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Original Article

Long-term efficacy of hepatic artery chemoembolization combined with cryosurgical for the treatment of primary liver cancer

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Abstract: Objective: This study aims to investigate the the long-term efficacy of hepatic artery chemoembolization combined with cryosurgery for the treatment of primary liver cancer. Methods: Between June 2013 and June 2014, 86 cases of primary liver cancer patients were enrolled in the study. Random number table was used to divided the patients into observation and control group. In observation group, patients were treated with hepatic artery chemoembolization combined with cryosurgery. Patients in control group recived only cryosurgery. Baseline data of the two groups, efficacy, liver function score, safety and long-term efficacy and data analysis were compared between groups. Results: Gender, age, duration, liver function, AFP, tumor size and Karnofsky score and other basic clinical data in two groups showed no significant difference ($P > 0.05$). The total effective rate in the treatment group was 79.5%, which was significantly better than the effective rate in the control group (66.7%) ($P < 0.05$). In the observation group Child-Pugh score was (12.6±2.8), which was also significantly improved ($P < 0.05$). The incidence of adverse reactions was 18.2% and 19.0%, respectively ($P > 0.05$). The overall effective rate in one-year follow-up were 59.1% and 42.9%, respectively ($P < 0.05$). Conclusions: Hepatic artery chemoembolization combined with is a safe and effective approach for primary liver cancer.

Keywords: TACE, cryocare, hepatocellular carcinoma, feasibility, long-term efficacy

Introduction

Primary liver cancer is a common malignant tumor in clinical. Its mortality rate is higher, occupying the 3rd of digestive tumor. According to the statistics from ministry of health, the death of liver cancer is 110000 people per year in China. Not only does it directly affect the life quality of the patients, but also affects the family, even the society [1]. Thus the research on the method and curative effect of primary liver cancer treatment were of great value. Although traditional surgery has significant curative effect, those affect the application of the surgery because of the strict indications, big traumas and so on. In recent years, with the application of the new treatments such as the technology of hepatic artery embolism chemotherapy, argon-helium knife and minimally invasive surgery, the curative effect of primary liver cancer significantly increased. However it still needs to be improved [2]. Studies have confirmed that hepatic artery embolism chemotherapy combined argon-helium knife has significant value in the treatment of primary liver cancer. But the research is still lack of sufficient data to support. Thus this study has the important value for clinical guidelines.

Subjects and methods

Inclusion and exclusion criteria

Patients' including criteria was formulated by diagnosis and treatment of primary liver cancer as well as clinical experience. The objectives of the study were screened rigorously in order to ensure the security of scientific research and data. Its selection criteria are as follows: (1) inclusion criteria: ① comprehensive diagnosed with primary liver cancer [3]; ② lymph node metastasis did not occur, and the prediction of survival time more than 1 year; ③ health tolerated treatment, Karnofsky score not was

Table 1. Baseline data of the two groups

Parameter	Observation group (44)	Control group (42)	t or X^2	P
Sex ratio	26:18	22:20	1.936	0.826
Age (Year)	52.5±4.6	52.6±4.8	1.638	0.462
Course of disease (year)	2.4±0.6	2.3±0.7	1.532	0.372
The Child-Pugh score (points)	6.3±1.5	6.5±1.4	1.589	0.438
AFP (ng/ml)	563.8±56.6	566.5±58.2	1.652	0.475
Tumor diameter (cm)	4.5±1.6	4.6±1.5	1.768	0.513
Karnofsky score (points)	82.6±10.3	83.2±11.4	1.836	0.623

Table 2. Efficacy comparison between the two groups

	n	CR	PR	SD	PD	The total benefit rate (%)
Observation group	44	6	18	11	9	79.5
Control group	42	3	18	7	14	66.7
X^2						4.868
P						0.042

Table 3. Child-Pugh score comparison between the two groups (points)

	Observation group		Control group	
	Before treatment	After treatment	Before treatment	After treatment
Child-Pugh score	6.3±1.5	12.6±2.8	6.5±1.4	10.3±2.6
t	13.685		13.465	
P	0.038		0.042	

less than 70 minutes [4]; ④ liver function Child-Pugh score was between 5 and 9 points [5]; ⑤ meet the informed consent of the relevant principles and medical ethics; (2) Exclusion criteria: ① in blood test, blood platelet count was less than 5.0 * 10^9/L; ② 15th before treatment or during the study were treated with chemotherapy or hormone therapy [6]; ③ patients with acute and chronic infectious diseases; ④ pregnancy, breast-feeding women and persons with mental disorders.

General information

According to selection criteria, between June 2013 and June 2014 primary liver cancer patients were screened, and 86 cases were selected fro the study, the basic information were as follows: (1) Gender: male 48 cases, female 38 cases; (2) Age: 48-56 years; (3) Course: 1-3 years; (4) Liver function: Child-Pugh score between 5 and 9 points in; (5) Serum alpha-fetoprotein (AFP): 400-750 ng/ml; (6) tumor size: 3-8 cm in diameter; (7) Karnofsky score: 70-90 points.

Treatment for the control group

Control subjects were treated with simple cryoablation; the treatment operation was as follows: (1) Preoperative intramuscular injection of pethidine 100 mg, anesthesia with 0.1 g, 2% lidocaine, treatment with argon-helium superconducting surgical treatment systems (Endocare, USA); (2) In selected puncture site, a 0.5 cm incision was made; CT-guided core puncture was performed in the intercostal; needle tip was directly penetrated into the bottom of the tumor; after removal of the inner core guidewire was introduced; cryocare was inserted in the tumor central along the outer sheath; (3) Knife tip temperature was quickly dropped to -140°C; 15 min later it was warmed to 20°C; after 5 min it was cooled and freezed for 15 min again; this was the first treatment; if the tumor was too large or the efficacy was poor, treatment was performed again after one week; (4) Argon-helium knife was removed; After compression bandage for 12 h, anti-infection, hemostasis, liver protection, complication treatment and routine care were performed.

Treatment for observation group

Observation group was treated with hepatic arterial chemoembolization combined with cryosurgery; the cryosurgery operation was consistent with the control group; hepatic artery chemoembolization was as follows: (1) Before treatment catheterization was performed through the femoral artery by modified Seldinger method, and arterial angiography was conducted; according to angiographic results tumor blood supply was analyzed; (2) The micro-catheter was inserted into the tumor feeding arteries; 750 mg FUDR, 100 mg oxaliplatin, and 10 mg pirarubicin were slowly inject-

Table 4. Adverse reaction incidence comparison between the two groups

	Fever	Abdominal pain	Urinary retention	Puncture The hematoma	Other	The incidence of adverse reactions (%)
Observation group (44)	2	1	2	0	3	18.2
Control group (42)	2	2	1	1	2	19.0
X^2						2.689
P						0.092

ed through the catheter; (3) After drug liquid injection, under DSA monitoring, artery embolization was performed using a mixture of 10 mg pirarubicin and 10 ml ultra-liquid iodinated oil; (4) After one month of treatment, patients with poor efficacy may receive the treatment again.

Projects and standards evaluation

(1) baseline information: statistics including gender, age, course, liver function, AFP, tumor size, the Karnofsky score and other data, and they were compared between groups; (2) efficacy: 1 week before and 4 week after treatment, enhanced CT was used for check. According to WHO on solid tumor evaluation standard for effect evaluation, its is divided into CR, and PR, and SD and the PD, level. The benefit rate = (CR+PR+SD) cases number/ research cases number *100%. Benefit rate is more high, the effect is much better [7]; (3) liver function: according to liver function Child-Pugh score method, liver function was scored before and after the treatment. As liver function evaluation content, the score is more high, the liver function is much better [8]; (4) security: in treatment process, the appearance of bad reaction was calculated. Adverse reaction occurrence rate was calculated, and the both were negative related [9]; (5) long-term efficacy: After treatment, image check was performed after one year follow-up. According to the WHO evaluation criteria in solid tumors, the results were evaluated and the benefit rate was calculated as the long-term effect content.

Data processing method

Research data were processed with SPSS 20.1 statistical software; measurement data were expressed as Mean ± SD; count data were expressed by X (%); Comparison between groups was performed using t-test (Continuous variables) and X^2 (Count variables); when $P < 0.05$, the difference was significant.

Results

Baseline data

Gender, age, duration, liver function, AFP, tumor size and Karnofsky score and other basic clinical data were compared between groups. The data of the two groups showed no significant difference ($P > 0.05$), and the research data were comparable. The specific data were shown in **Table 1**.

Short-term efficacy

In observation group there were 6 CR cases, 18 PR cases, 11 SD and 9 PD cases. The total effective rate was 79.5%, which was significantly better than the control group (66.7% of the total benefit rate) ($P < 0.05$). That is, short-term effect in the observation group was significantly better than the control group. The specific data were shown in **Table 2**.

Liver function

According to Child-Pugh score method, liver function was scored after the treatment. The Child-Pugh scores were significantly improved than before ($P < 0.05$). As comparisons between surgery group, in the observation group Child-Pugh score was (significantly better than the 12.6±2.8) points which was better than that in the control group ($P < 0.05$). That is, liver function in the observation group was better than that in the control group. Specific data are shown in **Table 3**.

Security

There was no serious adverse events during the treatment. Some cases of mild adverse reactions occurred, after treatment they were improved. The incidence of adverse reactions were 18.2% and 19.0% respectively, without significant difference between groups ($P > 0.05$). It meant the safety showed no significant

Table 5. Long-term effect between two groups

	n	CR	PR	SD	PD	The total benefit rate (%)
Observation group	44	3	15	8	18	59.1
Control group	42	2	10	6	24	42.9
X^2						5.873
P						0.026

difference between the two groups. Specific data were shown in **Table 4**.

Long-term efficacy

The total efficiency and the overall effective rate were 59.1% and 42.9% in one-year follow-up of the two groups of, respectively. Long-term efficacy in observation group was significantly better than that in the control group ($P < 0.05$). Specific data were shown in **Table 5**.

Discussion

Primary liver cancer is the most common liver cancer in clinical, it is a critical illness affecting the quality of life of patients and threatening their life. Although currently there are various clinical treatment methods, the efficacy cannot meet the clinical needs, there is still vast room for improvement. With the improvement of hepatic artery chemoembolization, Argon-Helium cryoablation and other treatment methods, their application in the treatment of primary liver cancer is more and more common, and the value is also confirmed by some studies, but because of the lack of clinical experience, the efficacy is poor; so hepatic artery chemoembolization is often combined with cryosurgical treatment [10]. Therefore, the feasibility of hepatic arterial chemoembolization + cryosurgical treatment for primary liver cancer was studied, with great value for liver cancer treatment and therapy promotion.

Argon-Helium cryoablation uses ultra-low temperature target freezing technology to destroy cancerous tissue, and thus achieve therapeutic purposes. With its combination with imaging techniques, the treatment accuracy, efficacy and safety have been significantly improved; and clinical studies have proven that Argon-Helium cryoablation surgery for the treatment of primary liver cancer has the advantages of flexible operation, high security, rapid onset, less invasiveness and faster recovery, which has become the most commonly-used local ablation therapy [11]. Hepatic arterial chemoembolization achieves chemotherapy drug infusion and embolization through liver cancer artery; it can kill tumor cells as well as block tumor blood supply to play a therapeutic role. It has advantages of less trauma, safety and repeated treatment, especially suitable for advanced patients who cannot accept surgical treatment [12]. Efficacy and value of hepatic artery chemoembolization in combination with cryosurgery still need to be confirmed by clinical research, laying a foundation for its promotion.

This study took primary liver cancer patients as subjects; patients were treated with simple cryosurgical treatment and hepatic artery chemoembolization combined with cryosurgery, respectively, and the short-term and long-term efficacy, safety and liver function were compared between groups, in order to confirm the value of hepatic arterial chemotherapy combined cryosurgery and support its promotion in primary liver cancer. The results confirmed that the short-term and long-term efficacy and liver function in the combined treatment group were significantly better than those in cryosurgery group; while there was no significant difference in safety between two groups, thus confirming the promotional value of hepatic artery chemoembolization combined with cryosurgery in primary liver cancer. But limited by the study interval and time, there were some defects, such as the sample size was small, the long-term efficacy evaluation time was shorter, and the treatment technology and experience need to be improved; while the randomized grouping, double-blind experiment, and randomly assignment of medical staffs would reduce the impact of human factors on the comparison between groups, to ensure the scientificalness and validity of research data and conclusions. Therefore the findings have important guiding values for the treatment of primary liver cancer.

In summary, the hepatic artery chemoembolization combined with cryosurgery for the treatment of primary liver cancer has advantages of significant short-term and long-term efficacy, high safety and significantly improved liver function, with a promotional value.

Disclosure of conflict of interest

None.

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