Research on mechanism of Jin-Shui-Liu-Jun-Jian and Acupoint Application combined therapy for chronic bronchitis

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ABSTRACT

Objective: To investigate the influencing mechanism of Jin-Shui-Liu-Jun-Jian and Acupoint Application combined therapy on hemorheology, inflammatory factors and pulmonary functions in patients with chronic bronchitis, thus to offer relevant help for clinical therapies on patients with chronic bronchitis. Methods: 120 cases of patients with chronic bronchitis treated in our hospital were selected and randomly divided to be the therapeutic group and the control group, 60 cases each. Patients in control group were provided some basic treatments, such as spasmolysis, anti-inflammation, asthma relieving, oxygen inhalation and dissolve phlegm. For therapeutic group on this basis, Jin-Shui-Liu-Jun-Jian and Acupoint Application combined therapy was provided. Hemorheology, inflammatory factors and pulmonary functions in the two groups of patients were detected before and after treatment.

Results: Differences of hemorheology indexes, inflammatory factors and pulmonary function relevant indexes between the two groups of patients with chronic bronchitis before treatment showed no statistical significance (P>0.05). Compared with prior treatment, hemorheology relevant indexes [whole blood high shear viscosity (WHV), whole blood low shear viscosity (WLV), packed cell volume (PCV), plasma viscosity (PV) and red cell assembling index (RCAI)], inflammatory factors [IL-8 (interleukin-8) and TNF-α (tumor necrosis factor-α)] were significantly decreased and pulmonary function relevant indexes [forced vital capacity (FVC), forced expiratory volume in one second (FEV1.0), peak expiratory flow (PEF), maximal voluntary ventilation (MVV) and expiratory flow rate when exhale vital capacity was 0.50], inflammatory factors (IL-4, IL-2) were significantly increased in the two groups of patients with chronic bronchitis after relevant treatments; The differences between the groups showed statistical significance (P<0.05). After combined therapy provided, pulmonary function relevant indexes (FVC, FEV1.0, PEF, MVV and V0.50) and inflammatory factors (IL-4, IL-2) in therapeutic group were significantly higher than control group after basic therapy. Hemorheology relevant indexes (WHV, WLV, PV, PCV and RCAI) and inflammatory factors (IL-8 and TNF-α) in therapeutic group were significantly lower than control group; Differences between the two groups showed statistical significance (P<0.05). Conclusions: Combination of Jin-Shui-Liu-Jun-Jian and Acupoint Application significantly improved the levels of hemorheology, inflammatory factors and pulmonary functions in patients with chronic bronchitis. It has a great important clinical significance on therapies for patients with chronic bronchitis.

1. Introduction

Chronic bronchitis is a more common chronic inflammatory disease[1]. Symptoms of expectoration, cough, wheeze, etc., often appeared when suffering from it. The course of disease is long and hard to be cured. Eventually it could lead to appearance of some other diseases, such as COPD and pulmonary heart disease[2] and seriously affect the physical, mental health and daily life of patients. Searching for a suitable therapeutic project for chronic bronchitis becomes urgent affairs for many medical workers[3,4]. Chinese medicines become ideal medications for chronic bronchitis therapies because of their properties of less side effects, long-time administration and not easy to induce drug intolerance[5]. Our research investigated the influence of Jin-Shui-Liu-Jun-Jian and Acupoint Application combined Therapy on hemorheology, inflammatory factors and pulmonary functions in patients with chronic bronchitis.
chronic bronchitis, and offered help for clinical therapies on patients with chronic bronchitis.

2. Materials and Methods

2.1. General information

120 cases of patients with chronic bronchitis treated in our hospital from Jan 2013 to Jan 2015 were collected and randomly divided to be two groups, namely, the therapeutic group and the control group. There were 60 cases in therapeutic group (30 male cases, 30 female cases), ages ranged from 40 to 70 years old, the course of diseases were 6–12 years, average course was (9.5±2.4) years; Diseases of patients in this group were classified to be 17 cases of grade I, 31 cases of grade II and 12 cases of grade III based on Clinical Research Guiding Principles for Chinese Medicine Treatment of Chronic Bronchitis. There were 60 cases in control group (31 male cases, 29 female cases), ages ranged from 40 to 70 years old, , the course of diseases were 6–12 years, average course was (9.8±2.2) years; Diseases of patients in this group were classified to be 16 cases of grade I, 30 cases of grade II and 14 cases of grade III. No difference existed in ages, genders, sick times, severity of diseases, physical conditions between the two groups of patients ($P>0.05$).

2.2. Selected and excluded standards

All the patients were met with diagnose standards of chronic bronchitis; No other diseases in heart, liver, blood, kidney or endocrine existed in all the patients. They could actively coordinate the treatment, and had no hypersensitive symptoms to relevant therapeutic medications; The patients started to accept relevant treatments after other medicines discontinued for 2 weeks, and they had detail materials before treatment; Our research was approved by ethics committee in our hospital and conducted after informed consent forms signed by patients.

2.3. Therapeutic methods

For patients in control group, basic treatments, like spasmolysis, anti-inflammation, asthma relieving, oxygen inhalation and dissolve phlegm were provided; For patients in therapeutic group, Jin-Shui-Liu-Jun-Jian was provided on the basis of the above treatments. Jin-Shui-Liu-Jun-Jian was composed of Angelica (6 g), Rehmannia Glutinosa (15 g), Tangerine Peel (4.5 g), Pinellia ternate (6 g), Poria (6 g) and Prepared Liquorice Root (3 g). Water was added to it and decocted to 300 mL. Warm administered without food for one dose a day, twice a day; Acupoint application was also provided to the patients. Medicines included in acupoint application were mustard seed, asarum, raw ephedra, lumbricus, raw pinellia ternate and almond; Therapeutic durations were 4 weeks for the two groups of patients with chronic bronchitis.

2.4. Blood sample selection

5 mL peripheral blood was separately extracted from fasting patients with chronic bronchitis in control group and therapeutic group before and 4 weeks after treatment for relevant indexes detection.

2.5. Hemorheology Detection

Full-automatic hemorheology detector (Zhongchi ZL6000 automatic hemorheology detector) was utilized to detect packed cell volume (PCV), plasma viscosity (PV), whole blood high shear viscosity (WHV), red cell assembling index (RCAI) and whole blood low shear viscosity (WLV). Experimental operations were conducted strictly following the instructions.

2.6. Inflammatory factors detection

ELISA method was used to detect IL-4 (interleukin-4), IL-2 (interleukin-2), IL-8 (interleukin-8) and TNF-α (tumor necrosis factor-α). The kits were provided by Shanghai Crystal Anti Biological Engineering Co., Ltd., Jiangsu Jing Mei Biotechnology Co., Ltd. and Shanghai Enzyme Research Biological Technology Co., Ltd. Enzyme micro-plate analyzer (Nanjing Germany Iron laboratory equipment Co., Ltd., Model: HBS-1096A) was utilized to measure OD value at 450 nm. And corresponding concentrations were calculated by standard curves. Operational processes were strictly conducted following the instructions.

2.7. Pulmonary function detection

Spirograph (Ming Yuan Medical Treatment, Model: FGC-A+) was used to measure forced vital capacity (FVC), forced expiratory volume in one second (FEV1.0), peak expiratory flow (PEF), maximal voluntary ventilation (MVV) and expiratory flow rate when exhale vital capacity was 0.50 (V0.50) for the patients. Experimental operations were strictly processed following the instructions.

2.8. Statistical methods

SPSS 17.0 statistical software was utilized to count and analyze relevant data. Hemorheology, inflammatory factors and pulmonary function indexes were indicated by average number ± standard deviation. Comparisons between and within therapeutic group and control group were processed by $t$ test. If $P<0.05$, difference showed
Compared with the same group before treatment, comparison of pulmonary functions before and after treatment between two groups of patients with chronic bronchitis (Table 2). Comparison of hemorheology before and after treatment between two groups of patients with chronic bronchitis (Table 1). The two groups of patients with chronic bronchitis before and after treatment, comparison of hemorheology relevant indexes, namely, WHV, WLV, PV, PCV and RCAI were significantly decreased in patients of therapeutic group who received Jin-Shui-Liu-Jun-Jian and Acupoint Application combined therapy. The difference showed statistical significance (P<0.05). As for patients in therapeutic group after treatment, hemorheology relevant indexes WHV, WLV, PV, PCV and RCAI were significantly decreased in patients of control group. The difference showed statistical significance (P<0.05). See Table 1.

3.2. Comparison of pulmonary functions before and after treatment between two groups of patients with chronic bronchitis

Spirograph was used to measure and analyze pulmonary functional relevant indexes, namely, FVC, FEV1.0, PEF, MVV and V0.50 in the two groups of patients with chronic bronchitis before and after treatment. Before treatment, comparison of pulmonary functional relevant indexes in the two groups of patients showed no statistical significance (P>0.05); Compared with the same group before treatment, pulmonary functional relevant indexes FVC, FEV1.0, PEF, MVV and V0.50 were significantly increased in patients of therapeutic group who received Jin-Shui-Liu-Jun-Jian and Acupoint Application combined therapy. The difference showed statistical significance (P<0.05). As for patients in therapeutic group after treatment, pulmonary functional relevant indexes FVC, FEV1.0, PEF, MVV and V0.50 were significantly higher than patients in control group after treatment, the differences between the two groups showed statistical significance (P<0.05). See Table 2.

3.3. Comparison of inflammatory factors before and after treatment between two groups of patients with chronic bronchitis

ELISA method was used to measure and analyze inflammatory factors, namely, IL-4, IL-2, IL-8 and TNF-α in the two groups of patients with chronic bronchitis before and after treatment. Before treatment, comparison of inflammatory factors in the two groups of patients with chronic bronchitis before and after treatment, the differences between the two groups showed no statistical significance (P>0.05); Compared with the same group before treatment, inflammatory factors IL-4, IL-2 were significantly increased, IL-8 and TNF-α were significantly decreased in patients of therapeutic group who received Jin-Shui-Liu-Jun-Jian and Acupoint Application combined therapy. The difference showed statistical significance (P<0.05); Compared with the same group before treatment, inflammatory factors IL-4, IL-2 were significantly increased, IL-8 and TNF-α were significantly decreased in patients of control group after treatment, the differences between the two groups showed statistical significance (P<0.05). See Table 1.

### Table 1

Comparison of hemorheology before and after treatment between two groups of patients with chronic bronchitis (n=60, \( \bar{x} \pm s \)).

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>WHV (mPa/s)</th>
<th>WLV (mPa/s)</th>
<th>PV (mPa/s)</th>
<th>PCV (%)</th>
<th>RCAI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapeutic g.</td>
<td>Before</td>
<td>5.65±0.62</td>
<td>11.42±3.35</td>
<td>2.17±0.41</td>
<td>51.24±5.07</td>
<td>2.66±0.38</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>4.08±0.25*</td>
<td>9.57±1.02*</td>
<td>1.52±0.37*</td>
<td>44.96±5.62*</td>
<td>2.45±0.32*</td>
</tr>
<tr>
<td>Control g.</td>
<td>Before</td>
<td>5.67±0.59</td>
<td>11.38±1.30</td>
<td>2.18±0.44</td>
<td>51.17±4.91</td>
<td>2.65±0.36</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>4.82±0.37*</td>
<td>10.46±1.11</td>
<td>1.80±0.36</td>
<td>47.03±4.58</td>
<td>2.55±0.35</td>
</tr>
</tbody>
</table>

 Compared with the same group before treatment, \( ^*<0.05 \); Compared with control group after treatment, \( ^P<0.05 \).

### Table 2

Comparison of pulmonary functions before and after treatment between two groups of patients with chronic bronchitis (n=60, \( \bar{x} \pm s \)).

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>FVC (L)</th>
<th>FEV1.0 (L)</th>
<th>PEF (L/s)</th>
<th>MVV (L)</th>
<th>V0.50 (L/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapeutic g.</td>
<td>Before</td>
<td>72.87±3.14</td>
<td>68.97±2.24</td>
<td>7.48±1.03</td>
<td>63.54±3.11</td>
<td>1.36±0.27</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>81.54±3.27*</td>
<td>79.35±2.67*</td>
<td>8.31±1.11*</td>
<td>78.87±3.34*</td>
<td>2.06±0.34*</td>
</tr>
<tr>
<td>Control g.</td>
<td>Before</td>
<td>72.66±2.94</td>
<td>71.12±2.36</td>
<td>7.45±1.06</td>
<td>63.89±3.17</td>
<td>1.34±0.24</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>77.50±3.10*</td>
<td>75.04±2.45*</td>
<td>7.87±1.20*</td>
<td>71.26±3.08*</td>
<td>1.65±0.31*</td>
</tr>
</tbody>
</table>

 Compared with the same group before treatment, \( ^*<0.05 \); Compared with control group after treatment, \( ^P<0.05 \).
Table 3
Comparison of inflammatory factors before and after treatment between two groups of patients with chronic bronchitis (n=60,  = 0.05).

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>IL-2 (pg/L)</th>
<th>IL-4 (pg/L)</th>
<th>IL-8 (pg/L)</th>
<th>TNF-α (pg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapeutic group</td>
<td>Before treatment</td>
<td>415.33±7.82</td>
<td>92.39±8.08</td>
<td>800.81±8.12</td>
<td>30.14±2.78</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>526.27±6.24*</td>
<td>115.01±9.17*</td>
<td>338.38±6.08*</td>
<td>14.26±2.21*</td>
</tr>
<tr>
<td>Control group</td>
<td>Before treatment</td>
<td>412.47±7.51</td>
<td>92.41±7.11</td>
<td>802.82±9.10</td>
<td>30.19±2.80</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>490.68±6.84</td>
<td>101.70±9.68</td>
<td>765.60±7.07</td>
<td>22.69±2.64</td>
</tr>
</tbody>
</table>

Compared with the same group before treatment, *P<0.05; Compared with control group after treatment, *P<0.05.

4. Discussion

Chronic bronchitis is a more common disease in respiratory tract[6]. In recent years, with the rapid development of our Chinese economy, air pollutions have been aggravated. Population with chronic bronchitis increased year by year, the incidence rate was as high as 3.8%. And incidence rate in elder patients has been arrived at 15%. Therefore, relevant researches regarding to chronic bronchitis become of vital important[7]. Chronic bronchitis is a non-specific inflammatory reaction appears in bronchial mucosa, trachea and surrounding tissues. Patients with it always repeatedly experience expectoration, coughing and wheezing. At the same time, it was always accompanied by decline of respiratory function. The course of disease is quite long and hard to be cured. With the developing of disease, chronic bronchitis could be eventually developed to COPD, pulmonary heart disease, pulmonary hypertension or other diseases, which could seriously influence on lives, families and relationships of patients[8–11]. Searching for a suitable therapeutic project becomes an urgent issue for many medical workers[12].

Currently, some therapeutic effects have been received by utilization of western medicine therapeutic methods on antitussive and expectorant, infection controlling, spasmyosis and asthma, etc. However, since relevant medicines have large side effects, drug tolerance could easily appear, and long-term effects are not ideal, utilization of western medicine therapeutic methods for chronic bronchitis could not meet the requirements of many patients[13,14]. Therapeutic mechanisms of Chinese medicines become more clearness with the large amount of researches on Chinese medicines by many medical workers, which provided theoretical supports for application of Chinese medicines[15]. Herbalist doctors believe the appearance of chronic bronchitis is due to endogenous phlegm, unsubstantial defense, long-term renal deficiency, shortness of breath, diffusion of pulmonary disease to spleen or endogenous phlegm retention, finally the disease could lead to imbalance of pulmonary, renal and spleen. Hence the treatments of chronic bronchitis are mainly focused on drying dampness and resolving phlegm, and nourishing the negative parts of pulmonary and kidney[16,17]. Jin-Shui-Liu-Jun-Jian was derived from Jing-yue Complete Works. It is composed of Angelica, Rehmannia Glutinosa, Tangerine Peel, Pinellia ternate, Poria and Prepared Liquorice Root, etc. It plays important roles in treatment of deficiency and cold in lung and kidney, insufficient blood, coughing, vomiting and nausea, water flooding to be phlegmy, panting and profuse sputum, etc[18]. Acupoint application operates effects by skin absorbing. When in summertime, human sweat glands and capillaries are generally open. Blood circulations are prosperous, which make a fast rapid to develop drug effects and more gentle curves of medicine concentrations, thus effects on liver and gastrointestinal tract could be avoid. And medicines functions could be adequately and effectively developed[19,20].

Our research found that Jin-Shui-Liu-Jun-Jian and acupoint application combination significantly improved hemorheology (WHV, WLV, PV, PCV and RCAI), inflammatory factors (IL-4, IL-2, IL-8 and TNF-α) and pulmonary function levels (FVC, FEV1.0, PEF, MVV AND V0.50) in patients with chronic bronchitis, which showed important clinical significance on treatment of the patients. Because of airway obstruction and poor ventilation, patients with chronic bronchitis experienced long-time chronic hypoxia, which affected their micro-circulations. As for the patients, amount of non-oxygen metabolism were increased, and amount of ATP generation were decreased, which altered the distort capability of red blood cells, and enhanced high shear viscosity. In the status of oxygen deficiency, red blood cells compensatory and accumulation were increased, blood viscosity were increased on the patients. Jin-Shui-Liu-Jun-Jian and acupoint application play important roles in nourishing yin and blood, drying dampness and resolving phlegm and regulating flowing for activating stagnancy. It made the breathing smoothly in pulmonary and provided sufficient oxygen for the patients, which was benefit to the improvement of micro-circulation, and ultimately improved hemorheology for patients. Angelica could regulate pulmonary, kidney and golden water intercrescence. Prepared Liquorice Root could strengthen spleen and regulate all the medicines; Acupoint application could accelerate smooth of meridian patency, eliminate unhealthy trends, cold and phlegm, promote flow and activate blood circulation, which could let medicines access
to pulmonary effectively and let all the organs receive regulation. Therefore, pulmonary functions of patients with chronic bronchitis could be improved. IL-2 is secreted by Th1 cells. It has function of immune cells proliferation and differentiation. It could regulate Th1 type immune reaction to prevent damage of immune over-reaction; IL-4 could induce Th2 reaction, and suppress activity of Th1 cells.[21] Jin-Shui-Liu-Jun-Jian and acupoint application combination could regulate IL-2 and IL-4 levels to enhance immune regulation capability, and diminish inflammatory reactions, thus the disease state of chronic bronchitis could be relieved. IL-8 is an important chemokine. It could affect neutrophils and eosinophils; TNF-α could improve blood capillary permeability and moisturizing of inflammatory cells, which lead to organs damage; Jin-Shui-Liu-Jun-Jian and acupoint application combination could diminish IL-8 and TNF-α levels, thereby inflammatory reaction of patients could be relieved, pulmonary tissues could be protected from injury, and rehabilitation of chronic bronchitis could be promoted.

Above all, our research detected the influences of Jin-Shui-Liu-Jun-Jian and acupoint application combination on levels of hemorheology (WHV, WLV, PV, PCV and RCAI), inflammatory factors (IL-4, IL-2, IL-8 and TNF-α) and pulmonary function (FVC, FEV1.0, PEF, MVV and V0.50) for patients with chronic bronchitis, and discussed the mechanisms of in-Shui-Liu-Jun-Jian and acupoint application combination on treatment of chronic bronchitis, which offered significant assistance for treatment of chronic bronchitis.

References


