Effect of Kanglaite Injection combined with chemotherapy in treating advanced non-small-cell lung cancer

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[Abstract] Objective: To evaluate GP regimen alone and GP regimen combined with Kanglaite Injection (KLT) on efficacy, side effect and improvement of quality of life in the treatment of advanced non-small-cell lung cancer (NSCLC). Methods: 35 patients with NSCLC in stage III and IV were treated by GP regimen combined with KLT, and 35 patients were treated with GP regimen alone. KLT was used on the first day of each chemotherapy cycle for consecutive 10 days, and dosage was 200ml/d. GP regimen included gemcitabine 1000mg/m² on 1st and 8th days and cisplatin 25mg/m² from 1st to 3rd day. The treatment was repeated every 3 weeks. Efficacy, side effect and quality of life were compared after 2 cycles of chemotherapy. Results: Response rate was 42.86% in treatment group and 34.28% in control group (P<0.05). Quality of life in treatment group was significantly higher than that in control group after treatment (P<0.05). Incidence of side effect in treatment group was lower than that in control group, and degree was also slighter. Conclusion: KLT in combination with GP regimen can be used for treatment of advanced NSCLC. It can improve efficacy and quality of life, and reduce side effect of chemotherapy.

[Key words] Kanglaite; chemotherapy; non-small-cell lung cancer


Lung cancer has become the first death factor to threat people's life and ITS mortality is as high as 80%. Major causes are that patient has been at advanced stage when discovered and that there is extensive metastasis in lymph node or far viscera. Chemotherapy may prolong survival for advanced lung cancer patient but total response rate is only 20%~35% with severe adverse reaction. Active ingredient of KLT is semen coicis that is extracted with modern technology and presents effect to reduce toxicity and enhance immune function. Between March 2008 and October 2010, we adopted KLT combined with chemotherapy to treat advanced lung cancer and reached better therapeutic effect as compared with chemotherapy along group. Following is the summary.

1. Data and methods
2. 1.1 General information
70 cases with NSCLC admitted between March 2008 and October 2010 were randomly divided into treatment group and control group with 35 cases in each group.

Treatment group: male 21 cases, female 14; age 59~74 years with average 66.1 years; squamous 22 cases, adenocarcinoma 12, adenosquamous carcinoma 1; stage III 12 cases, stage IV 23.

Control group: male 23 cases, female 12; age 60~71 years with average 64.8 years; squamous 19 cases, adenocarcinoma 15, adenosquamous carcinoma 1; stage III 10 cases, stage IV 25. Comparison on general information between the two groups had no statistical significance ($P>0.05$) with comparability.

1.2 Enrollment and exclusion criteria
Enrollment criteria: ① NSCLC diagnosis confirmed with pathological or cytological examination with focus measurable in lung (chest CT and chest X-ray film); ② Karnofsky score (KPS) >60 with normal cardiac, hepatic and renal functions; ③ Estimated survival > 3 months. Exclusion criteria: ① Not tolerable with chemotherapy regimen; ② Estimated survival <3 months; ③ KPS < 60 scores.

1.3 Regimen
Two groups accepted GP protocol. Gemcitabine (Jiangsu Hansoh) 100mg/m$^2$, iv drip, D$_1$, D$_8$; cisplatin (Qilu Pharmaceutical) 25mg/m$^2$ +0.9% sodium chloride injection 500ml, iv drip, D$_1$~D$_3$. KLT 200ml was added to patients in treatment group from 1$^{st}$ day of chemotherapy (Zhejiang Kanglaite), iv drip, qd for consecutive 10 days. Concomitant treatment included anti-vomiting, protection of gastric mucosa, and anti-allergy while cisplatin was routinely hydrated in administration. 21 days were as a cycle for the two groups and evaluation of response rate was made after completion of chemotherapy for 2 cycles.

1.4 Observatory evaluation
1.4.1 Clinical response rate
Response rate was evaluated based on RECIST 1.1 criteria. Response rate included: CR -disappearance of all target lesions; PR –shrinkage of long diameter sum of basal line in lesion ≥30%; SD –shrinkage of long diameters sum of basal line in lesion not reaching that of PR or increase but not reaching PD; PD –increase of long diameters sum of basal line in lesion ≥30% or occurrence of new lesion. Total response rate = (CR cases + PR cases) / total cases x 100%.

1.4.2 Evaluation of life quality
Based on KPS criteria: Improvement -KPS score increased by ≥10 points after treatment;
Stability - KPS score increased or decreased by 1 < 0 points; Decrease - KPS score decreased by > 10 points. Effective rate = (improved cases + stable cases) / total cases x 100%.

1.4.3 Adverse reaction
Based on criteria for grading adverse reaction of antineoplastic agent formulated by WHO. Indexes were observed such as blood routine result, WBC count, platelet change, hepatic and renal function damage, and gastrointestinal reaction, etc. Grade III or IV was serious adverse reaction.

1.5 Statistical method
SPSS 11.0 software was used for analysis. Measurement data was processed with t test and categorical data used $X^2$ test with $P < 0.05$ suggesting statistical difference.

2. Results
2.1 Comparison on clinical efficacy between the two groups
Comparison on total effective rate between the two groups showed that data from treatment group was apparently better than those from control group with significant statistical differences ($P < 0.05$), see Tab. 1.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>CR</th>
<th>PR</th>
<th>SD</th>
<th>PD</th>
<th>CR+PR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>35</td>
<td>3</td>
<td>12</td>
<td>13</td>
<td>7</td>
<td>42.86</td>
</tr>
<tr>
<td>Control</td>
<td>35</td>
<td>2</td>
<td>10</td>
<td>14</td>
<td>9</td>
<td>34.28</td>
</tr>
</tbody>
</table>

2.2 Comparison on survival quality between the two groups
KPS scores in treatment group was better than that in control group with statistical difference ($P < 0.05$), see Tab. 2.

<table>
<thead>
<tr>
<th>Group</th>
<th>n (%)</th>
<th>Improve</th>
<th>Steady</th>
<th>Decline</th>
<th>ER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>35</td>
<td>6</td>
<td>18</td>
<td>11</td>
<td>68.57</td>
</tr>
<tr>
<td>Control</td>
<td>35</td>
<td>3</td>
<td>12</td>
<td>20</td>
<td>42.86</td>
</tr>
</tbody>
</table>

2.3 Comparison on adverse reaction between the two groups
Bone marrow inhibition rate in treatment group was 22.86% (8/35) and 65.71% (23/35) in control group. Comparison between the two groups had significant difference ($P < 0.05$). Incidence of gastrointestinal reaction in treatment group was 48.57% (17/35) without any degree III~IV reaction. The same incidence in control group was 68.57% (24/35) with degree III~IV reaction in
2 cases, accounting for 5.71%. Comparison between the two groups had significant difference \((P<0.05)\), see Tab. 3.

<table>
<thead>
<tr>
<th>Adverse reaction</th>
<th>Treatment group</th>
<th>Control group</th>
<th>(%)</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I</td>
<td>II</td>
<td>III</td>
<td>IV</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>3</td>
<td>4</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>8</td>
<td>9</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Nausea &amp; vomiting</td>
<td>10</td>
<td>7</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Impaired liver/renal function</td>
<td>7</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

3. Discussion

NSCLC is one of the malignant tumors with high morbidity and mortality. Its incidence kept increasing in recent years. Due to the fact that most patients have lost opportunity for operation when diagnosed, only 20% could receive operational treatment but with \(\geq 50\%\) postoperative recurrent or metastatic rate. Although chemotherapy remains the means of first choice in treating advanced lung cancer, it could lead to a series of adverse reaction in patient such as bone marrow inhibition, gastrointestinal reaction, and liver/kidney function impairment, etc. Most patients could tolerate chemotherapy after symptomatic treatment while some cases have to give up the treatment due to intolerance so that therapeutic effect is greatly reduced \(^1\). Therefore during chemotherapy, how to improve control rate of lung cancer, to improve patient survival quality, and to raise tolerance to chemotherapy shall be concerned by clinical doctors. TCM has apparent advantages to be recognized by clinicians in stabilizing lesions, improving patient life quality, and prolonging survival period \(^2\).

Kanglaite Injection (KLT) is a category II anticancer TCM invented and developed by China and a new type of emulsive formulation for intravenous infusion with its active substance coix seed oil extracted from natural coix seed by advanced technology \(^3\text{~}^4\). As a biphasic broad spectrum anticancer medicine, KLT can effectively kill cancer cells while notably enhance body immune function and can reduce adverse reaction caused by chemotherapy and radiation therapy \(^5\text{~}^7\). Its extract coix triglyceride is able to retard cancer cell at \(G_2\text{-}M\) phase, inhibit multiplication of cancer cells, and induce apoptosis. KLT has effect to notably reverse multi-drug resistance of cancer cells and can improve patient immune function and life quality through regulating cell factor levels \(^6\text{~}^8\).
Major treatment objective for advanced lung cancer is to improve life quality. Symptom improvement, enhancement of immune function, and reduction of adverse reaction caused by chemotherapy are important component part in improving life quality. This clinical study shows that Kanglaite Injection has advantage in raising clinical therapeutic efficacy, improving clinical symptoms, improving life quality, relieving bone marrow inhibition, enhancing body immune function, and prolonging survival period. It has reached the objective to enhance effect while reduce toxicity. No apparent adverse reaction was observed during the treatment. KLT is recommended to be applied in treating lung cancer.

[References]


