Effect of TACE on liver function indexes in patients with primary liver cancer

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ABSTRACT
Objective: To explore effect of transcatheter arterial chemoembolization (TACE) on coagulation function, liver function and liver fibrosis index in patients with primary liver cancer.
Method: 118 cases of patients with primary liver cancer as observation group and 100 cases of persons with health check-up as control group. After treatment for one week with TACE, compared coagulation function (APTT, PT and FIB), liver function (TBIL, DBIL, IBIL, ALB and ALT) and liver fibrosis indexes (LN, HA, PⅢP and PⅣC) in control group and observation group before and after treatment.
Results: Levels of APTT, PT in observation group after treatment were higher than before treatment in group, moreover were lower than the control group, there was statistical significant difference, level of FIB after treatment in observation group was significantly lower than before treatment and obviously higher than control group, difference was significant; Compared with observation group before treatment, levels of TBIL, DBIL, IBIL, ALT increased dramatically, ALB level decreased obviously after treatment, moreover levels of TBIL, DBIL, IBIL, ALT in observation group before and after treatment were significant higher and ALB level was lower than that in control group, difference was significant; levels of LN, HA, PⅢP and PⅣC in observation group before and after treatment exceeded significantly in control group, levels of LN, HA, PⅢP and PⅣC after treatment was higher when compared with before treatment, the difference comparison was statistical significant.
Conclusion: It could effectively improve coagulation function through treating primary liver cancer patients with TACE, however chemotherapy drug and embolotherapy would damage liver cells of patients and affect the liver function and liver fibrosis at some extent.

1. Introduction

Primary liver cancer was one of the common and high lethality cancers in clinic. Surgical operation was one of main means, however related research found that there was only 10%-15% patients who could be treated with Surgery in our country.[1,2]. Efficacy of hepatic arterial chemoembolization (TACE) in primary liver cancer was significant, therefore it was the first choice of patients who were not suitable for operative treatment[3,4]. Liver was the primary site where compounded blood coagulation factors.

If liver was damaged, coagulation function of patients would be dysfunction. Liver function and liver fibrosis index were important indexes that evaluated liver lesion and outcome. In order to define clinical efficacy of TACE in patients with primary liver cancer, this study researched from three aspects: coagulation function, liver function and liver fibrosis. The detail was following.

2 Research object and method
2.1 General data

Selected 118 cases of patients with primary liver cancer who were admitted into our hospital from April 2015 to March 2017 as research object, all patients were diagnosed through pathological, clinical diagnosis, iconography (B ultrasound, CT or MRI) and
Dosage of lipiodol was determined according to tumor diameter and vascular condition. The maximal dose was not above 30 mL. As for patients whose blood-supply artery thickened obviously, used proper gelfoam particles to embolism. All of the tumor blood-supply vascular should be embolized, DSA arteriography was used for detect tumor vascular embolization after operation, removed catheter. Postoperative management: electrocardiograph monitoring was not less than 6 hours, intravenous drip of antibiotic for 3 d to prevent infection, took orally analgesic and liver protection, vomiting stopping.

2.3. Observation indexes

Extracted fasting peripheral venous blood when the control group was health check-up and observation group was before and after treatment (one week after operation) to measure coagulation function, liver function and liver fibrosis index in patients. Prothrombin time (PT), activated partial thromboplastin time (APTT) and fibrinogen (FIB) were measured by French Stago Evolution coagulometer, operation was in strict accordance with introduction; Liver function indexes including total bilirubin (TBIL), direct bilirubin (DBIL), indirect bilirubin (IBIL), albumin (ALB), alanine aminotransferase (ALT); Laminin (LN), hyaluronic acid (HA), III procollagen (PIIIP) and collagen type IV (IVC) and other indexes were detected by radioimmunoassay.

2.4 Statistical method

Statistical Software SPSS 17.0 was used for research data processing and analyzing, all the indexes were in accord with normal distribution, representing methods was (±x), t-test was applied to comparison of two sample averages intra-group before and after treatment and interblock, P<0.05 indicated the difference was statistical significant.

3. Results

3.1. Comparison of coagulation function in two groups

Levels of APTT, PT and PIB in observation group before and after treatment were shown in Table 1. In observation group, levels of APTT, PT and PIB were (30.43±5.74) s, (13.16±0.81) s and (3.24±1.18) g/L respectively after treatment, compared with before treatment, APTT and PT levels significantly decreased and FIB increased dramatically, the difference was significant (P<0.05); FIB level was lower and APTT, PT levels was higher in observation group before and after treatment than control group, difference comparison was statistical significant (P<0.05).

<table>
<thead>
<tr>
<th>Table 1.</th>
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<tbody>
<tr>
<td>Comparison of coagulation function in two groups.</td>
</tr>
<tr>
<td>Group</td>
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<tr>
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</tr>
<tr>
<td>Control group</td>
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<td>Observation group</td>
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</tbody>
</table>

Note: Compared with control group, *P<0.05; compared with observation group before treatment, **P<0.05.
Primary liver cancer was one of common malignant tumor, with high grade malignancy and fast rate of progress, its lethality was up to third in related tumor death[7]. Due to liver cancer lacked specific clinical feature in early phase and difficult to find, once a definite diagnose was made it had been in middle and advanced stage[8], therefore, patients with primary liver cancer in our country almost accounted for 55% of liver cancer in world. Pathogenesis of this disease was complicated, it was considered that polygenes, multi-factors, multi-mutation together led to this results[9,10]. The relative researches have demonstrated that HBV and HCV were important factors resulted in liver cancer. In primary liver cancer, almost 1/3 patients with history of chronic hepatitis disease, 80% patients had factors resulted in liver cancer. In primary liver cancer, almost 1/3 patients with history of chronic hepatitis disease, 80% patients had factors resulted in liver cancer.

### Table 2
Comparison of liver function indexes level in two groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>Case</th>
<th>Treatment time</th>
<th>TBIL (µmol/L)</th>
<th>DBIL (µmol/L)</th>
<th>IBIL (µmol/L)</th>
<th>ALB (g/L)</th>
<th>ALT (U/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>100</td>
<td>Before treatment</td>
<td>15.42±2.09</td>
<td>3.51±0.83</td>
<td>11.24±1.07</td>
<td>40.19±1.80</td>
<td>20.07±3.22</td>
</tr>
<tr>
<td>Observation group</td>
<td>118</td>
<td>Before treatment</td>
<td>21.82±8.42*</td>
<td>8.09±3.67*</td>
<td>14.83±4.87*</td>
<td>35.19±1.22*</td>
<td>39.42±7.71*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>35.12±13.35**</td>
<td>15.36±6.71**</td>
<td>20.72±7.11**</td>
<td>31.28±2.63**</td>
<td>132.26±33.49**</td>
</tr>
</tbody>
</table>

Note: Compared with control group, *P<0.05; compared with observation group before treatment, **P<0.05.

### Table 3
Comparison of serum liver fibrosis indexes level in two groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>Case</th>
<th>Treatment time</th>
<th>LN (µg/L)</th>
<th>HA (mg/L)</th>
<th>PIIIP (µmol/L)</th>
<th>IVC (µg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>100</td>
<td>Before treatment</td>
<td>115.63±17.29</td>
<td>72.48±15.06</td>
<td>107.25±11.53</td>
<td>69.15±18.26</td>
</tr>
<tr>
<td>Observation group</td>
<td>118</td>
<td>Before treatment</td>
<td>161.34±24.03*</td>
<td>236.41±34.82*</td>
<td>264.50±18.82*</td>
<td>88.15±15.02*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>194.47±11.98*</td>
<td>269.85±21.06*</td>
<td>307.33±20.27*</td>
<td>101.67±18.85*</td>
</tr>
</tbody>
</table>

Note: Compared with control group, *P<0.05; compared with observation group before treatment, **P<0.05.

### 3.2. Comparison of liver function indexes in two groups

TBIL, DBIL, IBIL, ALT levels were (35.12±13.35) µmol/L, (15.36±6.71) µmol/L, (20.72±7.11) µmol/L and (132.26±33.49) U/L respectively in observation group after treatment, significantly exceeded intra-group before treatment and control group, there was statistical significant difference (P<0.05); after treatment ALB level was (31.28±2.63) g/L in observation group was significantly lower than before treatment and control group, difference comparison was statistically significant (P<0.05). As shown in Table 2.

### 3.3. Comparison of serum liver fibrosis indexes level in two groups

Levels of LN, HA, PIIIP and IVC were (194.47±11.98) µg/L, (269.85±21.06) mg/L, (307.33±20.27) µg/L and (101.67±18.85) µg/L respectively in observation group after treatment, dramatically exceeded intra-group before treatment and control group, there was statistical significant difference (P<0.05). As shown in Table 3.

### 4. Discussion

Primary liver cancer was one of common malignant tumor, with high grade malignancy and fast rate of progress, its lethality was up to third in related tumor death[7]. Due to liver cancer lacked specific clinical feature in early phase and difficult to find, once a definite diagnose was made it had been in middle and advanced stage[8], therefore, patients with primary liver cancer in our country almost accounted for 55% of liver cancer in world. Pathogenesis of this disease was complicated, it was considered that polygenes, multi-factors, multi-mutation together led to this results[9,10]. The relative researches have demonstrated that HBV and HCV were important factors resulted in liver cancer. In primary liver cancer, almost 1/3 patients with history of chronic hepatitis disease, 80% patients had history of liver cirrhosis[11,12]. The outcome of primary liver cancer was badly, recurrence rate of surgery was extremely high and easily caused hepatic failure, surgical risk was high. TACE was a method that embolized artery of hepatic tumor tissue blocking arterial blood supply and infused chemotherapy drugs to inhibit and kill hepatic tumor cell, hepatic tumor volume shrank obviously and AFP level decreased significantly, the efficacy was reliable. However, some researches pointed that patients appeared feeble, jaundice, ascites and other clinical features after TACE, this affected liver function at some extent[13,14]. This study was aimed to explore effect of TACE on coagulation function, liver function and liver fibrosis index in patients with primary liver cancer.

In normal body physiologic hemostatic system, coagulation system and fibrinolytic system interacted with each other, being in dynamic equilibrium, to maintain normal blood circulation[15]. This study detected coagulation function index of patients with primary liver cancer and healthy persons, results revealed that the levels of APTT, PT was higher and lower level FIB in primary liver cancer than in healthy people. The reason might be that in addition to coagulation dysfunction, patients with primary liver cancer also had hypercoagulability of malignant tumor, large necrosis of tumor cell would release multiple cytokines which activated coagulation system and resulted in coagulation dysfunction[16]. After interventional therapy, levels of APTT, PT and PIB in patients were improved, however still abnormal when compared with normal people. It might be related to that hepatic tumor cell was inhibited, level of coagulant secretions decreased, compound of coagulation factor was greater than consumption, regeneration of hepatic normal tissue and so on[17,18]. After treatment, compared with healthy people, coagulation function was still abnormal. It may be due to that interventional therapy and chemotherapy, embolization drugs caused hepatocyte damaged, coupled with a large number of apoptotic tumor cell that was able to stimulate tissue release massive activated factors and then activated coagulation function, eventually resulted in the extension. While FIB level was lower than normal people, this was mainly related to liver cirrhosis in patients with liver cancer. These results revealed that coagulation function index could serve as the effective index of TACE efficacy and outcome in patients with primary liver cancer.

Some related researches indicated that TACE therapy would affect hepatic function at different extent[19]. It was found that levels of TBIL, DBIL, IBIL and ALT in patients were dramatically higher than normal people, ALB level was lower than healthy people, indicating hepatic dysfunction in patients through comparing hepatic function between patients with healthy people. However, after interventional therapy, all levels of TBIL, DBIL, IBIL and ALT were increased at different extent, ALB level was decreased, it might due to that most chemotherapy drugs could enter target tissue to perform lethal function in interventional therapy process, however, there existed a little of drugs that entered healthy tissue around tumor and led to lesion; embolization caused hypoxia of periphery healthy tissues and emulsion of ultra-fluid lipiodol and chemotherapy drug...
sediment in healthy tissues and without removing in short time, these would result in hypoxia, ischemia of liver tissue, at last damaged hepatic cell[20,21].

Liver cirrhosis and infection were important risk factors that caused liver cancer genesis. Hepatic fibrosis was the pathogenic basis of liver dysfunction. Four items of serum hepatic fibrosis (LN, HA, PIIIP and IVC) were recognized as critical indexes that evaluated severity of liver fibrosis and liver cirrhosis, it also indicated the lesion of liver function[22]. This study manifested that LN, HA, PIIIP and IVC in patients were higher than in healthy people at different lesion of liver function severity of liver fibrosis and liver cirrhosis, it also indicated the PIIIP and IVC) were recognized as critical indexes that evaluated liver dysfunction. Four items of serum hepatic fibrosis (LN, HA, PIIIP and IVC) were recognized as critical indexes that evaluated liver dysfunction.

Due to liver cancer patients always with liver cirrhosis and hepatic dysfunction, chemotherapy drugs could not only kill target tissue and cells but also kill periphery normal cell. Almost all of the chemotherapy drugs could promote apoptosis, and a large dose of chemotherapy drugs could enhance hepatic cell damaged (heaven non-tumorous hepatic cell apoptosis), aggravated liver cirrhosis severity. Generally, using superselective intubation could properly reduce the dose of chemotherapy drugs and decrease liver function lesion[24].

In conclusion, TACE treatment in patients with primary liver cancer could improve effectively coagulation function however it also affected liver function and liver fibrosis index. Consequently, in practical clinical application, all kinds of factors should be considered. The scheme which could treat liver cancer validly and affected liver function mildly was selected, in order to enhance efficacy and outcome of liver cancer.

Reference


