Clinical Observations

Effects of Jingyuankang Capsules (精元康胶囊) on Leukocyte Level in AIDS Patients

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Objective: To observe the therapeutic effects of Jingyuankang capsules (精元康胶囊) for leukopenia in AIDS patients.

Methods: In this randomized double-blind trial, 58 patients orally took Jingyuankang capsule, analog Leucogen tablet and the HAART (highly active anti-retroviral therapy) drugs, and the other 58 patients took Leucogen tablet, analog Jingyuankang capsule and the HAART drugs all for 6 months, during which the peripheral hemogram was periodically examined to observe the therapeutic effects of Jingyuankang capsule for leukopenia of the AIDS patients.

Results: With good therapeutic effect for leukopenia of the AIDS patients, Jingyuankang capsule can enhance leukocyte level as effective as Leucogen tablet in treating grade I and grade II leukopenia, and more effectively than Leucogen tablet in treating grade III leukopenia. No toxic side-effects and adverse reactions were found during the treatment and in the follow-up visit.

Conclusion: Jingyuankang capsule can effectively treat leukopenia of the AIDS patients.

Keywords: Jingyuankang Capsules; HIV/AIDS; HAART therapy; TCM therapy; leukopenia; clinical research

The HAART (highly active anti-retroviral therapy) drugs now used in China are all imitations of the drugs early developed abroad with severe toxic side-effects, mainly manifested by leukopenia due to arrest of bone marrow. The patients often stop taking the drugs because of the intolerable toxic side-effects, thus seriously influencing therapeutic effect. At present, there are no drugs special for leukopenia of AIDS patients in the world. Therefore, it is of important significance to develop drugs for treating and preventing leucopenia of the AIDS patients.

Based on the previous study, Jingyuankang capsule (精元康胶囊), which has obvious therapeutic effect for arrest of bone marrow caused by radiotherapy and chemotherapy of cancer¹, was used to treat leucopenia of 116 AIDS patients in Shangcai County, Henan Province in a period clinical from January 2006 to June 2007. now the authors reported as follows.

METHODS

General Data
The 116 AIDS patients, conforming to the Standards for Diagnosing and the Principles for Treating HIV/AIDS promulgated by the Health Ministry of China, were randomly divided into two groups using SPSS 13.0 random number program.

The patients, all definitely diagnosed in AIDS general survey among the high risk people in Henan Province in 2003, were infected with HIV (short for human immunodeficiency virus) via blood supply from 1989 to 1994. They voluntarily took part in the trial (signing a consent after being informed about the facts, and the trial was permitted by Health Care Ethics Committee) and were randomly divided into two groups. Fifty-eight patients were in the treatment group, aged 26–62, 42.4 on the average; the 58 patients were in the control group, aged 29 to 62, 43.6 on the average, both with a ratio about 1:2 between men and women. All the patients of the two groups had taken HAART drugs before the trial for 4–36 months.

There were no significant difference between the two groups in the score of symptoms and signs, peripheral hemogram, Karnofsky score, body weight, and CD4+, hence comparable.

Case Selection

1. Diagnostic Standards:
Standards for diagnosing HIV/AIDS are drawn up according to the Standards for Diagnosing and the Principles for Treating HIV/AIDS promulgated by the Health Ministry of China.²

Standards for classifying the toxic side-effects of HAART drugs are drawn up in reference to the Standards for Grading Toxic Side-effects of Anti-cancer Drugs promulgated by WHO.³

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This study was supported by a grant from the National Key Technology R&D Program of the Ministry of Science and Technology of China (No.2004BA719A09-0203).
Standards for diagnosing leukopenia are worked out in reference to the Standards for Diagnosing Hemotopathy and Evaluating the Therapeutic Effect compiled by ZHANG Zhi-nan.4

Standards for diagnosing TCM syndromes are worked out according to the Instructive Principles for Clinical Researches of New TCM Drugs compiled by ZHENG Xiao-yu.5

Standards for classifying and quantifying the symptoms and signs are drawn up in reference to the Instruction Principles for Clinical Researches of New TCM Drugs compiled by ZHENG Xiao-yu and the TCM Technical Plan (Trial) Implemented in 5 Provinces for Clinical Treatment of AIDS promulgated by the State TCM Administration.5,6

Standards for classifying the quality of life are drawn up according to the Karnofsky Scale quoted from Practical Internal Medicine for Tumors compiled by ZHOU Ji-chang.3

2. Standards for case inclusion:
The patients conforming to the standards for diagnosing HIV/AIDS in Western medicine have taken HAART drugs. The patients with peripheral blood WBC <4.0 × 10^9/L but ≥1.0 × 10^9/L, neutrophilic granulocyte ≥0.5 × 10^9/L, in men Hb <120 g/L but ≥80 g/L, in women Hb <100 g/L but ≥65 g/L, and PLT <100 × 10^9/L but ≥50 × 10^9/L. The patients conform to the standards for diagnosing TCM syndromes with deficiency of both the spleen and kidney. The patients, aged ≥18 but ≤65, predicted to survive for 6 months. The Karnofsky’s score ≥60. The patients have signed a consent after being informed about the facts.

3. Standards for case exclusion:
The patients have severe diseases of the heart (Grade III/IV), liver (ALT ≥200 μ/L), kidney and blood. The patients do not conform to inclusive standards. The patients have severe mental disease or dementia. The patients have taken drugs for less than 6 months. The patients with malignant tumors. The patients have one or more active opportunistic infections such as pneumocystis carinii pneumonia, herpes zoster and pulmonary tuberculosis. The patients have severe symptoms of the whole body, such as inability to take care of their daily life, faint or coma, headache like epileptic attack, and cachexia. The patients can not stop excessive drinking. Women in the period of pregnancy or lactation.

4. Standards for exfoliation and rejection:
Standards for exfoliation: 1) The patients voluntarily quit from the trial. 2) The patients have obvious adverse reactions closely related to the medication. 3) The patients have severe complications during the trial.

Standards for rejection: 1) The patients do not take drugs according to the instruction or do not come for reexamination in time. 2) The patients additionally take other drugs with similar actions, affecting evaluation of therapeutic effects. 3) The patients not conforming to the inclusive standards are found after taking part in the trial.

Group and Medication
For treatment group: 1) HAART: a) AZT: 300 mg, twice one day, oral (note: AZT will be replaced with D4T when WBC <2.0×10^9/L and Hb <90 g/L), b) DDI: 250 mg, Bid, Po for body weight ≥60 kg; and 167 mg, twice one day, oral for body weight <60 kg. c) NVP: 200 mg, once one day (14 days later, once/d is replaced with twice/d). 2) 5 Jingyuankang capsules, three times one day, oral. 2 analog Leucogen tablets, three times one day, oral.

For control group: 1) HAART: the same as in treatment group’s. 2) 2 Leucogen tablets (20 mg), three times one day, oral. Five analog Jingyuankang capsules, three times one day, oral.

The treatment course: the patients take drugs for 6 months in 2 courses of treatment with 3 months as one therapeutic course.

Additional use of drugs: 1) For mild opportunistic infection, additional drugs should be used according to relevant rules. However, it should be avoided to use the drugs influencing peripheral hemogram. 2) For other complicated diseases, drugs should be given according to medical routine. 3) It is prohibited to use the drugs possibly influencing peripheral hemogram.

The Indexes Observed
Peripheral blood routine (including leukocyte, granulocyte, lymphocyte, hemoglobin, blood platelet and red blood cell) should be examined once every half a month.

Criteria for Evaluating Therapeutic Effects
Markedly effective: The leukocyte level returned to normal (≥4.0×10^9/L) in 2 consecutive examinations. Effective: The leukocyte level raised by 100% or to ≥3.0×10^9/L, and granulocytes >1.5×10^9/L in several consecutive examinations. Ineffective: no obvious increase in leukocyte level after treatment.

Statistical Analysis
SPSS13.0 software is used for the statistical analysis. Bilateral examination is used for all the statistical examinations. P<0.05 will be regarded as having statistical difference. Average value ± standard difference is used to statistically describe numerical variables, and t tests were performed. Frequency is used to statistically describe classified variables, and rank test was used.

RESULTS
Through 6 months of systematic observation, no patient died and one case exfoliated (accounting for 0.8% of the 116 patients). Peripheral hemogram in the patients of the 2 groups improved in varying degrees.
Comparison of the Therapeutic Effects
Changes in WBC of the patients before and after treatment in the 2 groups: Among the 57 patients in the treatment group, marked effect was found in 35 cases, effectiveness in 19 cases and ineffectiveness in 3 cases, with an effective rate of 94.7%. Among the 58 patients in the control group, marked effect was found in 26 cases, effectiveness in 20 cases and ineffectiveness in 10 cases with an effective rate of 82.8%. There was a significant difference in therapeutic effects between the 2 groups (P<0.05, Table 1).

Comparison of the Leukocyte Levels of the Patients before and after Treatment
According to the leukocyte levels of patients before treatment and the WHO standards for classifying toxic side-effects of drugs (grade I: WBC 3.0–3.9, grade II: 2.0–2.9, grade III: 1.0–1.9), the 2 groups were divided respectively into 3 subgroups of grade, II and III leukopenia for comparing the change of WBC before and after treatment.

Comparison of the leukocyte levels in patients with grade I leukopenia before and after treatment showed that there was an obvious difference in both groups, indicating that both the drugs can enhance the leukocyte level (P<0.05). However, there was no obvious difference (P>0.05) before treatment (0 month) and after treatment (6 months) between the two subgroups, indicating that the two drugs have similar effect on enhancing leukocyte level for grade I leukopenia (Table 2).

There were 4 patients with grade III leukopenia before treatment in both the two groups. After treatment, the leukocyte level returned to normal in all the 4 patients of the treatment group but only in one patient of the control group, showing that Jingyuankang capsule has better therapeutic effect than the contrast drug for grade III leukopenia, as shown in Table 3.

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Toxic side-effects and adverse reactions caused by Jingyuankang capsules were not found during the treatment and in the follow-up visit.

Table 1. Comparison of changes in WBC of the patients before and after treatment between the 2 groups (cases)

<table>
<thead>
<tr>
<th>Group</th>
<th>Cases</th>
<th>Markedly effective</th>
<th>Effective</th>
<th>Ineffective</th>
<th>Effective rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>57</td>
<td>35</td>
<td>19</td>
<td>3</td>
<td>94.7</td>
</tr>
<tr>
<td>Control</td>
<td>58</td>
<td>26</td>
<td>22</td>
<td>10</td>
<td>82.8</td>
</tr>
</tbody>
</table>

Note: Z=2.096, P<0.05.

Table 2. Comparison of the leukocyte levels in patients with grade I leukopenia before and after treatment in the two groups (x±s, ×10⁹/L)

<table>
<thead>
<tr>
<th>Group</th>
<th>Cases</th>
<th>0 month</th>
<th>6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>34</td>
<td>3.41±0.31</td>
<td>5.22±1.53</td>
</tr>
<tr>
<td>Control</td>
<td>36</td>
<td>2.52±0.29</td>
<td>4.90±1.89</td>
</tr>
</tbody>
</table>

Notes: *P<0.05 compared with that of 6 months; *P>0.05 compared with the treatment group.

Table 3. Comparison of the leukocyte levels in patients with grade II leukopenia before and after treatment in the two groups (x±s, ×10⁹/L)

<table>
<thead>
<tr>
<th>Group</th>
<th>Cases</th>
<th>0 month</th>
<th>6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>19</td>
<td>2.52±0.29</td>
<td>5.84±1.39</td>
</tr>
<tr>
<td>Control</td>
<td>18</td>
<td>2.60±0.27</td>
<td>4.90±1.89</td>
</tr>
</tbody>
</table>

Notes: *P<0.05 compared with that of 6 months; *P>0.05 compared with the treatment group.

Table 4. Comparison of the leukocyte levels in patients with grade III leukopenia before and after treatment in the two groups

<table>
<thead>
<tr>
<th>Group</th>
<th>The coding number</th>
<th>0 month</th>
<th>6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>7</td>
<td>1.5</td>
<td>6.4</td>
</tr>
<tr>
<td></td>
<td>67</td>
<td>1.4</td>
<td>4.7</td>
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<tr>
<td></td>
<td>68</td>
<td>1.8</td>
<td>4.8</td>
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<tr>
<td></td>
<td>100</td>
<td>1.9</td>
<td>7.9</td>
</tr>
<tr>
<td>Control</td>
<td>9</td>
<td>1.1</td>
<td>7.5</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>1.9</td>
<td>3.7</td>
</tr>
<tr>
<td></td>
<td>48</td>
<td>1.6</td>
<td>3.9</td>
</tr>
<tr>
<td></td>
<td>82</td>
<td>1.7</td>
<td>1.7</td>
</tr>
</tbody>
</table>

Notes: *P<0.05 compared with that of 6 months; *P>0.05 compared with the treatment group.

CONCLUSION
Jingyuankang capsule can obviously enhance the leukocyte level in patients with leukopenia caused by AIDS and HAART. The total therapeutic effect is better than that of Leucogen tablet.

Jingyuankang capsule can enhance the leukocyte level as effective as Leucogen tablet in treating patients with grade I and II leukopenia and more effectively than Leucogen tablet in treating grade III leukopenia, preliminarily showing the good therapeutic effect of
Jingyuankang capsule for severe leukopenia. Because of few cases involved in the test, the therapeutic effect of Jingyuankang capsule remains to be further studied.

DISCUSSION
All the similar researches in the past were completely separated from the pathogenic circumstances, that is to say, drugs were used for observation after radiotherapy and chemotherapy. Because of the specialty, AIDS can not be treated without HAART, so Jingyuankang capsule should be used together with HAART. The results from the present study shows that the more advantages of TCM can be reflected.

The previous researches put the patients with WBC \( \geq 2.5 \times 10^9/L \) under observation. We expanded the range to \( \geq 1.0 \times 10^9/L \), making it much more difficult the research, but still obtained good therapeutic effect of TCM.

The present study shows that Jingyuankang capsule, with good therapeutic effects, less toxic side-effects, and can improve the leukocyte level in AIDS patients, reduce the toxic side-effects of HAART, thus guarantee a smooth-going of the treatment.

REFERENCES

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