Effects of DCRT Combined with Kanglaite Injection on Patients with Advanced Unresectable Hepatocellular Carcinoma

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[Abstract] Objective: To evaluate the effects of TACE and DCRT combined with KLT injection on patients with advanced unresectable hepatocellular carcinoma. Method: There are totally 80 cases of patients with advanced unresectable hepatocellular carcinoma who are divided into treatment group (KLT injection+ radiation therapy+ TACE) and control group (radiation therapy+ TACE) randomly, with each group of 40 cases. Observe changes in clinical symptoms, Karnofsky evaluation, serum biochemical index and recent effect, and analyze clinical data. Results: Clinical symptoms have been improved; hepatocellular carcinoma has been restrained; Karnofsky evaluation has been increased; toxic reaction of radiation therapy and TACE (decrease of WBC and PLT) has been mitigated; treatment group is significantly superior to the control group (P<0.05). However, the difference in decrease of HGB and damage of liver and kidney functions between the two groups is insignificant statistically (P>0.05). Conclusion: Clinical observation shows that KLT injection can significantly improve the life quality of patients with advanced unresectable hepatocellular carcinoma; relieve toxic reaction of radiation therapy and TACE; enhance comprehensive effect. Therefore, it is worth promoting clinically.

[Key words] Hepatocellular carcinoma; KLT injection; DCRT; TACE

HCC is a common cancer in our country, which bears a dormant onset. It is often at middle and later period once found. Due to rapid progress, difficult treatment and bad prognosis, the natural survival rate will be no more than 6 months. Its annual mortality rate ranks second and first¹,² in cancer of city and village respectively. The five-year survival rate will not exceed 5%³. From August 2003 to December 2005, our hospital has observed the clinical effect in treating 80 cases of patients with advanced unresectable hepatocellular carcinoma by combining KLT injection and TACE and three³/dimensional conformal radiotherapy (3DCRT). It is hereby reported as follows.

1. Materials and method

1.1 General data
There are totally 80 cases, where: male patients of 64 cases and female patients of 16 cases,

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with age ranging from 25 to 72. The average age is 51.2. All the cases, after examination of histopathology or liver puncture cytology pathology, are proved to be HCC, and have no chance for operation. In accordance with the classification of UICC in 1997, there are 51 in period III and 29 cases in period IV. The Karnofsky evaluation is above 60 points, with estimated lifetime of more than 3 months. There is no absolute radiation therapy and contraindication for TACE. The 80 patients are randomly divided into two groups: 40 cases for group A—treatment group (traditional Chinese medicine+TACE+3DCRT), where: 31 male patients and 9 female patients with age between 28 and 72. Their average age is 51.5. There are 25 cases in period III and 15 cases in period IV. There are 80 cases in group B—control group (TACE+3DCRT), where: 33 male patients and 7 female patients with age between 25 and 70. Their average age is 50.5. There are 26 cases in period III and 14 cases in period IV.

1.2 Treatment method
Adopt TACE for 2~3 times first, and 3DCRT afterwards. The interval between the last TACE and 3DCRT shall be 3~4 weeks. Adopt Seldinger method for TACE. Carry out hepatic angiography through femoral artery intubation. Select target artery with one-off large doses of shock therapy. Meanwhile, treat by TACE. Chemotherapeutics and dose: FUDR of 10g and PDD of 40~60mg. Prepare fixed device of radiation therapy position for 3DCRT first with vacuum pad. Carry out positioning CT scan of treatment position under fixed phantom. Deliver the CT pictures to the DCRT design system produced by Shanghai Topslane Medical Equipment Co., Ltd.. Doctors and physicists draw target region and dangerous organs. Comprehensively evaluate radiation therapy plan with DVH, isodose picture and cloud picture. Isodoses with optimized index ≥90% surround PTV; the uniformity of PTV dose is 90%~107%; dangerous organs do not exceed the tolerance dose. 3DCRT plan is input into treatment unit by means of floppy disk. Radioactive source is from 6-15MV X linear accelerator manufactured by Siemens with hepatocellular carcinoma dose of 2Gy/ time for 5 times per week. The total dose is 40~60 Gy. Simultaneously apply KLT injection of 200ml once per day for radiation therapy of treatment group by means of intravenous instilling. 20 days is deemed as one course. Repeat at an interval of one month. The method of control group is the same with that of the treatment group except for KLT injection. During TACE and 3DCRT, examine blood routine and liver and kidney functions per week. Observe clinical symptoms, liver and kidney functions, electrocardiogram, chest radiograph and abdomen CT, etc. before treatment.

1.3 Observation indexes
Examine blood routine, liver and kidney functions, AFP, liver B ultrasonic and CT before and after treatment. Reexamine liver and kidney functions, AFP, liver B ultrasonic and CT. Measure focus after the course. Make follow-up visit for all the patients after treatment once every two months.
1.4 Standards for effect
(1) Evaluate as per standard for evaluating solid tumor issued by WHO, it can be divided into:
CR: all visible focuses totally disappear for at least 4 weeks; PR: focuses reduce by over 50% for
at least 4 weeks; NC: focuses reduce by less than 50% or increase by less than 25%; PD:
focuses increase by 25% or there is new focus. (2) In accordance with Karnofsky life quality
valuation: increase >20 points means improvement; increase >10 points means stability;
decrease <10 points means worsening. (3) Toxic reaction and side effect: WHO toxic grading
evaluation is adopted.

1.5 Statistical analysis
SPSS10.0 statistical software is adopted.

2. Results
2.1 CR+PR 40.0% of the treatment group is significantly higher than that of the control group
25.0%. The difference is significant statistically (P<0.05). See details in Tab.1.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>CR</th>
<th>PR</th>
<th>NC</th>
<th>CR+PR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment group</td>
<td>40</td>
<td>1 (0) 15</td>
<td>15 (37.5)</td>
<td>20 (50.0)</td>
<td>16 (40.0)</td>
</tr>
<tr>
<td>Control group</td>
<td>40</td>
<td>0 (0) 10</td>
<td>10 (25.0)</td>
<td>18 (45.0)</td>
<td>10 (25.0)</td>
</tr>
</tbody>
</table>

2.2 By comparing the clinical symptoms before and after treatment, the total improvement rate
of the treatment group is 67.8%; that of the control group is 34.9%. The difference is significant
statistically (P<0.05). See details in Tab.2.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>Hepatalgia</th>
<th>Abdominal distension</th>
<th>Poor appetite</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment group</td>
<td>40</td>
<td>Before treatment</td>
<td>25</td>
<td>16</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>8</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Control group</td>
<td>40</td>
<td>Before treatment</td>
<td>21</td>
<td>18</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>15</td>
<td>13</td>
<td>16</td>
</tr>
</tbody>
</table>
2.3 The difference in improvement rate of the two groups by Karnofsky evaluation is significant statistically ($P<0.05$). See details in Tab.3.

**Tab.3 Comparison for Karnofsky evaluation of the two groups**

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Improvement</th>
<th>Stability</th>
<th>Worsening</th>
<th>Improvement rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>40</td>
<td>17</td>
<td>19</td>
<td>4</td>
<td>42.5</td>
</tr>
<tr>
<td>Control group</td>
<td>40</td>
<td>6</td>
<td>23</td>
<td>11</td>
<td>15.0</td>
</tr>
</tbody>
</table>

2.4 WBC and PLT of the two groups have all decreased after treatment to a varied degree. However, the effect of control group is more significant than that of the treatment ($P<0.05$). The difference in decrease of HGB, damage to kidney function and nausea and vomiting is insignificant statistically ($P>0.05$). See details in Tab.4.

**Tab.4 Comparison for toxic reaction and side effect of the two groups after treatment**

<table>
<thead>
<tr>
<th>Toxic reaction and side effect</th>
<th>Treatment group</th>
<th>Control group</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decrease of WBC</td>
<td>21</td>
<td>17</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Decrease of PLT</td>
<td>34</td>
<td>5</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Decrease of HGB</td>
<td>33</td>
<td>6</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>29</td>
<td>8</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Damage to liver function</td>
<td>30</td>
<td>8</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Damage to kidney function</td>
<td>40</td>
<td>0</td>
<td>-</td>
</tr>
</tbody>
</table>
3. Discussion

3.1 HCC bears high morbidity and bad prognosis. In early period, it is mainly treated by operation cutting. However, most of cases are patients with advanced unresectable hepatocellular carcinoma in treatment. Currently, the operation cutting rate only accounts for about 10%~20%. Non-operation method is of great importance in treating patients with advanced unresectable hepatocellular carcinoma. TACE is the major non-operation method for HCC. However, due to the specialty of HCC blood-supply, blood-supply PVTT and collateral circulation form. Pure TACE is hard to make tumor thanatosis, especially for large tumor block. It is reported that when the diameter of tumor >3cm, the thanatosis for tumor after TACE will be no more than 44% \(^4\). Moreover, the tolerance and liver function of tumor will be damaged after several times of TACE. 3DCRT is irradiated by multiple interfaces or non-interface irradiation field so that stereoscopic distribution of high-dose region consist with the stereoscopic shape of tumor. Therefore, the tumor dose can be significantly improved without increasing the dose of normal liver organ; focuses can be positioned more accurately; the effect of radiation therapy for HCC can be improved. The combination of TACE and 3DCRT can overcome demerits of TACE. By taking the advantages of accurate positioning, position and treatment, unsatisfactory NBCA and (or) tumor edge can be further treated. It is reported \(^5-8\) to have better effect. The effective rate of the treatment group in the study achieves 40.0%, in compliance with report.

3.2 KLT injection extracted from traditional Chinese medicine coix seed with modern scientific approach. It is proved to be a duplex broad-spectrum anti-cancer drug with functions of restraining cancer cells and enhanceing immunity by drug clinical and basic study. Function mechanism: cut G2 in cell cycle and cells in M, and help reduce cells in S period so as to decrease mitosis and DNA synthesis; restrain growth of tumor cells; and apoptosis\(^9\) of affected celles. On the other hand, by activating NK cell and IL-2, KLT injection boosts phagocytic function of phagocyte and growth of SP to improve immunity and nonspecific disease-resistant ability\(^9\).

The study compare treatment of patients with advanced unresectable hepatocellular carcinoma between methods of combining KLT injection and TACE+3DCRT (treatment group) and TACE+3DCRT (control group). The tumor in treatment group has reduced CR+PR40.0%, significantly higher than that of the control group (25.0%). The difference is significant statistically \((P<0.05)\). It may be related to the reported hypersensitivity \(^10\) and tumor apoptosis\(^11\) of KLT injection. Meanwhile, it is observed that KLT injection is better in relieving clinical symptoms (hepatalgia, abdominal distension, poor appetite and weak) than that of the control group \((P<0.05)\). Karnofsky evaluation of the treatment group has been improved more than that of the control group \((P<0.05)\). Additionally, the result shows that the treatment group can
significantly reduce toxic reaction of chemotherapeutics. Though the peripheral blood of patients in the two groups have all decreased to a varied degree (mainly in WBC and PLT), the treatment group is lower than that of the control group. The difference is significant statistically ($P<0.05$). It reveals that KLT injection may protect the marrow of patients with TACE and radiation therapy, especially in WBC and PLT. The difference in decrease of HGB, damage to liver function, nausea and vomiting is insignificant statistically ($P>0.05$). To conclude, TACE and DCRT combined with Kanglaite injection can significantly improve the effect of patients with advanced unresectable hepatocellular carcinoma; improve clinical symptoms; reduce toxic reaction and side effect of TACE and DCRT. Therefore, it is worth promoting.

Reference


