Efficacy Evaluation for Depression with Somatic Symptoms Treated by Electroacupuncture Combined with Fluoxetine

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Objective: This study is to investigate the clinical therapeutic effects and safety of treating mild or moderate depression with somatic symptoms with electroacupuncture combined with Fluoxetine. Methods: 95 cases of mild or moderate depression with somatic symptoms were randomly divided into a Fluoxetine group, and an electroacupuncture plus Fluoxetine group. Hamilton Depression Scale (HAMD) was used for the assessment of clinical therapeutic effects and Treatment Emergent Symptom Scale (TESS) was used for assessment of adverse reactions. Results: The total effective rate was 77.27% in the Fluoxetine group and 78.26% in the electroacupuncture plus Fluoxetine group, showing no statistically significant difference between these two groups (P>0.05). However, the treatment took effect after two weeks in the electroacupuncture plus Fluoxetine group but after four weeks in Fluoxetine group. During this time, a better therapeutic effect on depression with mild or moderate somatic symptoms was found in the electroacupuncture plus Fluoxetine group, which also had fewer adverse reactions than the Fluoxetine group. Conclusion: Electroacupuncture combined with Fluoxetine takes effect faster for relieving the somatic symptoms with fewer adverse reactions. It is worth popularizing clinically.

Key words: electroacupuncture; somatic symptoms; Fluoxetine; depression

Depression is a common emotional mental disorder characterized by significant and long-lasting depressed emotion, anhedonia or fatigue, with somatic symptoms such as discomfort and declining ability. Most patients go to general hospitals for treatment with complaints of somatic symptoms. Somatization is a phenomenon by which psychic complaints are expressed as somatic symptoms, and by which personal psychological processes as well as various problems of social groups are interpreted, expressed and experienced as somatic symptoms. It is a modus in which patients deal with psychological and social difficulties. Somatic symptoms include insomnia, headache, dizziness, fatigue, poor appetite, breath holding and/or unfixed chronic pain (including gastrointestinal pain, precordial pain, headache or backache, which cannot be relieved with analgetics). Although the occurrence and duration of these symptoms are closely correlated with the unhappiness, difficulties or conflicts, patients often deny the existence of psychological factors and attribute the depressed emotions to physical problems. Long-term symptomatic treatment without obvious efficacy may delay the pathogenetic condition and lead to chronic diseases.

For mild to moderate depression, medical intervention is not the only treatment. The clinical application and research into using traditional medicine, including acupuncture therapy, for treatment of depression has been carried out for many years and has resulted in some marked achievements. According to the internationally recognized criteria for diagnosis and therapeutic effect, the clinical efficacy, effect-onset and safety of the treatment have been observed in two different ways, electroacupuncture plus Fluoxetine and Fluoxetine alone, to determine the different therapeutic effects.
CLINICAL MATERIALS

General Data

This study was approved by the Hospital Ethics Committee. All 95 cases in this series were in- and outpatients from Department of Neurology and Department of Psychology in the PLA General Hospital. They were randomly divided into a Fluoxetine group and an electroacupuncture plus Fluoxetine group. The general data is shown in Table 1.

Table 1. General Data in Both the Fluoxetine Group and the Electroacupuncture Plus Fluoxetine Group (\(\bar{X} \pm s\))

<table>
<thead>
<tr>
<th>Group</th>
<th>Cases</th>
<th>Sex</th>
<th>Age (year)</th>
<th>Course (month)</th>
<th>HAMD Score (before treatment)</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoxetine</td>
<td>47</td>
<td>Male</td>
<td>19</td>
<td>28</td>
<td>37±11.22</td>
<td>Mild</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Female</td>
<td></td>
<td></td>
<td></td>
<td>22</td>
</tr>
<tr>
<td>Fluoxetine + Acupuncture</td>
<td>48</td>
<td>Male</td>
<td>17</td>
<td>31</td>
<td>38±10.17</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Female</td>
<td></td>
<td></td>
<td></td>
<td>23</td>
</tr>
</tbody>
</table>

The general data was statistically compared between the two groups of patients. There were no significant differences in sex (df=1, \(\chi^2=0.4314, P=0.806\)), age (df=73, \(t=0.67, P=0.5157\)), course of disease (df=73, \(t=0.6458, P=0.62\)), HAMD score before treatment (df=73, \(t=1.40, P=0.1669\)), and severity of disease (df=1, \(\chi^2=0.48, P=0.8059\)), indicating that the baseline data were comparable between the two groups.

Diagnostic Criteria

The diagnosis of depression in the study was consistent with the diagnostic criteria ICD-10 for mild or moderate psycholepsy. The patients with two typical symptoms and two other core symptoms were diagnosed as having mild depression; patients with two typical symptoms and three other core symptoms were diagnosed as having moderate depression.

Standard for severity: According to the Hamilton Depression Scale (HAMD) and the cut-off score by Davis JM, 20–26 of HAMD score was considered as mild depression, and 27–34 was considered as moderate depression.

Inclusive Criteria

1) The patients were 18–60 years met the above diagnostic criteria; 2) with a HAMD score for somatic symptoms between 20–34; 3) with no serious, organic brain diseases and somatic disease history; 4) with no history of mental disorder; 5) voluntarily signed the informed consent.

Exclusive Criteria

1) Patients who had schizophrenia or other mental disorders; 2) complications with organic diseases such as tumors and central nervous system diseases; 3) pregnant women, lactating women, or women who were pregnant during the treatment; 4) patients with psychiatric symptoms; 5) patients with severe depression evidenced by HAMD score ≥35 and suicidal tendencies; 6) patients who were intolerant or hypersensitive to Fluoxetine, or who had severe adverse reactions in the past.

METHODS

For Fluoxetine Group

A 5-HT antidepressant Fluoxetine was used (trade name: Fluoxetine; Common name: Fluoxetin hydrochloride capsule, produced by Suzhou Eli Lilly and Company of the United States; Specification: 20 mg/pill). It was orally taken 20 mg/day for six weeks.

For Electroacupuncture Plus Fluoxetine Group

Patients were treated with oral Fluoxetine and by electroacupuncture. Baihui (GV 20) and Yintang
(EX-HN3) were connected to G68052-I electro-acupuncture treatment device. The output wave was continuous at a frequency of 120–250 per minutes, the intensity was set according to the patient’s tolerance, and each session of treatment lasted 30 minutes. Meanwhile, conventional body acupuncture was adopted: for stagnation of liver qi, Taichong (LR 3) and Hegu (LI 4) were selected; for stagnated qi transforming into fire, Xingjian (LR 2) and Xiaixi (GB 43) were selected; for melancholy disturbing the mind, the sleeping point, Shenmen (HT 7), and Neiguan (PC 6) were selected; for deficiency of both the heart and spleen, Sanyinjiao (SP 6) and Zusanli (ST 36) were selected; for excessive fire due to deficiency of yin, Taixi (KI 3) and Zhaohai (KI 6) were selected. The patients were treated once a day, with a one-day interval in a week, for six weeks.

Criteria for Therapeutic Effects
The patients were assessed with HAMD by two doctors of psychology who had rich clinical experience and were not responsible for the treatment. The doctors were requested to achieve 98%–100% consistency in scoring the results of the assessments.

The therapeutic effects were evaluated by examining changes in the HAMD scores expressed as the “score reducing rate”. The assessment was done before treatment and once a week during the treatment.

The score-reducing rate = (total score before treatment − total score after treatment) / total score before treatment × 100%;

The score-reducing rate >75% was considered to be clinically controlled, 50%–75% markedly relieved, 25%–49% improved, and <25% failed.

The General HAMD Scoring Assessment
The general HAMD scoring assessment includes seven categories of factors. Four of these were observed in this study: somatic symptoms, sleep disorders, depressive retardation and cognitive disturbance. The somatic symptoms consisted of 5 items, which were psychic anxiety, somatic anxiety, gastrointestinal symptoms, hypochondriasis and insight. The sleep disorders consisted of 3 items, i.e. difficulty in falling asleep, light sleep and early awakening. The depressive retardation consists of 4 items, including depressive emotions, fatigue/ inability to work, intestinal blockage and sexual symptoms. The cognitive disturbance consists of 6 items, including self-acusation, suicide, agitation, depersonalization and derealization, paranoid symptoms and obsessive compulsive symptoms. For a better understanding of the characteristics of depression, the factor analysis can accurately reflect the changes of target symptoms before and after the treatment.

Each of the factor scores equals the total score of the factor / the number of items. The assessment was carried out before and after the treatment.

Assessment of the Adverse Effects with the TESS Scale
The Treatment Emergent Symptom Scale (TESS) was formulated by NIMH in the United States in 1973. It involves the most complete items and widest coverage among similar scales, including the common adverse signs and symptoms as well as several laboratory results. It is used frequently in WHO collaborative research.

The original TESS requests assessment of each symptom in terms of the severity, the medicine-symptom relationship and the measures adopted. The symptoms clearly related to the medical treatment were assessed in the “severity” column. The score was 0 for no symptoms; one for the light or suspicious symptoms; two for the mild symptoms that did not affect functioning but were somewhat troublesome, if there was ambiguous evidence for the existence of the symptoms according to complaints from patients; three for moderate symptoms that affected functioning to a certain degree, but with no serious impacts on daily life, although the patients may feel uncomfortable or uneasy, and the presence of symptoms can be observed; and four for severe symptoms that seriously affected the patient’s daily life and activities.
Blood pressure, blood and urine routine, liver function and electrocardiograms were examined for the patients of both groups, including those who gave up the treatment because of serious adverse effects induced by Fluoxetine, at the end of the second, fourth and sixth week of the treatment. Assessments were made based on physical examinations and laboratory reports. And the family members of patients were asked to provide additional information. The total score of “severity” was calculated for each patient to get the average value for each group.

**Statistical Analysis**

The patients who dropped out of the study due to the adverse effects of Fluoxetine were not assessed with HAMD, but they were assessed and analyzed with TESS.

**Measurement Data**

The paired-sample $t$ test was used for intragroup comparison; and the independent sample $t$ test was used for intergroup comparison.

**Numerical Data**

The single ordinal Chi-square test (Row Mean Score Differ) was used.

**RESULTS**

In the Fluoxetine group, dizziness and postural hypotension appeared in one patient one week after taking Fluoxetine, and panic and pyknosphygmia showed by EKG were found in another patient four weeks after taking Fluoxetine. The treatment was terminated for these patients because of the serious adverse effects. In addition, one patient’s emotions were stimulated by the death of his mother, and he was hospitalized for integrated therapy because the illness was aggravated to severe depression. In the acupuncture plus Fluoxetine group, the treatment was terminated for one patient because of sexual dysfunction, and for another patient with drug-induced dysuria. These 5 cases were not included in the statistical analysis, but the 4 patients with serious drug-induced adverse effects were assessed by TESS.

**The Total Therapeutic Effects**

The total therapeutic effects of the two groups are shown in Table 2.

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of Subjects</th>
<th>Clinically Controlled N (%)</th>
<th>Significantly Relieved N (%)</th>
<th>Improved N (%)</th>
<th>Failed N (%)</th>
<th>Total Effective Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoxetine</td>
<td>44</td>
<td>6 (13.63)</td>
<td>17 (38.64)</td>
<td>11 (25.00)</td>
<td>10 (22.73)</td>
<td>77.27</td>
</tr>
<tr>
<td>Fluoxetine+Acupuncture</td>
<td>46</td>
<td>8 (17.39)</td>
<td>18 (39.13)</td>
<td>10 (21.74)</td>
<td>10 (21.74)</td>
<td>78.26</td>
</tr>
</tbody>
</table>

The data in table 2 was compared by Row Mean Scores Differ ($df=1, \chi^2=0.05, P=0.83$). There was no significant difference between the Fluoxetine group and the acupuncture plus Fluoxetine group.

**The HAMD Scoring Assessment**

The HAMD scores of the two groups are shown in Table 3.

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline</th>
<th>Endpoint</th>
<th>Reduction Rate</th>
<th>Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Df</td>
<td>$t$</td>
<td>$P$</td>
<td></td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>25.1±3.7</td>
<td>12.7±5.5</td>
<td>50.8±17.6</td>
<td>33</td>
</tr>
<tr>
<td>Fluoxetine+acupuncture</td>
<td>23.8±4.0</td>
<td>10.1±5.1</td>
<td>56.8±15.2</td>
<td>35</td>
</tr>
</tbody>
</table>
Table 3 shows the intragroup comparison of the HAMD scores in the two groups before and after treatment, with statistically significant differences between baseline and endpoint scores indicating marked therapeutic effects in both groups.

The independent samples t test was used for intergroup comparison of the score-reducing rate between two groups, with no significant difference indicating a similar therapeutic effect in both the Fluoxetine group and electroacupuncture plus Fluoxetine group.

**HAMD Scores of the Factors**

The HAMD factor scores between the two groups before and after treatment are shown in Table 4.

**Table 4. Comparison of the HAMD Factor Scores Between Two Groups (X \( \pm s \))**

<table>
<thead>
<tr>
<th>Factor</th>
<th>Group</th>
<th>Baseline</th>
<th>Endpoint</th>
<th>Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Df</td>
<td>t</td>
<td>P</td>
</tr>
<tr>
<td>Somatic symptoms</td>
<td>Fluoxetine</td>
<td>68</td>
<td>8.33</td>
<td>0.002</td>
</tr>
<tr>
<td></td>
<td>Fluoxetine+ acupuncture</td>
<td>33</td>
<td>1.42</td>
<td>0.21</td>
</tr>
<tr>
<td>Sleep disorder</td>
<td>Fluoxetine</td>
<td>68</td>
<td>8.59</td>
<td>0.007</td>
</tr>
<tr>
<td></td>
<td>Fluoxetine+ acupuncture</td>
<td>33</td>
<td>2.07</td>
<td>0.04</td>
</tr>
<tr>
<td>Retardation</td>
<td>Fluoxetine</td>
<td>68</td>
<td>1.3</td>
<td>0.26</td>
</tr>
<tr>
<td></td>
<td>Fluoxetine+ acupuncture</td>
<td>33</td>
<td>2.39</td>
<td>0.03</td>
</tr>
<tr>
<td>Cognitive disturbance</td>
<td>Fluoxetine</td>
<td>68</td>
<td>1.04</td>
<td>0.34</td>
</tr>
<tr>
<td></td>
<td>Fluoxetine+ acupuncture</td>
<td>33</td>
<td>1.07</td>
<td>0.37</td>
</tr>
</tbody>
</table>

Table 4 suggests significant differences in the factor scores for depressive retardation and sleep disorder before and after treatment in the Fluoxetine group, and in the factor scores for somatic symptoms, depressive retardation and sleep disorder before and after treatment in the electroacupuncture plus Fluoxetine group. Symptoms that failed to show significant alleviation included the somatic symptoms and cognitive disturbance in Fluoxetine group, and the cognitive disturbance in electroacupuncture plus Fluoxetine group. The intergroup comparison showed a significant difference in the therapeutic effect for the somatic symptoms between the two groups.

**Assessment for the Clinical Effect–Start Time**

Table 5 shows that in the Fluoxetine group there were significant differences in HAMD scores starting from the fourth week of treatment; and that there were significant differences in HAMD scores starting from the second week of treatment in the electroacupuncture plus Fluoxetine group.

**Table 5. Comparison of the HAMD Scores Between the Two Groups During Treatment (X \( \pm s \))**

<table>
<thead>
<tr>
<th></th>
<th>Fluoxetine</th>
<th>Fluoxetine+acupuncture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>25.1±3.7</td>
<td>23.8±4.0</td>
</tr>
<tr>
<td>Week 1</td>
<td>23.3±4.3</td>
<td>20.3±3.9</td>
</tr>
<tr>
<td>Week 2</td>
<td>22.7±4.6</td>
<td>16.9±4.3</td>
</tr>
<tr>
<td>Week 3</td>
<td>20.9±4.7</td>
<td>15.3±4.7</td>
</tr>
<tr>
<td>Week 4</td>
<td>17.6±5.6</td>
<td>13.7±5.3</td>
</tr>
<tr>
<td>Week 5</td>
<td>14.2±6.3</td>
<td>11.8±5.9</td>
</tr>
<tr>
<td>Week 6</td>
<td>12.7±5.5</td>
<td>10.7±5.1</td>
</tr>
</tbody>
</table>

Note: *P<0.05

**Assessment for Adverse Effects**

The comparison of TESS scores between the two groups is shown in Table 6.
Table 6. TESS Scores for the Fluoxetine Group and the Electroacupuncture Plus Fluoxetine Group (X ±s)

<table>
<thead>
<tr>
<th></th>
<th>Fluoxetine</th>
<th>Fluoxetine + acupuncture</th>
<th>Analysis (df=68)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 2</td>
<td>12.3±5.3</td>
<td>8.3±1.7</td>
<td>t     2.31</td>
</tr>
<tr>
<td>Week 4</td>
<td>11.2±3.3</td>
<td>5.7±1.3</td>
<td>t     3.85</td>
</tr>
<tr>
<td>Week 6</td>
<td>9.9±2.3</td>
<td>4.2±1.6</td>
<td>t     3.97</td>
</tr>
</tbody>
</table>

From Table 6, a significant difference can be found between the two groups in the second week of treatment, and there are markedly significant differences in the 4th and 6th week of treatment.

As the treatments continued, the TESS scores gradually declined in both groups. On the one hand, four patients suffered from so severe adverse effects that the treatment and the assessment had to be terminated. On the other hand, the decline may be related to the mitigating effect of electroacupuncture in the electroacupuncture plus Fluoxetine group.

**DISCUSSION**

Like most of the selective serotonin reuptake inhibitors (SSRIs), slow onset is one of the defects of Fluoxetine, which may show effect 2–4 weeks after medication. It is one of the main reasons for low compliance among patients. Therefore, to increase the compliance for antidepressant medicines, there is an urgent demand for new medication with faster, more stable and better long-term effects. 11-15

Depression is a disease manifested by both somatic and mental symptoms, which should be treated by expectant medications. For example, to alleviate the somatic symptoms, sedative hypnotics, anticoagulant medicines and antipsychotic medicines should be added. However, the combined use of medications may cause a risk of medicine interaction, and lead to a reciprocal causative vicious cycle. 2, 11-12, 15-17

For patients who suffer depression accompanied by somatic symptoms, the adverse effect of Fluoxetine is another problem. 18 The adverse effects may increase the psychological burden of patients, and lower the compliance for treatment. Psychotherapy can directly explore the psychogenic factors, so it is effective for relieving the psychological symptoms, but it is not effective for patients with mainly somatic symptoms who are reluctant to expose their psychological factors.

The electroacupuncture treatment may take effect within two weeks, and may show immediate effects for somatic symptoms in some patients. Therefore, the combined use of acupuncture and medicines for depression patients cannot only reduce their suffering, but also increase their trust in the treatment. 19-21

And during the acupuncture treatment, the patients may have more opportunities to communicate with the doctors and other patients, which may enhance their confidence, and play a role in their health rehabilitation. 15

The present observations showed that both treatments were effective for mild and moderate depression. However, Fluoxetine had a stronger effect for improving physical fatigue, while electroacupuncture showed a better effect for relieving sleep and appetite disorders. Electroacupuncture can improve some of the somatic symptoms of depression, especially the gastrointestinal symptoms, chronic pain and sleep disorders. 13, 19-21 And electroacupuncture can directly treat the somatic symptoms, without the need for additional medications, without physical and mental dependence and without withdrawal symptoms, but with good compliance. For patients suffering from depression with serious somatic symptoms and for elderly patients and patients in poor physical condition, acupuncture combined with medicine would be their first choice.

In this study, the treatment with Fluoxetine was terminated in 4 patients because of serious adverse effects. And the majority of patients had different degrees of adverse effects in the process of taking Fluoxetine. However, during electroacupuncture treatment, there were no adverse effects except the normal needling sensations. Electroacupuncture plus Fluoxetine could reduce the adverse effects caused by
antidepressants, such as headache, dry mouth, nausea, vomiting, anorexia, diarrhea, constipation, and low blood pressure. The therapeutic efficacy was felt after 2 weeks, and became more obvious four weeks after the treatment.

To summarize, clinical practice has shown that we can combine the TCM syndrome differentiation with the disease diagnosis of Western medicine. The prescription of points for electroacupuncture treatment of depression should vary according to different symptoms. Electroacupuncture therapy is applicable for patients who cannot tolerate antidepressant medications, for patients with aggravated somatic symptoms after medical treatment and for elderly depressed patients.²²

REFERENCES


