CLINICAL EXPERIENCES

Clinical Observation on Treatment of Chronic Aplastic Anemia by Shengxuening (生血宁) and Cyclosporin A

ZHANG Xue-zhong (张学忠), XU Yan-li (徐燕丽), JIN Juan (金娟)
ZHANG Xiu-qun (张秀群), ZHANG Lei (张磊), and SU Ai-ling (苏爱玲)

ABSTRACT
Objective: To explore the therapy to further elevate the efficacy of the treatment of chronic aplastic anemia (CAA). Methods: Forty-five patients with CCA were assigned into two groups, the 26 patients in the treated group were treated by Shengxuening (生血宁, a Chinese herbal preparation) and cyclosporin A (CsA), and the 19 patients in the control group were treated with androgen alone, with the therapeutic course lasting for over 3 months. Changes of peripheral blood picture, and the colony productivity of burst forming unit-erythroid (BFU-E), colony forming unit-erythroid (CFU-E) and colony forming unit-granulocyte macrophage (CFU-GM) in bone marrow were observed before and after 3 months treatment. The amount of erythrocyte and platelet infusion, frequency of infection, condition of hemorrhage and relevant death were also observed. The follow-up study was conducted for over half a year. Results: The total effective rate in the treated group was 84.6%, which was significantly higher than that in the control group (52.6%, P<0.05). Levels of hemoglobin, reticulocyte, neutrophil and platelet increased after treatment in the treated group, as compared with those before treatment, with significant difference (P<0.05), and the colony productivity of BFU-E, CFU-E and CFU-GM in bone marrow also got significantly increased (P<0.01), and showed significant difference from those in the control group (P<0.05). Conclusion: Shengxuening-assisting CsA therapy is an effective measure for treatment of CAA.

KEY WORDS Shengxuening, cyclosporin A, aplastic anemia

Chronic aplastic anemia (CAA) is a disease of bone marrow hemopoietic function failure due to chemical, physical, biological or unknown factors, characterized by hemopoietic stem cell injury and peripheral whole blood cell decrease. Nowadays, there is no method for radical cure of the disease, with the previously commonly used drug as androgen, of which the effective rate is about 40% - 50%.

In the recent ten years, several domestic hospitals have been using cyclosporin A (CsA) in treating CAA, and according to comprehensive report, the effective rate is 60% - 70%. In China, the effect of traditional Chinese medicine (TCM) on CAA has been researched on all the while. Shengxuening (生血宁, SXN) tablet made of extract from excrementum bombycis, with its chief component as chlorophyll derivative, has been proved by animal experiment to be able to promote the proliferation of bone marrow erythron and granulo-macrophagous progenitor(1). In order to find more effective method for treatment of CAA, SXN and CsA were used in this study and certain efficacy was obtained. The result is reported as follows.

METHODS

Clinical Materials
All the 45 CAA patients, diagnosed according to the reference(2), were either in-patients or out-patients of the authors’ hospital from Aug. 2002 to Sept. 2005. They were assigned according to their financial condition into two groups.

The 26 patients in the treated group were 15 males and 11 females, with the mean age of 40 years (20 - 72 years old), their course of disease 4 - 78 months, 21.3 ± 12.5 months on average. The 19 patients in the control group, who were too hard up to pay for the medicine of CsA, were 10 males and 9 females, with the mean age of 38 years (18 - 69 years old), their course of disease 4 - 82 months, 21.6 ± 12.4 months on average. Statistical analysis showed that the clinical materials of the two groups were similar and so they were comparable.

...
Treatment

Stanozolol was used to treat the control group patients, with 4 - 6 mg given per day, while the treated group was treated with CsA (product of Huabei Pharmaceutical Factory), 3 - 5 mg/kg per day, and SXN (product of Wuhan Union Pharmaceutical Co. Ltd.), 6 tablets per day. All the drugs were administered orally in three times. The therapy lasted for 3 - 20 months. The clinical efficacy was assessed after 3 months’ treatment, and the patients were followed up from 6 months to 2 years.

Items and Methods of Observation

Changes of hemoglobin (Hb), reticulocyte, neutrophil and platelet were observed before and after 3 months treatment.

Changes of bone marrow burst forming unit-erythroid (BFU-E), colony forming unit-erythroid (CFU-E) and colony forming unit-granulocyte macrophage (CFU-GM) in part of the patients (18 in the treated group and 14 in the control group) were detected and recorded before and after 3 months treatment by using methyl cellulose semi-solid culture method.

The incidence and frequency of infection, condition of general or local hemorrhage, the infusion amount of erythrocyte suspension and platelet suspension needed in the therapeutic course were recorded and the relevant causes of death were analyzed.

Standard for Efficacy Evaluation

In reference to the "Standard for Diagnosis and Therapeutic Efficacy Evaluation of Hematopothy" [2], the effects of treatment were classified into 4 grades: (1) Basically cured: anemia and hemorrhage disappeared, amount of Hb reached 120 g/L in male or 100 g/L in female, count of white blood cell reached $4 \times 10^9$/L, and count of platelet reached $80 \times 10^9$/L; (2) Alleviated: anemia and hemorrhage disappeared, amount of Hb reached 120 g/L in male or 100 g/L in female, count of white blood cell reached $3.5 \times 10^9$/L, and count of platelet was somewhat increased; (3) Markedly improved: anemia and hemorrhage got markedly improved, with no need for blood perfusion, Hb increased over 30 g/L more than that before treatment, and the effect could be maintained for 3 months; (4) Ineffective: no obvious improvement was revealed in symptoms or blood picture.

Statistical Analysis

Data were expressed by $\bar{x} \pm s$, measurement data were compared by t-test and the enumeration data were compared by $\chi^2$ test.

RESULTS

Comparison of the Therapeutic Effect

In the treated group, 8 out of the 26 patients were evaluated as basically cured, 5 as alleviated, 9 as markedly improved and 4 as ineffective, the total effective rate being 84.6% (22/26 cases). In the control group, 1 out of the 19 patients were evaluated as basically cured, 3 as alleviated, 6 as markedly improved and 9 as ineffective, the total effective rate being 52.6% (10/19 cases). The difference in total effective rate between the two groups was significant ($P<0.05$).

Comparison of the Changes in Hemoglobin and Reticulocyte between the Two Groups

As shown in Table 1, the level of hemoglobin and count of reticulocyte got increased after treatment in the treated group, significantly higher than those before treatment respectively ($P<0.05$), and as compared with those in the control group after treatment, it was also higher in the treated group but showed no statistical significance ($P>0.05$).

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>Hemoglobin (g/L)</th>
<th>Reticulocyte (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treated 26</td>
<td>BT</td>
<td>43.75 $\pm$ 13.47</td>
<td>1.02 $\pm$ 0.42</td>
<td></td>
</tr>
<tr>
<td></td>
<td>AT</td>
<td>77.84 $\pm$ 30.23*</td>
<td>1.45 $\pm$ 0.92*</td>
<td></td>
</tr>
<tr>
<td>Control 19</td>
<td>BT</td>
<td>44.11 $\pm$ 15.86</td>
<td>1.08 $\pm$ 0.52</td>
<td></td>
</tr>
<tr>
<td></td>
<td>AT</td>
<td>63.31 $\pm$ 21.78</td>
<td>1.28 $\pm$ 0.75</td>
<td></td>
</tr>
</tbody>
</table>

Notes: * $P<0.05$, compared with BT in the same group.

Comparison on the Changes of Neutrophil and Platelet

As shown in Table 2, the count of neutrophil and platelet got increased significantly after treatment in the treated group, as compared with those

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>Neutrophil ($\times 10^9$/L)</th>
<th>Platelet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treated 26</td>
<td>BT</td>
<td>0.57 $\pm$ 0.14</td>
<td>32.65 $\pm$ 14.16</td>
<td></td>
</tr>
<tr>
<td></td>
<td>AT</td>
<td>0.93 $\pm$ 0.26*</td>
<td>58.74 $\pm$ 19.02*</td>
<td></td>
</tr>
<tr>
<td>Control 19</td>
<td>BT</td>
<td>0.61 $\pm$ 0.13</td>
<td>33.01 $\pm$ 15.77</td>
<td></td>
</tr>
<tr>
<td></td>
<td>AT</td>
<td>0.74 $\pm$ 0.21</td>
<td>45.92 $\pm$ 15.65</td>
<td></td>
</tr>
</tbody>
</table>

Notes: * $P<0.05$, compared with BT in the same group