Kanglaite Injection combined with chemotherapy & radiotherapy in treating non-Hodgkin’s lymphoma

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[Abstract] This study was to determine effectiveness of Kanglaite Injection (KLT) combined with chemotherapy and radiotherapy in treating Non-Hodgkin Lymphoma (NHL). 45 cases of NHL were treated with KLT combined with chemotherapy and radiotherapy as treatment group and 35 cases of NHL were treated by chemo and radiotherapy alone as control group. The response rate (RR) of treatment group and control group was 86.7% and 57.1% respectively, \( P<0.05 \). Recurrence rate of 3 and 5 years in treatment group was 15.0% and 21.0% separately, which was much lower than 31.3% and 46.7% in control group, \( P<0.05 \). In addition, improvement of clinical symptoms and toxicity reduction in treatment group were much higher than that in control group \( (P<0.01) \). KLT combined with chemotherapy and radiotherapy could effectively alleviate toxicity caused by chemotherapy and radiotherapy, improve quality of life, strengthen effectiveness and reduce local recurrence rate.


45 patients with non-Hodgkin’s lymphoma, NHL received treatment of Kanglaite Injection (KLT) combined with chemotherapy and radiotherapy in our department between Jan. 20, 1994~Dec. 31, 1998 with 35 cases receiving pure chemotherapy and radiotherapy in control group. Following is the summary.

1. Clinical data
   1.1 General information
   All 80 cases were pathologically confirmed NHL patients with 65 male and 15 female. Age: 60~72 years with average age as 50 years. 80 cases were classified as follows. Low-malignancy group: small lymphocytic 9 cases, mycosisfungoides 4 cases, cleaved-non-cleaved cell (follicular) 3 cases; medium-malignancy group: cleaved-non-cleaved cell (widespread) 7 cases; high-malignancy group: non-cleaved cell (widespread) 10 cases, histiocytic 14 cases, lymphoblastic 11 cases, immunoblastic 10 cases; non-classified group: 12 cases; phase I 7 cases, phase II 13 cases, phase III 50 cases and phase IV 10 cases. 45 patients randomly entered treatment group (KLT combined with chemo- and radio therapy) and 35 entered control group (pure chemo-and radio therapy). There was no significance in difference of sex, age, clinical staging and pathology between the two groups. Head & neck neoplasm 41 cases, abdominal mass 11 cases, inguinal mass 10 cases, tonsillar mass 3 cases, systemic superficial lymphadenopathy 6 cases, mediastinum tumor 5 cases, and whole-body subcutaneous nodule 4 cases. Primary intranodal 58 cases and extranodal 22 cases.

1.2 Treatment method
45 cases in treatment group received 100ml KLT iv drip, once a day with 25~30 days as a cycle. Regimen of chemo-radiotherapy in control group was the same as that for treatment group. Chemotherapy protocol was mainly CHOP with CTX 750mg/m², iv injection, d1; ADM 40mg/m² (E-ADM 50mg/m²), iv injection, d1; VCR 1.4mg/m², iv injection, d1, d8; PDN 100mg/m², orally d1~d5, 21 days as a cycle and 3 cycles as a course. Linear accelerator was used for extracorporeal and local involved field irradiation. Primary lesion was given radical radiation therapy with DT 50~55Gy for 5~7 weeks. Reduced field was applied for remaining mass at dose of 5Gy for 2~3 times. Adjacent nodal irradiation was employed for prevention at dose of 45Gy for 5~6 weeks. Dose of fractionated irradiation was 1.8~2.0Gy, 5 times a week.

### 1.3 Criteria for efficacy

WHO criteria were followed i.e. CR, PR, NC, and PD with CR+PR as effectiveness. Toxic and side effects were also based on WHO standard with 0~8 degrees in toxicity. Survival started from beginning of treatment to death that was counted from date of loss of contact in follow-up. All results were tested with $X^2$.

### 1.4 Results

#### 1.4.1 Comparison in toxic and side effect

See Tab. 1 for comparison in clinical symptom improvement after treatment and toxic/side-effect between the 2 groups.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Treatment Group</th>
<th>Control Group</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal reaction</td>
<td>15/45 (33.3)</td>
<td>25/35 (71.4)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Bone marrow inhibition</td>
<td>26/45 (57.8)</td>
<td>31/35 (88.6)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Increase in bodyweight</td>
<td>39/45 (86.7)</td>
<td>6/35 (17.1)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Reduction in fatigue</td>
<td>30/45 (66.7)</td>
<td>8/35 (22.9)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Improvement of appetite</td>
<td>29/45 (64.4)</td>
<td>6/35 (17.1)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Alleviated pain</td>
<td>36/45 (80.0)</td>
<td>15/35 (42.9)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Alleviated low fever</td>
<td>36/45 (80.0)</td>
<td>16/35 (45.7)</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>

#### 1.4.2 Response rate

In treatment group: CR 17 cases (37.8%), PR 22 cases (48.9%), NC 4 cases (8.9%), PD 2 cases (4.4%), CR+PR 86.7%; in control group: CR 6 cases (17.1), PR 14 cases (40%), NC 9 cases (25.8%), PD 5 cases (14.3%), CR+PR 57.1%. Statistical differences were significant ($P<0.05$) with data in treatment group much better than that in control group.

#### 1.4.3 Local recurrence rate

3-year recurrence rate in treatment group was 6/40 (15.0%) and 5-year rate was 8/38 (21.0%). In control group the 3-year and 5-year figures were 10/32 (31.3%) and 14/30 (46.7%) respectively with significant statistical difference ($P<0.05$).
1.4.4 Distant metastasis rate
3-year metastasis rate in treatment group was 9/40 (22.5%) and 5-year rate was 10/38 (26.3%). In control group 3-year and 5-year figures were 9/32 (28.1%) and 10/30 (33.3%) respectively without significant statistical difference ($P > 0.05$).

1.4.5 Survival rate
3-year survival rate in treatment group was 24/40 (60.0%) and 5-year rate was 19/38 (50.0%). In control group 3-year and 5-year figures were 16/32 (50.0%) and 14/30 (46.7%) respectively without significant statistical difference ($P > 0.05$).

2. Discussion
KLT is an O/W white emulsion with natural coix seed oil as active ingredient extracted from *semen coicis* and prepared with natural emulsifier and isotonic agent. KLT has double-phasic anticancer action. Its major mechanism is to block cells at $G_2$-$M$ phase, reduce cells entering $G_0$-$G_1$ phase to cause reduction in percentage of cells of $S$ phase so as to decrease cell mitosis, inhibit cell multiplication and induce apoptosis of tumor cells. KLT can prevent invasion and metastasis of tumor cells. Treatment of NHL includes chemotherapy and radiation therapy. Chemotherapy has action to kill normal cells and easily causes drug resistance while KLT can reverse multi-drug resistance. Therefore KLT presents synergistic action in combination with chemotherapy. A large number of in vitro studies and animal experiments proved that KLT could activate NK cell, IL-2 and T-lymphocyte, promote multiplication of splenic lymphocyte to improve body immuno function, strengthen phagocytic function of macrophage, enhance hematopoiesis of bone marrow, improve activity of SOD, notably raise body’s nonspecific ability to resist disease and present significant analgesic action.

This study showed that KLT, in combination with chemo-radiotherapy, could alleviate gastrointestinal reaction and bone marrow inhibition caused by chemo-radiotherapy, increase bodyweight, reduce fatigue, improve appetite, reduce pain and alleviate low fever so as to improve quality of life. The study also showed that response rate in treatment group was 86.7% against 57.1% in control group with significant statistic difference. 3 and 5 year local recurrence rate in control group was 31.3% and 46.7% separately, which were obviously higher than 15.0% and 21.0% in treatment group with significant difference. So, KLT combined with chemo-radiotherapy could reduce patient local recurrence rate. 3 year distant metastasis rate in treatment group was 22.5% and 5 year figure was 26.3% without significant difference as compared with control group. 3 year survival rate in treatment group was 60.1% and in control group 50.0% without significance in difference as compared with control group. KLT combined with chemo-radiotherapy could reduce toxic and side effect caused by chemo-radiotherapy, improve patient quality of life, raise response rate, and reduce local recurrence rate. KLT has become an effective drug in comprehensive treatment of NHL.

[References]

