Effects of transcatheter arterial chemoembolization combined with Kanglaite Injection on patients with advanced unresectable hepatocellular carcinoma

Lu Hao, Zhou Jiansheng, Xu Xun, Deng Nan. Dept. of Medicine, Huainan Union University, Huainan 232001, Anhui; Dept. of Oncology, the Red Cross Chaoyang Hospital of Huainan, China

[Abstract] Objective: To evaluate effects of transcatheter arterial chemoembolization (TACE) combined with Kanglaite injection on patients with advanced unresectable hepatocellular carcinoma. Methods: Forty-eight patients suffered with hepatocellular carcinoma (HCC) were randomly distributed into two groups. In treatment group, 24 patients received KLT after TACE, and 24 patients in the control group were treated with TACE simply. The serum α-fetal protein (AFP) was detected by radio-immunological technology. At the same time, the observed indexes including the changes of symptoms and signs, side effects, ultra-sound, CT and liver or kidney, kidney functions were considered. Results: In the treatment group, ten cases were evaluated as 10 CR, 8 PR, 5 NC and 1 PD, compared with the control group (CR, PR, NC and PD were 3, 10, 5 and 4 cases respectively). The effects response rate (CR+PR) was 75% in the treatment group were superior to those in the control group 54.17% (P < 0.05). AFP in the treatment group decreased more significantly than that in the control group (P < 0.05). Conclusion: The treatment for HCC combined KLT with TACE could inactivate the tumor cells effectively. It is an effective method for HCC patients who have lost the surgical chance.

[Key words] Hepatocellular carcinoma, Kanglaite injection, chemotherapy, embolization

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 first in cancer of city and village respectively. The five-year survival rate will not exceed 5% [3]. From August 2001 to December 2003, we have acquired good clinical effect in treating patients with advanced unresectable hepatocellular carcinoma by combining KLT injection and TACE. It is hereby reported as follows.

1. Date and method
1.1 Clinical data
In 48 cases, there are 37 male patients and 11 female patients; with age ranging from 21 to 69. The average age is 43.7. All the cases, after clinical symptoms, sign, AFP, B ultrasonic, CT, hepatic angiography and liver puncture cytology pathology, are proved to be HCC, and comply with Regulations for Diagnosis and Treatment of Common Cancers in China. Pathological types:
9 cases of massive type, 24 cases of node and 5 cases of diffuse type. Clinical types: 12 cases of period I, 25 cases of period II and 11 cases of period III. Liver function grading: 23 cases of grade A, 19 cases of grade B and 6 cases of grade C. There are 36 cases of positive AFP and 48 cases of positive GGT-II. There are 8 cases of which the diameters of TM I>10cm, 21 cases of which the diameters are 5~10cm and 19 cases of which the diameters<5cm. The patients all have no chances for operation. Their Karnofsky evaluation ≥50 points. Estimated lifetime≥3 months. They are randomly divided into two groups. Treatment group: 19 cases of male patients and 5 cases of female patients; control group: 18 cases of male patients and 6 cases of female patients. After statistical treatment, there is no significance for the difference between the clinical data of the two groups (p>0.05). It is comparable.

1.2 Method
Adopt Seldinger technology to intubate into proper hepatic artery through skin biopsy femoral artery for TACE. Angiography succeeds. Determine blood-supply artery. Orderly inject MMC of 10mg/m², 5-FU of 1000mg/m² and cis-platinum of 40mg/m² to carry out chemotherapy. Use 40% iodized oil for NBCA. Inject with the mixture of MMC and iodized oil of 10ml and gelatin sponge fragments. Carry out the second TACE every 4~6 weeks. Use KLT injection of 200ml for 24 cases of patients in the treatment group after operation per day for continuously 21d. Carry out the next course every 3~5d. Slowly instill for the first time with speed of 20 drops/ min for the first 10 min; continuously increase after 20min. Control the speed at 40~60 drops/ min.

1.3 Observation indexes
Collect venous blood from the external elbow one week before and after treatment to examine blood routine, liver and kidney functions, AFP and liver B ultrasonic. Reexamine WBC, 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. Calculate survival rate by means of Kaplan-Meier method.

1.4 Statistical analysis
Express data with $\overline{x} \pm s$; test with $\chi^2$ and $t$.

2 Results
2.1 Standards for effect
As per the statistical evaluation standard issued by the WHO in 1981, the effect can be divided into CR, PR, SD and PD. Toxic reaction and side effect ranges from 0 to IV\[4\]. In accordance with Karnofsky life quality evaluation, >10 points means improvement; <10 points means worsening;

increase or worsening <10 points means stability. Make a detailed record for each toxic reaction and side effect during treatment.

### 2.2 Recent effect

Two months later, among 24 cases of treatment group, there are 10 cases of CR, 8 cases of PR, 5 cases of SD and 1 case of PD, boasting effective rate of 75.00% and progressive rate of 4.11%; among 24 cases of control group, there are 3 cases of CR, 10 cases of PR, 5 cases of SD and 4 case of PD, boasting effective rate of 54.17% and progressive rate of 16.67%. There is statistical significance for the difference of effective rate and progressive rate of the two groups \((P<0.05)\).

### 2.3 Lifetime with tumor

Till December 2005, the average lifetime for the two groups with tumor: \((22±11)\) months for the treatment group, with the longest lifetime of 38 months; \((22±6)\) months for the control group. There is statistical significance for the difference of survival rate of the two groups \((P<0.05)\). See details in Tab.1.

### Tab.1 Comparison for survival rates of cancer patients between the two groups (%)

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of cases</th>
<th>Survival rate 6 months</th>
<th>Survival rate 12 months</th>
<th>Survival rate 18 months</th>
<th>Survival rate 24 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment group</td>
<td>24</td>
<td>91.7(22/24)</td>
<td>62.5(15/24)</td>
<td>37.5(9/24)*</td>
<td>16.7(4/24)*</td>
</tr>
<tr>
<td>Control group</td>
<td>24</td>
<td>79.2(19/24)</td>
<td>50(12/24)</td>
<td>12.5(3/24)</td>
<td>0(0/24)</td>
</tr>
</tbody>
</table>

Note: compared with control group, * \(P<0.05\)

### 2.4 Changes in serum biochemical index

AFP of the two groups has all decreased to a varied degree after treatment. However, it is more significant for that of the treatment group. The treatment effect is more significant than that of the control group before treatment. See details in Tab.2.

### Tab.2. Comparison for AFP of cancer patients between the two groups before and after treatment \((\bar{x} ± s)\)

<table>
<thead>
<tr>
<th>Group</th>
<th>Item</th>
<th>No. of cases</th>
<th>AFP(μg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment group</td>
<td>Before treatment</td>
<td>24</td>
<td>1427±103</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>24</td>
<td>721±98*(^{△})</td>
</tr>
<tr>
<td>Control group</td>
<td>Before treatment</td>
<td>24</td>
<td>1432±124</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>24</td>
<td>1087±113*(^{△})</td>
</tr>
</tbody>
</table>
Note: compared with that of the group before treatment, *\( P<0.05 \); compared with that of two groups after treatment, *\( ^{\Delta} P<0.01 \).

### 2.5 Life quality evaluation

The improvement in treatment group accounts for 59.4% while the worsening accounts for 7.7%; the improvement in control group accounts for 27.3% while the worsening accounts for 39.7%. Compare the improvement rate and worsening rate of the life quality between the two groups, the difference is significant statistically (\( P<0.05 \)). See details in Tab.3.

### 2.6 Toxic reaction and side effect

The numbers of WBC of the two groups have all decreased after treatment. Therefore, the difference is insignificant statistically (\( P>0.05 \)). There are 19 cases (79.2%) and 20 cases (83.3%) in the treatment and control group that have I-IV gastrointestinal tract reaction respectively. Therefore, the difference is insignificant statistically (\( P>0.05 \)).

**Tab.3 Comparison for life quality evaluation of cancer patients between the two groups [case (%)]**

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of cases</th>
<th>Improvement</th>
<th>Stability</th>
<th>Worsening</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment group</td>
<td>24</td>
<td>14(58.4)*</td>
<td>8(33.3)</td>
<td>2(8.3)*</td>
</tr>
<tr>
<td>Control group</td>
<td>24</td>
<td>8(33.3)</td>
<td>7(29.2)</td>
<td>9(37.5)</td>
</tr>
</tbody>
</table>

Note: compared with control group, *\( P<0.05 \)

### 3. Discussion

TACE for clinical treatment can display the dual function of chemotherapy and NBCA, which is a non-operation method with affirmative effect that is widely applied in curing HCC currently. It is the top choice for treating cancer without resection. Pathology section reveals that TACE may effectively destroy chief tumor of liver, sub-focus and PVTT, boasting significant recent effect [6]. However, due to the specialty of HCC blood-supply, blood-supply PVTT and collateral circulation form. Pure TACE is hard to make tumor thanatosis. There will be residual cancer cells even it is repeated for several times, boasting insignificant long-term effect [7]. The main ingredient of KLT injection is TG, which is an effective component extracted from traditional Chinese medicine coix seed. It has the function of destroying tumor cells and enhancing immunity, which mainly functions in G2/ m period to hinder mitosis and growth of tumor cells and lead to apoptosis. It is reported that [8] KLT injection may directly induce apoptosis of hepatocellular carcinoma cells, boasting apoptosis rate of 44.1%. The generation of new vessels is one of the critical conditions for quick growth and transfer of tumor. Restraint of the generation of tumor vessel is a feasible
approach for treating tumor. KLT injection is proved to exert restraint function for the generation of tumor vessel. The study shows that the combination of KLT injection with TACE can significantly narrow the cancer block. Its effect is superior to single use of TACE. It reveals that the two have synergy. Liver artery NBCA kills the majority of central cancer tissue of its blood-supply while the surrounding ones supplied by portal vein can be killed by KLT injection. Radiation therapy and chemotherapy will replaced, which may exert influence on different sub-group cells in one tumor. Moreover arterial chemotherapy synchronizes the cycle of tumor cells, reduces the resistance. It is in favor of killing residual cells for KLT injection. Combining chemotherapy can significantly improve the survival rate of patients while insignificant in toxic reaction and side effect. The analysis shows that the adverse reaction of patients is not incurred by KLT injection but by TACE.

Reference


