Effect of St. John’s wort extract on depressive disorder in elderly patients with unstable angina

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BACKGROUND: The elderly patients with coronary heart disease (CHD) are often accompanied with depression. This study aimed to assess the effect of St. John’s wort extract (SWE) on depressive disorder in elderly patients with unstable angina pectoris.

METHODS: Altogether 170 patients who met the set criteria were enrolled in this prospective study. They were randomly divided into SWE group (44 patients), Deanxit group (44), psychotherapy group (42), and control group (40). The effectiveness of SWE was evaluated by reduced percentage of Hamilton depression (HAMD) scale and reduced frequency of angina pectoris attack, which were measured before and at 12 weeks after the treatment with SWE.

RESULTS: The reduced percentages of HAMD scale were 79.5%, 56.8% and 57.1% in the SWE, Deanxit and psychotherapy groups, respectively. Compared with the control, the three groups had significant differences in the percentages (P<0.001). The improvement after the treatment was more significant in the SWE group than in the Deanxit or psychotherapy group (P<0.05). The improvement of angina pectoris attack, its frequencies, durations and electrocardiographic changes were significantly improved in the treatment groups than in the control group (F=6.05, 4.58, 5.12, P<0.01). They are markedly improved in the SWE group (P<0.05).

CONCLUSION: SWE can improve depressive symptoms more significantly in elderly patients with unstable angina pectoris than Deanxit or psychotherapy, proving that SWE contributes to better treatment of angina attack as well.

KEY WORDS: St. John’s wort extract; Depression; Elderly patients; Coronary heart disease; Unstable angina pectoris; Psychotherapy

INTRODUCTION

The morbidity and mortality of coronary heart disease (CHD) in China are increasing rapidly and the number of patients who died of CHD has reached over one million.\(^1\) It is common that the elderly patients with CHD are often accompanied with depression. The reported incidence of depression in CHD patients is 20%.\(^3\)\(^,\)\(^5\) This study was undertaken to assess the herbal antidepressant St. Johns Wort extract (St. John’s wort extract, SWE) in the treatment of elderly patients with unstable angina associated with depression and its effect on clinical symptoms of CHD.

METHODS

From October 2006 to September 2008, 170 elderly patients with unstable angina pectoris and depression were admitted to the Second Hospital of Tianjin Medical University. The patients aged 65-75 years met the criteria set by ISFC and WHO, and 17 Hamilton Depression Rating Scale (Hamilton Depression Scale, HAMD) (HAMD-17)\(^6\) score≥17 points. Exclusion
criteria included bipolar disorder, severe mental illness and suicidal tendencies without use of anti-psychotropic substances for 3 months before treatment. The patients were randomly divided into 4 groups according to the time of admission: drug treatment I (SWE) (n=44), drug treatment II (Deanxit) (n=44), psychotherapy (n=42) and control (n=40). There was no significant difference in baseline between the 4 groups (Table 1).

Beside the conventional treatment of unstable angina pectoris, the patients in the SWE group were given oral SWE (Dr. Weimashupe's Pharmaceutical Companies, German, batch number 0650307) 300mg tid; those in the Deanxit group oral Deanxit (LUNDBECK Pharmaceutical Co., Ltd, batch number 1133) 10.5mg qd; those in the psychotherapy group cognitive therapy, suggestion therapy, supportive therapy and rational emotive therapy twice a week; and those in the control group oral oryzanol 20 mg tid, three times a day. All patients were treated for 12 weeks and provided informed written consent.

Efficacy scores were assessed with the following criteria: (1) healing: HAMD<8, reduced percentage \[\text{score}=(\text{before}-\text{after})/\text{before} \times 100\%\] >75%, and disappearance of all depressive symptoms; (2) marked improvement: HAMD 8-10, reduced percentage 50%-75%, and disappearance of some depressive symptoms; (3) improvement: HAMD 15, reduced percentage<25%, and slight improvement of depressive symptoms; (4) ineffectiveness: HAMD>15, reduced percentage<25%, and no improvement of depressive symptoms. Recovery and marked improvement were defined as marked effectiveness. The HAMD score before and after treatment was assessed by specialist physicians. Before and after treatment, the patients were subjected to 24-hour Holter, electrocardiography, laboratory tests of blood, urine, liver and kidney function. The criteria for efficacy of CHD treatment were consistent with the severity criteria of angina set up by the Canadian Cardiovascular Society (Canada Cardio Society, CCS): 2 or more for marked improvement, 1 for improvement, no improvement for ineffectiveness. The marked improvement of myocardial ischemia was determined by electrocardiogram showing restoration of ST-T to normal or generally normal, improvement for ST-segment depression rebound 0.05 mV, inverted T shallower than 50% or changing a flat upright, and no improvement for not meeting the criteria.

Data analysis
Data analysis were conducted using the SPSS version software for Windows. The measurement data were expressed as means ± SEM, and comparisons were made by the paired t test before and after treatment. Multiple comparisons of enumeration data were made by the chi-square test and the $F$ test. $P$ values less than 0.05 were considered statistically significant.

RESULTS
HAMD score
Comparison of HAMD scores before and after treatment revealed a significant difference between the SWE group, deanxit group, and psychotherapy group ($P<0.001$) (Table 2). Compared to the control group, the difference was significant in the efficacy rate ($\chi^2=29.9$, $P<0.001$), which was higher in the SWE group than in the Deanxit or psychotherapy group ($P<0.05$) (Table 3).

CCS classification
Compared to the control group, the efficacy rate for the treatment of angina pectoris evaluated by the Canada Cardiac Society classification was significantly better in the treatment groups (88.7%, 65.9%, 57.1%) than in the control group ($\chi^2= 15.4$, $P<0.001$), and the efficacy rate in the SWE group was even more significant than in the psychotherapy group ($P<0.05$) (Table 4).

Angina pectoris and ECG
At 12 weeks after treatment, the frequencies and duration of angina pectoris and ischemia were more significantly improved in the SWE group, Deanxit group and psychotherapy group than in the control group ($F=6.05$, 4.58, 5.12, $P<0.01$). The improvement of these variables in the SWE group was better than in the Deanxit group and psychotherapy group ($P<0.05$) (Table 5).

<table>
<thead>
<tr>
<th>Table 1. Baseline characteristics of the patients studied</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group</strong></td>
</tr>
<tr>
<td>SWE</td>
</tr>
<tr>
<td>Deanxit</td>
</tr>
<tr>
<td>Psychotherapy</td>
</tr>
<tr>
<td>Control</td>
</tr>
</tbody>
</table>
Adverse effects

In the SWE group, the main adverse effects were thirsty (3 patients, 6.8%), constipation (3 patients, 6.8%), nausea (2 patients, 4.5%), and dizziness (2 patients, 4.5%).

DISCUSSION

The pathological basis of CHD is coronary atherosclerosis and plaque formation. The relationship between CHD and depression in elderly people has attracted the interest of researchers. Hypotheses about the mechanism of CHD associated with depression include coronary sclerosis, cerebral arteriosclerosis, changes of blood oxygen content. Coronary artery disease causes myocardial ischemia, and thus the heart is unable to transfer enough blood to the brain, causing hypoxia and brain dysfunction manifested as neurological, psychiatric symptoms. The disease is often associated with cerebral arteriosclerosis affecting blood supply to the brain. Decreased arterial oxygen content and oxygen saturation may lead to appearance of neurological, mental symptoms. Reports suggested that depression increases not only the risk of serious cardiac events in patients with stable AP but also the risk of cardiac arrest. Huang et al found that 24% of patients with depressive symptoms in elderly CHD patients with reduced obedience and irregular treatment. Therefore, the early diagnosis of depression is particularly important, and antidepressant treatment should be given along with health education, professional psychological counseling.

St. John Wort extract is the only pure plant antidepressant, which has been used in other countries for many years. Hypericin and hyperforin are the main components of the alcohol extract from St. John Grass (Hypericum perforatum) leaves and buds. It was reported that 2-week SWE treatment decreased the levels of ACTH and cortisol by 40%-70% to regulate the function of patient's hypothalamus-pituitary-adrenal axis for an antidepressant effect. Rarely SWE has similar side-effects as traditional anti-depressant agents, like anti-cholinergic, sympathetic and cardiovascular symptoms. Twelve weeks of treatment in our study demonstrated that SWE, Deanxit and psychological treatment are effective in the treatment of depression in elderly patients with unstable angina pectoris, and the symptoms can be improved to some extent. But SWE is superior to Deanxit and psychological treatment. The present study shows that thirsty, constipation, nausea and dizziness are common adverse effects of SWE. Moreover when angina attacks, frequency, duration and ECG changes are markedly improved after antidepressant treatment, in addition to the overall efficiency of CCS. In recent years, there has been a concept of "bio-psycho medical model" for the prevention and control of cardiovascular diseases in China with an emphasis on psychological intervention for a better prognosis of CHD, but it is still in a clinical

### Table 2. HAMD scales measured before and after treatments (mean±SD)

<table>
<thead>
<tr>
<th>Group</th>
<th>Number</th>
<th>Before</th>
<th>After</th>
<th>t</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SWE</td>
<td>44</td>
<td>24.72±6.68</td>
<td>6.72±3.26</td>
<td>8.65</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Deanxit</td>
<td>44</td>
<td>24.56±6.88</td>
<td>7.76±4.82</td>
<td>7.24</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Psychotherapy</td>
<td>42</td>
<td>24.66±7.52</td>
<td>7.85±4.64</td>
<td>7.32</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Control</td>
<td>40</td>
<td>24.42±6.76</td>
<td>21.86±6.64</td>
<td>0.72</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

### Table 3. Therapeutic effects among different groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Number</th>
<th>Excellence (n/%)</th>
<th>Nulli-excellence (n/%)</th>
<th>Nullity (n/%)</th>
<th>Total effective rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SWE</td>
<td>44</td>
<td>15 (34.1) 20 (45.5)</td>
<td>5 (11.4) 4 (9.1)</td>
<td>59.5*</td>
<td></td>
</tr>
<tr>
<td>Deanxit</td>
<td>44</td>
<td>11 (25.0) 14 (31.8)</td>
<td>11 (25.0) 8 (18.2)</td>
<td>56.8*</td>
<td></td>
</tr>
<tr>
<td>Psychotherapy</td>
<td>42</td>
<td>12 (28.6) 12 (28.6)</td>
<td>9 (21.4) 9 (21.4)</td>
<td>57.1*</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>40</td>
<td>0 (0.0) 8 (20.0)</td>
<td>16 (40.0) 16 (40.0)</td>
<td>20.0</td>
<td></td>
</tr>
</tbody>
</table>

*P<0.001; compared with SWE, #P<0.05.

### Table 4. Changes of CCS classification after different treatments

<table>
<thead>
<tr>
<th>Group</th>
<th>Number</th>
<th>Excellence</th>
<th>Utility</th>
<th>Nullity</th>
<th>Total effective</th>
</tr>
</thead>
<tbody>
<tr>
<td>SWE</td>
<td>44</td>
<td>30 (68.2) 9 (20.5)</td>
<td>5 (11.3)</td>
<td>88.7*</td>
<td></td>
</tr>
<tr>
<td>Deanxit</td>
<td>44</td>
<td>14 (31.8) 15 (34.1)</td>
<td>15 (34.1)</td>
<td>65.9*</td>
<td></td>
</tr>
<tr>
<td>Psychotherapy</td>
<td>42</td>
<td>10 (23.8) 14 (33.3)</td>
<td>18 (42.9)</td>
<td>57.1*</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>40</td>
<td>10 (25.0) 9 (22.5)</td>
<td>21 (52.5)</td>
<td>47.5</td>
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</tr>
</tbody>
</table>

*P<0.001; compared with SWE, #P<0.05.

### Table 5. Angina pectoris attack frequencies, durations and electrocardiogram changes after 12 weeks of different treatments

<table>
<thead>
<tr>
<th>Group</th>
<th>Number</th>
<th>Frequency (min)</th>
<th>ST decline (mm)</th>
<th>Duration (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SWE</td>
<td>44</td>
<td>14.3 ± 3.12 1.02 ± 0.36 3.16 ± 0.69</td>
<td>3.59 ± 0.55*</td>
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<tr>
<td>Deanxit</td>
<td>44</td>
<td>16.5 ± 3.64* 1.23 ± 0.39*</td>
<td>3.67 ± 0.54*</td>
<td></td>
</tr>
<tr>
<td>Psychotherapy</td>
<td>42</td>
<td>17.5 ± 3.86* 1.32 ± 0.41*</td>
<td>4.35 ± 0.91</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>40</td>
<td>20.9 ± 4.23 1.90 ± 0.52</td>
<td>4.35 ± 0.91</td>
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</tr>
</tbody>
</table>

compared with Control P<0.01; compared with SWE P<0.05.
stage. Therefore, elderly patients with unstable angina pectoris accompanied with depression should receive early psychological intervention and antidepressant treatment, which can improve the prognosis of the disease and the quality of life of the patients.\cite{15}

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**Contributors:** Liu J proposed the study and wrote the first draft. All authors contributed to the design and interpretation of the study and to further drafts.

**REFERENCES**


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