Clinical Study on Effect of Fuzheng Kangbai Granule on Long-Term Survival of Patients with Acute Leukemia

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ABSTRACT

Objective: To observe the effect of Fuzheng Kangbai Granule (FZKBG) on long-term survival of patients with acute leukemia, and to study its mechanism in treating minimal residual leukemia. Methods: FZKBG was used to treat 90 cases of completely remitted acute leukemia to observe the effect of treatment on 5-year event free interval (EFI), over survival (OS) and the immune function of patients. Results: Five-year EFI and OS of the 90 cases were 62.4% and 77.2% respectively, and the immune functions after FZKBG therapy were improved significantly. Conclusion: FZKBG could increase the 5-year EFI and 5-year OS, which might be reached through improving immune function of patients.

KEY WORDS: Fuzhen Kangbai Granule, acute leukemia, quality of life span, immune function

At the present time, chemotherapy is the chief treatment of acute leukemia (AL). But while chemotherapy eliminates pathogens, it also damage the organism itself. And therefore, when AL has gotten complete remission by chemotherapy and entered into minimal residual leukemia (MRL) state, the patients would, inevitably, suffer from Deficiency, showing the characteristics of “body impairment after Evil pathogen removed” and “both Deficiency of Qi and Yin Syndrome” (1). The authors expected to rebuild and restore the immune function, and to prevent the recurrence and prolong the leukemia-free survival (LFS) of MRL patients by way of supporting healthy energy. This article reported the clinical study on effect of Fuzheng Kangbai Granule (FZKBG) on long-term survival of AL patients.

METHODS

Clinical Materials

The study included 90 in-patients who had achieved complete remission (CR) from July 1st, 1992 to June 30, 1997 in the authors’ or other hospitals. They were 56 males and 34 females, aged 13 – 59 years, and their CR period was 0.5 – 7.5 months. Among them 81 suffered from acute non-lymphocytic leukemia (5 from M1, 8 from M2, 66 from M3, 1 from M5 and 1 from M7), and 9 from acute lymphocytic leukemia (all L2). The diagnosis and therapeutic effect were evaluated according to the standard published by Zhang Zhinan (2).

Method of Treatment

For the M3 cases, 0.01% As2O3 injection (1.0 mg/ml) 10 ml was added in 5% glucose solution for intravenous drip per day and given for 14 days as one therapeutic course for 6 course. To other acute non-lymphocytic leukemia patients, DA (DNR + Ara-C) or NA (NVT + Ara-C) scheme was used for at least 6 courses. And for acute lymphocytic leukemia cases, VDLP, VDAP, HD-MTX were applied alternately for at least 6 courses. Among them 2 patients received auto-bone marrow transplantation. All patients took FZKBG 12 g, 3 times a day for 3 months successively as one course, 2 – 12 courses were received in general.

FZKBG consisted of Radix Ginseng, Radix Astragalus, Radix Polygoni Multiflori, Herba Epimedium, Radix Asparagus, Fructus Psoralea, Fructus Ligustrum Lucidum and Rhizoma Atractylodes Alba, containing 82.5 g of crude drugs in 12 g of preparation, which was supplied by the pharmaceutical factory of the authors’ hospital.
Laboratory Detection

1. Peripheral lymphocyte subsets (CD3, CD4, CD8, CD20) and NK cell were determined using monoclonal antibodies (McAb) CD3, CD4, CD8, CD20, CD16 + CD56 (NK) (products of Immunotech Co.) by flow cytometry (made by Coulter EPICS ELITE) with the method mentioned in the reference (3). The normal value set by determination in 64 healthy persons (30 males and 34 females, aged 21 - 57 years) were: CD3 66.3% - 92.3%, CD4 30.3% - 52.7%, CD8 16.9% - 38.9%, CD20 8.0% - 18.0%, NK cell 9.2% - 19.6%. Moreover, peripheral lymphocyte subsets and NK cells in 10 patients of AL non-remission were also assayed.

2. IgG, IgA, IgM and C3 were tested by immunodiffusion method. And lymphocyte transformation rate was calculated by lymphoblast/total lymphocyte × 100% after 72 hours culture.

Evaluation of Effectiveness

EFI and OS time were counted from the day of CR, the follow-up period was 16 - 60 months, ending on June 30, 1997.

Statistic Analysis

F test, t test and Kaplan-Meier method were adopted. 5-year survival rate and 5-year LFS rate were calculated with Kaplan and Meier product-limit method (4).

RESULTS

EFI and OS

Among the 90 cases, 2 were lost, 2 died from hepatic coma and veno-occlusive syndrome of liver respectively, 31 had a relapse and 55 got consistent CR. The 3- and 5-year EFI were 72.4% and 62.4% respectively, and the 3- and 5-year OS were 82.2% and 77.2% respectively. The 5-year EFI in different subtypes of AL were listed in table 1.

Peripheral Lymphocyte Subsets and NK Cells

The abnormal lymphocyte subsets in non-CR AL patients were improved after the patients got CR but remained lower than those in the healthy persons. And further improvement could be induced by FZKBG (see table 2).

Changes of CD4 after FZKBG treatment: (1) Before treatment, there were 11 cases with CD4 < 30.3%. The CD4 level was markedly increased after treatment, an increase from 24.9 ± 3.2% to 33.8 ± 2.4% in them, P < 0.05. (2) Among the 23 cases with their CD4 in the normal range before treatment, no changes was shown after treatment except the lowering to < 30.3% in 3 case.

Changes of CD8 after FZKBG treatment: (1) There were 5 cases with CD8 < 16.9% before treatment, and their level of CD8 was markedly increased after treatment, an increase from 15.1 ± 2.5% to 33.3 ± 9.3%, P < 0.05. (2) In the 9 cases with CD8 > 38.5% before treatment, the level of CD8 decreased significantly from 47.7 ± 9.2% to 37.9 ± 11.9%.

Table 1. The 5-Year LFS and Survival of Patients with Different FAB Subsets of Leukemia (Cases)

<table>
<thead>
<tr>
<th></th>
<th>M1</th>
<th>M2</th>
<th>M3</th>
<th>M5</th>
<th>M7</th>
<th>L2</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Patients</td>
<td>5</td>
<td>8</td>
<td>64</td>
<td>1</td>
<td>1</td>
<td>9</td>
<td>88</td>
</tr>
<tr>
<td>Died during CR</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Relapse</td>
<td>2</td>
<td>5</td>
<td>16</td>
<td>1</td>
<td>1</td>
<td>6</td>
<td>31</td>
</tr>
<tr>
<td>Died for Leukemia</td>
<td>1</td>
<td>4</td>
<td>7</td>
<td>1</td>
<td>1</td>
<td>4</td>
<td>18</td>
</tr>
<tr>
<td>Consistent CR</td>
<td>2</td>
<td>3</td>
<td>47</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>55</td>
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<tr>
<td>5-Year Survival(%)</td>
<td>60</td>
<td>50</td>
<td>87</td>
<td>0</td>
<td>0</td>
<td>55</td>
<td>77</td>
</tr>
<tr>
<td>5-Year LFS(%)</td>
<td>40</td>
<td>37</td>
<td>73</td>
<td>0</td>
<td>0</td>
<td>33</td>
<td>62</td>
</tr>
</tbody>
</table>

Notes: Cases who died for leukemia were included in relapse