Clinical treatment of depressive patients with Anshendingzhi decoction

Jianyu Yang, Lijuan Jiang, Yang Li, Qingwen Zhu, Dong Liu, Wugeng Xue, Bolong Cao, Yingke Liu, Xing Wang

OBJECTIVE: To determine the effects of Anshendingzhi decoction (ASDZD) on depression, to compare ASDZD with Danzhixiaoyao pill (DZXYP), and to provide evidence for the clinical treatment of depression with Traditional Chinese Medicine.

METHODS: Seventy-eight patients with depression were enrolled from 2011 to 2013 in this double-blinded study. Patients were randomly divided into two groups: ASDZD (treatment group, n=39) and DZXYP (control group, n=39). Hamilton Depressive Scale and TCM Syndrome Differentiation Scale were used to assess depression and efficacy before treatment and 2, 4, and 6 weeks after treatment. The Treatment Emergent Symptoms Scale (TESS) was used to evaluate adverse reactions, observe, and record treatment outcomes.

RESULTS: ASDZD was significantly more effective than DZXYP. There were significant differences between the two groups in terms of recovered patients, overall response rate, and TESS score (all \( P < 0.05 \)).

CONCLUSION: ASDZD is an effective treatment for depression. ASDZD could improve clinical symptoms and warrants further clinical research and application.

INTRODUCTION

Depression (or depressive disorder) is a common affective disorder characterized by an obvious and persistent reduction in mood. Emotions range from sadness to...
The diagnosis criteria used for depression were from the two groups (P<0.05). There were no significant differences in general demographics between the two groups (P>0.05).

Diagnosis criteria

The diagnosis criteria used for depression were from the Chinese Categories and Diagnosis Criteria of Mental Disorders.\(^\text{14}\)

**Inclusion criteria**

Inclusion criteria were: HAMD score>20; aged between 18 and 65 years; no treatment with anti-depressive or anti-anxiety drugs 1 week before admission; no alcohol or drug abuse history; adherent to treatment regimens; and signed informed consent.

**Exclusion criteria**

Patients were excluded if they: did not meet the diagnosis criteria; had heart, brain, kidney, liver, or other serious organ diseases; were pregnant or lactating; or had multiple drug allergies.

**Treatment**

The treatment group was given ASDZD orally, once per day after two infusions with warm water. Each course of treatment lasted 2 weeks. The ingredients of ASDZD were: Danshen (Radix Codonopis) 10 g; Huangqi (Radix Astragali Mongolicis) 10 g, Danshen (Radix Salviae Militirrhizae) 7 g, Fuxiaomai (Fructus Fructus Triticis) 15 g, Dazao (Frutus Jujubae) 10 g, Gancao (Radix Glycyrrhizae) 5 g, Fushen (Poria Cum Radix Pini) 10 g, fried Sanzaoren (Semen Ziziphi Spinoides) 10 g, Yujin (Radix Cnicumae Wenyujin) 10 g, processed Yuanzhi (Radix Polygalae) 10 g, Shichangpu (Rhizoma Acori Tatarinowii) 10 g, and Dengxincao (Medulla seu Medulla Alomii) 3 g. Drugs above were added or subtracted from the decoction according to different clinical symptoms (avoid fried granules, Guandong Yifang Pharmaceutical Co., Ltd., Guangdong, China).

The control group was given DZXYP 6 g each bag, 6-9 g each time, twice a day. The total courses of the two groups were 6 weeks. The formula for DZXYP includes: Mudanpi (Cortex Moutan Radicis), Zhizhi (Fructus Gardeniae), DZXYP has the advantages of ease of use and wide clinical adoption. Li et al.\(^\text{12}\) performed a randomized double-blind controlled study with 32 depressive patients treated with DZXYP, and 31 depressive patients treated with maprotiline. The results showed an approximately equal curative effect of DZXYP and maprotiline. Both treatments could significantly reduce the Hamilton Rating Scale for Depression (HAMD), Zung’s Self-Rating Depression Scale (SDS), and Zung Self-Rating Anxiety Scale (SAS) scores in patients with depression. Liu et al.\(^\text{13}\) also found that DZXYP was equally effective in patients with both hypertension and depression. We used Anshendingzi decoction (ASDZD) to treat depression, and compared it with Danzhixiaoyao pill (DZXYP), a commonly used TCM treatment for depression.

**MATERIALS AND METHODS**

**Subjects**

Seventy-eight patients with depression were enrolled between January 2010 and June 2013. This study was approved by the ethical committee of Beijing Hepingli Hospital and informed consent was obtained from all participants. Using the digital table method, patients were divided randomly into a treatment and control group. In the treatment group, there were 16 males and 23 females aged 20-49 years (mean, 29±8 years), with a mean course of disease (15±13) months. In the control group, there were 18 males and 18 females aged 20-49 years (mean, 30±8 years), with a mean disease course of (16±15) months. There were no significant differences in general demographics between the two groups (P>0.05).

**Efficacy evaluation criteria**

Efficacy was ranked as: cured, markedly effective, improved, and ineffective. Cured was considered when patients exhibited no psychiatric symptoms, and had a
HAMD score<8. Markedly effective was considered when patients’ psychiatric symptoms almost disappeared and when they had a HAMD score reduce over 50% from before treatment. Improved was considered when patients had improved psychiatric symptoms, and had a HAMD score reduce over 30% from before treatment. Ineffective was considered when the psychiatric symptoms and HAMD scores did not improve.

Total number of effective cases=cured+markedly effective+improved.

**Statistical analysis**

Data were analyzed by SPSS 19.0 (SPSS, Chicago, IL, USA). The data were expressed as mean±standard deviation (SD) and analyzed by t-test. The enumeration data were analyzed by χ² test. P<0.05 was considered statistically significant.

**RESULTS**

**Comparison of effects between groups**

Eighty patients recruited in this study were randomly divided into a treatment and control group with 40 patients in each. After the trial, all patients who completed the trial in two groups (treatment group 39 cases, 1 case lost to follow-up, control group 39 cases, 1 case discontinued intervention) conducted a follow-up. The flow diagram of the trial is shown in Figure 1.

After treatment, the overall response rate of ASDZD was 94.9%, which was significantly better than that of DZXYP (74.3%) (χ²=4.82, P<0.05) (Table 1).

**HAMD and CMSDS scores**

Compared with before treatment, the HAMD and CMSDS scores all significantly decreased after treatment (all P<0.05), and the scores in the treatment group were significantly lower than those in the control group after treatment (all P<0.05) (Tables 2, 3).

**Adverse reactions**

There were significant differences in adverse reactions between the two groups (all P<0.05). In the treatment group, there was one case of dizziness, two of nausea, two of sweating, and one of weakness. In the control group, there were three cases of headache, two of thirst, three of nausea, three of sweating, one of fibrillation, and one of weakness. All adverse reactions were reduced by adjustment of drug dosage (Table 4).

**DISCUSSION**

In TCM, depression is considered “Melancholia,” and is caused by stagnation of Qi and emotional disturbance. For example, Zhu considered that if Qi and blood are in harmony and flow smoothly, then they do not cause problems. However, in the depressed state, Qi and blood are affected. Qian considered that Qi is...
Table 2 HAMD score before treatment and 2, 4, and 6 weeks after treatment (score, ±s)

<table>
<thead>
<tr>
<th>Group</th>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>2 Weeks</td>
</tr>
<tr>
<td>Treatment</td>
<td>35.9±2.5</td>
<td>25.9±1.8</td>
</tr>
<tr>
<td>Control</td>
<td>34.9±4.6</td>
<td>28.6±1.0</td>
</tr>
</tbody>
</table>

Notes: the treatment group was treated with ASDZD (one dose a day) and the control group was treated with DZXYP (one dose a day). ASDZD: Anshendingzhi decoction; DZXYP: Danzhixiaoyao pill; HAMD: Hamilton Depressive Scale.

Table 3 CMSDS score before treatment and 2, 4, and 6 weeks after treatment (score, ±s)

<table>
<thead>
<tr>
<th>Group</th>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>2 Weeks</td>
</tr>
<tr>
<td>Treatment</td>
<td>29.3±2.5</td>
<td>22.9±1.6</td>
</tr>
<tr>
<td>Control</td>
<td>28.9±3.3</td>
<td>25.6±1.3</td>
</tr>
</tbody>
</table>

Notes: the treatment group was treated with ASDZD (one dose a day) and the control group was treated with DZXYP (one dose a day). ASDZD: Anshendingzhi decoction; DZXYP: Danzhixiaoyao pill; CMSDS: Chinese Medicine Syndrome Differentiation Scale.

Table 4 TESS scores between groups (score, ±s)

<table>
<thead>
<tr>
<th>Group</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2 Weeks</td>
</tr>
<tr>
<td>Treatment</td>
<td>1.5±0.4</td>
</tr>
<tr>
<td>Control</td>
<td>2.0±0.3</td>
</tr>
</tbody>
</table>

Notes: the treatment group was treated with ASDZD (one dose a day) and the control group was treated with DZXYP (one dose a day). ASDZD: Anshendingzhi decoction; DZXYP: Danzhixiaoyao pill; TESS: Asberg Treatment Emergent Symptom Scale.

The base of personality, and if Qi is in harmony, then all organs will function properly. However, improper diet or emotional states can cause Qi movement disturbances, which can cause internal organ stasis and subsequent disease. Therefore, depression treatment should begin with soothing the liver and regulating Qi. ASDZD is a popular formula prescribed for depression in China. The major functions include soothing the liver, regulating Qi, removing stasis, invigorating the spleen, and replenishing the heart. Among the ingredients of ASDZD, Dangshen (Radix Codonopsis) can supplement the center and boost Qi, strengthen the spleen, and tonify the lung. Huangqi (Radix Astragali Mongolici) can tonify Qi, nourish blood, and invigorate splendid yang. Danshen (Radix Salviae Miltiorrhizae) can remove stasis and activate blood circulation, regulate Qi, and nourish blood. Fushen (Portia Cocos) can calm the nerves and treat palpitations. Fried Shanzao (Semen Ziziphi Spinosae) can act as a sedative, analgesic, and hypnotic on the heart, spleen, liver, and gallbladder meridians, and can regulate Qi and nourish blood. Yujin (Curcuma Wenyujin) can clear heart-fire and resolve depression, activate Qi, and resolve stagnation. Dengxincao (Medulla Junci) can clear away the heart-fire and relieve restlessness. Chinese dates (Fructus Jujubae) can supplement the center and boost Qi, nourish blood, and calm the nerves. Gancao (Radix Glycyrrhiza Uralensis) can tonify the spleen and boost Qi. Dazao (Fructus Jujubae), Gancao (Radix Glycyrrhiza Uralensis), and Fuxiaomai (Fructus Tritici) combined with other drugs can mitigate drug properties, moderate herbal properties, and alleviate the adverse drug properties.

Syndrome differentiation has long been used to treat depression in TCM. The common therapeutic methods include soothing liver-Qi stagnation, regulating Qi and dispelling stagnation, and invigorating the spleen. To soothe the liver and regulate Qi, we added more herbs to activate blood circulation, dispel stagnation, strengthen the spleen, and nourish the heart. Therefore, this ASDZD formula can not only regulate Qi activity, but also activate Qi, nourish the heart, and calm the nerves, which fundamentally resolves the patient’s Qi and blood stagnation. We found that the cure rate of the treatment group was significantly better than that of the control group, which only soothed the liver and dispelled the stagnation. The scores of depression scales and clinical TCM symptoms were also better in the treatment group than those in the control group.

Tranquilizing mind therapy (therapy with Chinese herbs of tranquilizer in mind restless syndrome) using ASDZD is another effective TCM method for treating psychiatric disorders. The therapy can be used to treat pediatric hyperkinesis, insomnia, attention deficit hyperactivity disorder (ADHD), and cardiac neurosis. Liu et al. and Yin et al. studied the effects of ASDZD on the expression of the dopamine transporter in ADHD rat striatum, and the effects of ASDZD on the content of COMT in rats with ADHD. They found that ASDZD was able to moderate ADHD. These results also indicate that tranquilizing mind therapy...
could stabilize patient mood, enhance patient attention, and possibly improve clinical symptoms of some psychiatric disorders. Our results show that ASDZD can improve depression symptoms and adjust patient emotions. There were significantly fewer adverse events in the treatment group than in the control group, which indicates that ASDZD is a safe treatment method. However, the study sample size is small, which may affect our conclusions. In addition, depression is caused by many factors such as psychology, society, and biology. Factors not related to the treatment, such as the hospital environment, may also affect the treatment results. A larger sample size and combination with other therapies such as psychotherapy may achieve better, more reliable results.

REFERENCES