Data were analyzed using the χ2 test; †Compared with the control group, P < 0.05.

Table 2 Primary and secondary outcome measurements after 6 weeks of treatment ( ± ± s)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>After treatment</th>
<th>Change*</th>
<th>P value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Borg scale score</td>
<td>Treatment group</td>
<td>4.12 ± 0.13</td>
<td>2.02 ± 0.71</td>
<td>-2.08 ± 0.56</td>
</tr>
<tr>
<td></td>
<td>Control group</td>
<td>4.10 ± 0.21</td>
<td>5.01 ± 0.34</td>
<td>1.23 ± 0.76</td>
</tr>
<tr>
<td>6MWD (m)</td>
<td>Treatment group</td>
<td>303.25 ± 44.73</td>
<td>352.41 ± 72.91</td>
<td>49.26 ± 21.15</td>
</tr>
<tr>
<td></td>
<td>Control group</td>
<td>310.56 ± 39.74</td>
<td>331.15 ± 75.51</td>
<td>18.42 ± 12.01</td>
</tr>
<tr>
<td>lung function (FVC, L)</td>
<td>Treatment group</td>
<td>2.47 ± 0.57</td>
<td>2.73 ± 0.70</td>
<td>0.38 ± 0.11</td>
</tr>
<tr>
<td></td>
<td>Control group</td>
<td>2.50 ± 0.49</td>
<td>2.61 ± 0.62</td>
<td>0.09 ± 0.13</td>
</tr>
<tr>
<td>FEV1 (L)</td>
<td>Treatment group</td>
<td>1.47 ± 0.44</td>
<td>1.61 ± 0.45</td>
<td>0.29 ± 0.52</td>
</tr>
<tr>
<td></td>
<td>Control group</td>
<td>1.42 ± 0.38</td>
<td>1.59 ± 0.13</td>
<td>0.10 ± 0.47</td>
</tr>
<tr>
<td>FEV1% pre</td>
<td>Treatment group</td>
<td>53.67 ± 9.03</td>
<td>57.74 ± 10.19</td>
<td>3.9 ± 6.3</td>
</tr>
<tr>
<td></td>
<td>Control group</td>
<td>52.88 ± 10.01</td>
<td>55.79 ± 10.68</td>
<td>1.94 ± 0.06</td>
</tr>
<tr>
<td>Arterial blood gas analysis (%)</td>
<td>Treatment group</td>
<td>87.12 ± 0.31</td>
<td>94.26 ± 0.10</td>
<td>5.06 ± 0.23</td>
</tr>
<tr>
<td></td>
<td>Control group</td>
<td>88.41 ± 0.28</td>
<td>87.01 ± 0.12</td>
<td>-1.02 ± 0.09</td>
</tr>
</tbody>
</table>

Notes: the acupuncture group was treated with routine western medicine treatment (individualized standard treatment according to the Global Initiative for Chronic Obstructive Pulmonary Disease 2016), and 30-minute sessions of acupuncture therapy to reinforce the spleen to strengthen the lung, three times weekly for 6 weeks; the control group was treated with only routine conventional treatment for 6 weeks (individualized standard treatment according to the Global Initiative for Chronic Obstructive Pulmonary Disease 2016). 6MWD: 6-min walk distance; FVC: forced vital capacity; FEV1; forced expiratory volume in 1 s; FEV1% pre: forced expiratory volume in 1 s as a percentage of the predicted value; SaO2: oxygen saturation. Data are expressed as the mean ± standard deviation, and were analyzed with the independent t test. *Change from baseline to post-treatment measurements; †P values for between-group comparisons.

"earth can transform into metal". Therefore, the method of reinforcing the spleen to strengthen the lung is based on the theory of the five elements. Zusanli (ST 36) is the sea point of the stomach meridian, and the five elements theory states that the sea point belongs to the "earth" element; thus, acupuncture at this point has the effect of reinforcing the spleen and stomach and strengthening the lung.29 Pishu (BL 20) is the transport point at the back of the spleen, which has the effect of reinforcing spleen Qi. Feishu (BL 13) is the transport point at the back of the lung, which has the effect of tonifying lung Qi. Dingchuan (EX B1) is not located on a standard meridian, but has the specific effect of relieving dyspnea.20,31 In the present study, these four acupuncture points were used in combination to produce the effects of reinforcing the spleen to strengthen the lung for the treatment of patients with stable COPD with the lung-spleen Qi deficiency pattern.

In the present study, the post-treatment decreases in the Borg scale score after the 6MWT, and the post-treatment increases in the 6MWD, lung function (assessed via the FVC, FEV1, and FEV1% pre), and SaO2 were significantly greater in the acupuncture group than in the control group. These results suggest that the acupuncture therapy of reinforcing the spleen to strengthen the lung was effective in treating the symptoms of patients with stable COPD, especially dyspnea on exertion. These findings are consistent with the results reported in previous studies.17,21,30-32 In a previous randomized, single-blind, placebo-controlled trial, the Borg score significantly decreased from 5.5 before treatment to 1.9 after treatment, and the 6MWD increased from 373.2 m before treatment to 436.7 m after treatment in the real acupuncture group.23 These changes were significantly better than the changes seen in the placebo acupuncture group,22 and were similar
to the results of the present study. In addition, there were no adverse effects directly related to acupuncture treatment. These results show that the acupuncture therapy of reinforcing the spleen to strengthen the lung safely and effectively improves the exercise capacity of patients with stable COPD.

The present study has several limitations. First, the sample size was relatively small. Second, the long-term efficacy was not evaluated. Third, the acupuncturists and patients were not blinded, which may have influenced the results.

In conclusion, the present results indicate that the acupuncture therapy of reinforcing the spleen to strengthen the lung is a safe adjuvant therapy that effectively improves the exercise capacity of patients with stable COPD. However, the present findings require further confirmation in high quality trials with large sample sizes.

REFERENCES


