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Feasibility of Transcatheter Arterial Chemoembolization Combined with Microwave Ablation for Treating Primary Large Hepatocellular Carcinoma

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ABSTRACT

Objective: To explore the feasibility of transcatheter arterial chemoembolization (TACE) combined with microwave ablation for treating primary large hepatocellular carcinoma (HCC).

Methods: Thirty patients with primary large HCC receiving TACE (control group) and another thirty cases undergoing TACE combined with microwave ablation (observation group) in our hospital from January 2015 to January 2017 were selected, and the clinical data of the two groups of patients were retrospectively analyzed. The objective response rate, serum tumor markers, incidence rates of adverse reactions, long-term survival rate, long-term recurrence rate and long-term quality-of-life score were compared between the two groups.

Results: The objective response rate was 66.67% in observation group, which was higher than that in control group (40.00%) (P<0.05). The levels of serum carcinoembryonic antigen, alpha fetoprotein and carbohydrate antigen 125 declined in both groups after treatment compared with those before treatment, and they were lower in observation group than those in control group (P<0.05). There were no statistically significant differences in the incidence rates of adverse reactions such as nausea and vomiting, leucopenia, thrombocytopenia, anemia and transaminase elevation between the two groups (P>0.05). After 1 and 3 years of follow-up, observation group had higher survival rate and quality-of-life score but lower recurrence rate than those of control group (P<0.05).

Conclusion: The combined application of TACE and microwave ablation to patients with primary large HCC can augment the short-term therapeutic effects, regulate the expressions of serum tumor markers and reduce adverse reactions. This method can raise the long-term survival rate, decrease recurrence and enhance the long-term quality of life of surviving patients.

KEYWORDS: primary large hepatocellular carcinoma; transcatheter arterial chemoembolization; microwave ablation

INTRODUCTION

The fourth-largest among malicious tumours in China is mainly liver cancer, a common type of malignant tumour. Patients at relatively high risk of death with primary liver cancer, and the disease poses a major threat to the life and health of most people[1-3]. In particular, the risk of death is even greater from primary large hepatocellular carcinoma (HCC) of > 5 cm in tumour. The TACE is a major therapeutic approach for primary liver cancer in the clinic and intervening therapy may delay tumour progression to a certain degree[4,5]. Microwave TACE-based ablation can improve liver cancer treatment[6]. The follow-up was a retrospective analysis in our hospital between Janus 2015 and January 2017 in 60 patients with main HCC, who were treated with TACE and TACE, combined with the ablation of microwaves to

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evaluate TACE in combination with the microwave ablation on primary major HCC.

MATERIALS AND METHODS

Baseline clinical data

In the period from January 2015 to January 2017, 30 patients with primary major HCC received TACE (control group) and another 30 TaCE-treated patients were selected and the clinical data analysed retrospectively. There are 19 men and eleven women aged between 30 and 85, with an average of 56.67 ± 13.24 years in the observation group. In the clinical phase, 7 Phase II, 14 Phase III and 9 Phase IV have been present. The control group consisted of 18 men and 12 women between the ages of 29 to 86 and the average number of (56.23 ± 12.47). Stage II consisted of six patients, Stage III of 16, and Stage IV of 8 patients. Both groups compared gender, age and clinical conditions (P>0.05).

Inclusion criteria: (1) Patients diagnosed as primary large HCC through imaging examination, clinical symptom observation and pathological diagnosis, with a tumor diameter >5 cm, (2) those with indications for TACE, (3) those who were informed of and agreed with the treatment protocol, and signed the informed consent, and (4) those with completely preserved clinical data.

Exclusion criteria: (1) Patients complicated with severe infections, (2) those complicated with other malignant tumors, (3) those with a past history of liver surgery, (4) those with mental disorders, or (5) those with incomplete clinical data.

Methods

TACE was performed for control group. With the patients in the supine position, puncture and catheterization were performed on the right femoral artery. A catheter was inserted into the target feeding artery of liver tumor, through which contrast agent was injected to determine the location of the liver tumor. Furthermore, gelatin sponge particles and lipiodol were used as the embolic agents and the emulsion, respectively, and injected to embolize the hepatic artery.

The patients in observation group were subjected to TACE combined with microwave ablation, during which the procedures of TACE were identical to those in control group, and microwave ablation was implemented at 1 week after TACE. Local infiltration anesthesia was applied to the patients in the supine position, ultrasound-guided puncture was performed, and two ablation needles were placed in the central region of the liver tumor. Then microwave generator (ablation power: 55 W) was operated for 10-12 min.

Observation indices

The objective response rate, serum tumour markers and adverse reaction incidence rates were compared among both groups, long-term survival rates, long-term recurrence rates and long-term quality-of - life score.

The assessment of short-term effectiveness was carried out as follows[7]: (1) Complete remission (CR): the tumour foci was totally removed without new foci. (2) Partial remission (PR): The tumour 's concentration has fallen by 50%. (3) Stable disease (SD): the tumour focus decreased by under 50% or increased by under 25%. (4) Advanced Disease (PD): a 25% increase or a new centre of attention in the tumour. Response rate target: CR + PR.

Carcinoembryonic antigen, alpha fetoprotein and carbohydrate antigen 125 were part of the serum tumour markers.

Leucopenia, thrombocytopenia, and anaemia were the most common adverse reactions to adverse reactions, nausea and vomiting.

Long-term survival and recurrence rates were reported after 1 and 3 years of follow-up.

As regards the long-term quality-of - life score[8], the Quality of Life Brief Version of the World Health Organization was used to assess surviving patients in the first and third years of follow-up. The scale consisted of 4 dimensions, namely physiology, psychology, environment and social relationship, with 0-100 points for each dimension, and the score was directly proportional to the quality of life.

Statistical analysis

The statistical analysis was done using SPSS 26.0 software. A^2 test was used to examine numerical data (n) and t-test the quantitative data). P<0.05 indicated statistically significant differences.

RESULTS

Objective response rate

The objective response rate was higher in the observation group than in the control group. (66.67% *vs.* 40.00%) (P<0.05) (Table 1).

Levels of serum tumor markers

Carcinoembryonic Serum antigen, alpha fetoprotein, and carbohydrate antigene 125 declined compared to pre-treatment in both treatment groups, and were smaller in the observer group than in P<0.05 (Table 2).

Table 1. **Objective response rates [n (%)]**

Group	n	CR	PR	SD	PD	Objective response rate
Control	30	4 (13.33)	8 (26.67)	14 (46.67)	4 (13.33)	12 (40.00)
Observation	30	7 (23.33)	13 (43.33)	9 (30.00)	1 (3.33)	20 (66.67) *

*P<0.05 *vs.* control group.

Table 2. **Levels of serum tumor markers ($\bar{x} \pm s$)**

Group	Time	Carcinoembryonic antigen (ng/mL)	Alpha fetoprotein (ng/mL)	Carbohydrate antigen 125 (U/mL)
Control (n=30)	Before treatment	32.45±6.23	35.06±6.94	53.76±12.37
	After treatment	25.19±4.51#	27.48±5.13#	39.53±9.64#
Observation (n=30)	Before treatment	32.17±6.29	34.81±6.87	53.42±12.83
	After treatment	20.38±3.95#*	21.15±4.56#*	29.27±7.05#*

#P<0.05 *vs.* before treatment within the group, *P<0.05 *vs.* control group.

Incidence of adverse reactions

There were no statistically significant differences in the incidence rates of such adverse reactions as nausea and vomiting, leukopenia, thrombocytopenia, anaemia and transaminase elevation between the observation group and the control group (P>0.05) (Table 3).

Table 3. **Incidence rates of adverse reactions [n (%)]**

Group	n	Nausea and vomiting	Leucopenia	Thrombocytopenia	Anemia
Control	30	5 (16.67)	4 (13.33)	4 (13.33)	1 (3.33)
Observation	30	6 (20.00)	3 (10.00)	2 (6.67)	3 (10.00)

Long-term survival rate and recurrence rate

Observation group had a higher survival rate but a lower recurrence rate than those of control group after 1 and 3 years of follow-up (P<0.05) (Table 4).

Table 4. **Long-term survival rate and recurrence rate [n (%)]**

Group	n	1-year survival rate	3-year survival rate	1-year recurrence rate	3-year recurrence rate
Control	30	24 (83.33)	18 (60.00)	7 (23.33)	9 (30.00)
Observation	30	29 (96.67) *	25 (83.33) *	1 (3.33) *	2 (6.67) *

*P<0.05 *vs.* control group.

Quality-of-life score

The quality-of - life score for surviving patients was increased in the follow-up observation group for 1 and 3 years compared to that for the control group (P<0.05) (Table 5).

Table 5. **Quality-of-life scores of patients with long-term survival ($\bar{x} \pm s$, point)**

Group	Time (n)	Physiology	Psychology	Environment	Social relation
Control	1 year (n=24)	78.94±6.51	77.28±6.32	77.95±6.19	78.46±6.63
	3 years (n=18)	74.53±6.42	73.35±6.90	73.08±6.21	73.37±6.30
Observation	1 year (n=29)	86.47±7.69	84.56±7.21	85.29±7.57	85.96±7.24
	3 years (n=25)	82.18±7.75	81.46±8.13	81.65±7.94	81.50±8.09

*P<0.05 *vs.* control group.

DISCUSSION

Primary liver cancer is one of the most common malignant diseases in China, and its symptoms, including incipient hepatic pain, are characterised by high morbidity and mortality rates[9]. The malignancy of tumours in primary liver cancer patients is early and with progression of disease and invasive tissues, the volume of the tumour gradually increases and seriously endangers the safety of patients[10]. Larger than other types of liver cancer, the primary major HCC refer to cancer of the liver with a diameter of > 5 cm, with a poorer prognosis amongst the patients with the condition[11].

Therefore, great attention should be paid to the clinical treatment of primary large HCC. Certain therapeutic effects of TACE and microwave ablation on primary liver cancer have been obtained in recent years. As an interventional therapy, TACE embolizes the hepatic artery mainly *via* puncture,

catheterization and injection of gelatin sponge particles and lipiodol into the hepatic artery. In this way, it can block the blood supply to the liver tumor by the hepatic artery and stimulate the gradual atrophy of the liver tumor, thus decreasing the tumor volume and delaying tumor progression [12]. In microwave ablation, also an interventional therapy, the liver tumor is primarily oscillated by microwave current, during which heat is generated by friction. Moreover, the thermal tolerance of tumor tissues is weaker than that of normal tissues, and the tumor tissues are ablated gradually at a certain temperature. At this time, the mitochondria and lysosomes in cancer cells are destroyed, and apoptosis occurs, thereby exerting an anti-cancer effect [13]. In this study, patients with primary large HCC treated by TACE alone (control group) were compared with those given TACE combined with microwave ablation (observation group). It was found that (1) observation group exhibited a higher objective response rate (66.67% *vs.* 40.00%) as well as lower levels of serum carcinoembryonic antigen, alpha fetoprotein and carbohydrate antigen 125 after treatment than control group ($P<0.05$), suggesting that the short-term efficacy of TACE combined with microwave ablation is superior to that of TACE alone in treating primary large HCC. (2) The differences in the incidence rates of adverse reactions including nausea and vomiting, leucopenia, thrombocytopenia, anemia and transaminase elevation were not statistically significant between observation group and control group ($P>0.05$), illustrating that TACE combined with microwave ablation does not increase adverse reactions and has favorable safety. (3) After 1 and 3 years of follow-up, the survival rate and quality-of-life score were raised, while the recurrence rate was reduced in observation group in contrast with those in control group ($P<0.05$), implying that TACE combined with microwave ablation has a good long-term therapeutic effect on primary large HCC, and such a therapy can lower the recurrence risk, increase the long-term survival rate, extend the survival time of patients and improve their quality of life during survival.

In conclusion, the combined use of TACE and microwave ablation in patients with primary major HCC may stimulate short-term therapeutic effects, regulate the expression of serum tumour markers and reduce adverse reactions. In addition, this method can increase the long-term survival rate, decrease recurrence and benefit the long-term quality of life of surviving patients.

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