Analysis on therapeutic effect of Kanglaite Injection in treating advanced hepatic carcinoma

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[Instructive abstract] Methods: Randomized block method was adopted to compare clinical therapeutic effect and toxic side reaction between 67 cases of advanced hepatic carcinoma with Kanglaite Injection plus chemotherapy in treatment group and 70 cases with pure chemotherapy in control group. Results: There was certain difference in objective effect of tumor mass shrinkage between the 2 groups and major clinical symptoms in patients in treatment group got significant improved with survival quality raised, survival period extended and slight toxic side reaction. This gave patients an opportunity for comprehensive treatment.

[Key words] Hepatic carcinoma; Advanced stage; Treatment; Kanglaite Injection

Approved by Ministry of Health, Kanglaite Injection (KLT), a pure TCM formulation manufactured by Zhejiang Kanglaite Pharmaceutical Co., Ltd. had its phase III clinical study in 1996. KLT was used in our department between October 1997 and October 1999 in treating 67 cases with advanced hepatic carcinoma that had lost opportunity of surgical operations. Among all patients peripheral hemogram was not affected. There was neither injury to heart, liver or kidney, nor other apparent toxic and side reactions. KLT could improve hepatic function and had notable synergistic action to interventional or general chemotherapies. It could drastically minimize acute and sub-acute reactions of chemotherapeutic agents and prolonged survival period with satisfactory therapeutic effect. Following is the report.

1. Clinical data
1.1 Patient enrollment
137 cases with advanced hepatic carcinoma were admitted in our department between October 1997~October 1999; Male: 86, female: 53; Age: 23~76 years; Medium age: 55 years; Primary hepatic carcinoma: 52 among whom male 34 and female 17; Hepatic metastasis: 86 among whom male 50 and female 36. All cases were confirmed with ultrasound, CT and MRI examinations; 21 cases confirmed by hepatic puncture cytology and 40 cases by hepatic arteriography. Based on criteria in 1997 for staging and typing of hepatic carcinoma: Stage I: no apparent symptom and physical sign of hepatic carcinoma with diameter of single node less than 5cm in CT and ultrasound examinations; Stage II: symptom and single node diameter more serious than stage I but without evidence of stage III; Stage III: one of apparent cachexia, jaundice, ascites, or distant metastasis. In this study stage II 55 cases and stage III 82 cases.
1.2 Treatment method
Patients were randomly divided into 2 groups: 70 cases in control group with male 36 and female 34; 67 cases in treatment group with male 45 and female 22. Hepatic artery catheterization chemotherapy or infusion pump chemotherapy in name of local chemotherapy was applied for 20 cases in each group. Drugs for local chemotherapy were 5-Fu, CF, ADM or MMC. There were also 17 cases in each group received general chemotherapy with drugs as CF, 5-Fu/FuDR, DDP or ADM. Dosage was calculated on surface area in routine protocol. Part of patients had additional interferon and IL-2. Rest cases in the 2 groups had intravenous PAF protocol. KLT was applied in the whole course in treatment group, 100ml, iv drip, once per day for 20 days as a cycle or 200ml daily x 10 days as a cycle. The longest course lasted consecutive 3 months and the shortest course was 10 days.

1.3 Observation indexes
1) Evaluation criteria for tumor objective therapeutic effect were based on “Guideline for diagnosis & treatment of common malignant tumor-hepatic carcinoma in China” from Ministry of Health: Disappearance of tumor mass ≥ 1 month as CR; Shrinkage of tumor mass ≥ 50% for more than 1 month as PR. 2) Peripheral hemogram/gastro-intestinal reaction was based on WHO’s "Manifestation of antineoplastic drugs in acute & sub-acute toxic and adverse reactions and criteria for staging". 3) Improvement in life quality was based on KPS scoring i.e. to score points before and after each therapeutic course. 20 points increase after treatment against that before treatment is recorded as significant improvement, 10 points increase as improvement, no change as stability, 10 points decrease as reduction. 4) Hepatic function, EKG, cardiac function, and blood sugar were examined before and after the treatment. 5) Body weight 6) Survival period.

1.4 Results
Among 20 cases in treatment group 35% patients completed 4 local chemotherapeutic courses against only 20% in control group. 4 cases in treatment group obtained opportunity for general chemotherapy due to application of 1~4 cycles of KLT. 8 cases in treatment group completed 4 courses and above general chemotherapy as compared to 2 cases in control group. There was certain difference in objective therapeutic effect on shrinkage of tumor mass. In all chemotherapy cases, changes in peripheral hemogram and gastrointestinal reaction in treatment group were apparently lower than those in control group (Table 1) and there was no case with toxic and adverse reaction. Part of patients had their hepatic and renal function improved with different degree. In treatment group 50% of cases had KPS status improved with 7 cases as remarkable improvement and 1 case as reduction. In control group only 6 cases had KPS score improved, accounting for 16%, but 60% of patients had KPS score reduced. Most of cases in treatment group accepted repeated chemotherapy based on cycles. However in control
group, chemotherapy treatment was delayed to certain extent in some cases even after treatment of leucocyte increasing agent. In statistical data, incidence of infection in control group was apparently high due to reduction in KPS score, poor survival quality, and notable inhibition of bone marrow. Compared with treatment group its survival period had significant difference (Table 2).

Table 1 Drug toxic & side reaction in chemotherapy between the two groups

<table>
<thead>
<tr>
<th>Peripheral hemogram</th>
<th>Gastrointestinal reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>(I)</td>
<td>(II)</td>
</tr>
<tr>
<td>Treatment group</td>
<td>13</td>
</tr>
<tr>
<td>Control group</td>
<td>7</td>
</tr>
</tbody>
</table>

$P<0.01$

Table 2 Survival period between the two groups

<table>
<thead>
<tr>
<th>(Month)</th>
<th>3</th>
<th>6</th>
<th>9</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment group (67)</td>
<td>27</td>
<td>25</td>
<td>12</td>
<td>3</td>
</tr>
<tr>
<td>Control Group (70)</td>
<td>43</td>
<td>21</td>
<td>6</td>
<td>0</td>
</tr>
</tbody>
</table>

$P<0.05$

2. Discussion
Kanglaite Injection (KLT), with substance of TCM coix seed that is extracted with high technology, is a biphasic and broad spectrum anticancer new drug for intravenous infusion. KLT can completely improve body immune function, regulate levels of cell factor and protect cell function of normal tissue to reduce toxic and adverse reaction of chemotherapy. In this study, patients using KLT during chemotherapy had apparent reduction in bone marrow inhibition and gastrointestinal reaction. KLT could not only reduce acute and sub-acute reaction of chemotherapeutic agents but improve patient nutrition status in various degrees, regulate appetite, and increase body weight so as to ensure performance of chemotherapy punctually, effectively and smoothly. Confidence of patients is enhanced in “visual efficacy” and their psychological worry about chemotherapy is eliminated. 4 cases in the study obtained chemotherapy opportunity only after applying KLT treatment and this is evidently related to the fact that KLT can effectively inhibit growth and metastasis of cancer cells and both survival quality and survival period get improved. In addition KLT has no toxic and side reaction in heart, liver and kidney and it can improve liver and kidney functions. Action of KLT in synergy and toxicity reduction should be confirmed. To hepatic carcinoma patients who have lost general chemotherapy or radiotherapy, they will have opportunity for better treatment after application of
KLT. At present clinical use of KLT remains an ideal choice with prerequisite that there is no satisfactory treatment method for advanced patient with hepatic carcinoma. Synergistic function of KLT with chemotherapy should be duly confirmed.