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ABOUT COVER

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AIMS AND SCOPE

The primary aim of *World Journal of Gastrointestinal Surgery* (*WJGS*, *World J Gastrointest Surg*) is to provide scholars and readers from various fields of gastrointestinal surgery with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGS mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal surgery and covering a wide range of topics including biliary tract surgical procedures, biliopancreatic diversion, colectomy, esophagectomy, esophagostomy, pancreas transplantation, and pancreatectomy, *etc.*

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ORIGINAL ARTICLE

Retrospective Cohort Study

Application of radioactive iodine-125 microparticles in hepatocellular carcinoma with portal vein embolus

Peng Meng, Ji-Peng Ma, Xiao-Fei Huang, Kang-Le Zhang

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Abstract

BACKGROUND

Radioactive iodine-125 (^{125}I) microparticle therapy is a new type of internal radiation therapy that has shown unique advantages in the treatment of malignant tumors, especially hepatocellular carcinoma. Patients with hepatocellular carcinoma frequently experience portal vein embolism, which exacerbates the difficulty and complexity of treatment. ^{125}I particles, used in local radiotherapy, can directly act on tumor tissue and reduce damage to surrounding healthy tissue. Through retrospective analysis, this study discussed the efficacy and safety of radioactive ^{125}I particles in portal vein embolization patients with hepatocellular carcinoma in order to provide more powerful evidence supporting clinical treatment.

AIM

To investigate the effect of transcatheter arterial chemoembolization combined with portal vein ^{125}I particle implantation in the treatment of primary liver cancer patients with portal vein tumor thrombus and its influence on liver function.

METHODS

The clinical data of 96 patients with primary liver cancer combined with portal

vein tumor thrombus admitted to our hospital between January 2020 and December 2023 were retrospectively analyzed. Fifty-two patients received treatment with transcatheter arterial chemoembolization and implantation of ^{125}I particles in the portal vein (combination group), while 44 patients received treatment with transcatheter arterial chemoembolization alone (control group). The therapeutic effects on tumor lesions, primary liver cancer, and portal vein tumor embolisms were compared between the two groups. Changes in relevant laboratory indexes before and after treatment were evaluated. The *t* test was used to compare the measurement data between the two groups, and the χ^2 test was used to compare the counting data between groups.

RESULTS

The tumor lesion response rate in the combination group (59.62% *vs* 38.64%) and the response rate of patients with primary liver cancer complicated with portal vein tumor thrombus (80.77% *vs* 59.09%) were significantly greater than those in the control group (χ^2 = 4.196, 5.421; P = 0.041, 0.020). At 8 wk after surgery, the serum alpha-fetoprotein, portal vein main diameter, and platelet of the combined group were significantly lower than those of the control group, and the serum alanine aminotransferase, aspartate aminotransferase, and total bilirubin were significantly greater than those of the control group (t = 3.891, 3.291, 2.330, 3.729, 3.582, 4.126; P < 0.05). The serum aspartate aminotransferase, alanine aminotransferase, and total bilirubin levels of the two groups were significantly greater than those of the same group 8 wk after surgery (P < 0.05), and the peripheral blood platelet, alpha-fetoprotein, and main portal vein diameter were significantly less than those of the same group before surgery (P < 0.05).

CONCLUSION

In patients with primary liver cancer and a thrombus in the portal vein, transcatheter arterial chemoembolization plus portal vein ^{125}I implantation is more effective than transcatheter arterial chemoembolization alone. However, during treatment it is crucial to pay attention to liver function injury caused by transcatheter arterial chemoembolization.

Key Words: Radioactive iodine-125; Hepatocellular carcinoma; Transcatheter arterial chemoembolization; Portal vein embolus; Retrospective study

Core Tip: This study investigated the clinical value of radioactive iodine-125 (^{125}I) particles in the treatment of hepatocellular carcinoma with portal vein embolism. The study reviewed data from patients who received ^{125}I microparticle implantation to evaluate its effect on tumor control and survival. At the same time, monitoring treatment-related safety and complications provided a basis for evaluating the efficacy and risk of ^{125}I particles in this pathological scenario.

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INTRODUCTION

Primary hepatocellular carcinoma (PHC) is a common malignant tumor with high morbidity and mortality[1-3]. PHC patients often have portal vein tumor thrombosis (PVTTs), which are risk factors for tumor recurrence, metastasis and blood-borne transmission[4-6]. In particular, when the tumor thrombus grows along the main portal vein, the prognosis of patients is worse, and the tumor may metastasize extensively from the liver[7]. It induces esophageal and gastric varices, resulting in rupture bleeding and other fatal consequences[8-10]. For PHC combined with PVTT, surgical procedures, portal stent implantation, radiotherapy, radiofrequency ablation, alcohol embolization, transhepatic arterial chemoembolization (TACE), and other methods have been applied, but a standardized treatment scheme has not been established in the clinic[11].

Hepatocellular carcinoma (HCC) is one of the most common types of primary liver cancer worldwide[12]. Patients with PVTT have a poor prognosis and are difficult to treat[13]. There is much interest in using radioactive iodine-125 (^{125}I) particles as an interventional radiation therapy method in the current treatment plan. However, their use in patients with HCC who undergo portal vein embolization is still in the exploratory stage[14-16]. Therefore, the goal of this study was to evaluate the use of ^{125}I particles in this treatment method, to determine how well the particles worked and whether they were safe, and to provide doctors with a better foundation for their work. This study investigated how well ^{125}I particles worked in treating HCC with portal vein embolization and how they affect survival, quality of life, and the number of complications[17].

Traditional treatment methods, such as interventional embolization or radiotherapy, have limited efficacy in treating HCC with portal vein embolization and are prone to serious side effects[18-20]. In recent years, ^{125}I particles have gradually attracted increased amounts of attention as a means of interventional radiation therapy because of their ability to accurately target tumor tissue and release high doses of radioactive energy[21]. However, its application in patients with HCC who underwent portal vein embolization has not been fully verified or demonstrated. The results of this study will contribute to a comprehensive understanding of the efficacy and safety of ^{125}I particles in the treatment of HCC combined with portal vein embolization and provide a scientific basis for the promotion of this treatment mode in clinical practice[22-24]. At the same time, exploring the possible challenges and solutions in the course of treatment is highly important for improving therapeutic efficacy and reducing the incidence of complications[25].

This study evaluated the efficacy and safety of ^{125}I particles in the treatment of HCC combined with portal vein embolization through retrospective analysis of collected clinical data and explored possible intraoperative challenges and corresponding solutions. Ultimately, we hope to provide scientific treatment strategies and recommendations for clinical practice and promote improvements in treatment efficacy and quality of life for HCC patients with PVTT.

MATERIALS AND METHODS

Research subjects

The clinical data of PHC patients with PVTT admitted to our hospital between January 2020 and December 2023 were retrospectively analyzed, and the patients were divided into a combination group and a control group according to treatment method.

Inclusion criteria: (1) PHC and PVTT confirmed by computed tomography (CT), magnetic resonance imaging, and pathological diagnosis; (2) Lesions that could be measured by imaging; (3) American Eastern Cancer Collaboration score < 2; (4) Liver function Child-Pugh grade A-B; and (5) Provided informed consent to the patient before treatment.

Exclusion criteria: (1) Had metastatic liver cancer; (2) Had tumors at other sites; (3) History of hepatic fibrosis; and (4) Cerebrovascular diseases, respiratory diseases, thyroid dysfunction, *etc.*

Treatment method

The control group was treated with TACE only. Briefly, after successful puncture of the right femoral artery by the Seldinger technique under local anesthesia, superselective intubation was performed into the tumor-supplying artery, and 1 g of fluorouracil, 40 mg of epirubicin, and a liodol emulsifier were injected. The injection dose of iodized oil was determined according to the tumor volume, and the dose was 2-3 mL/cm^3. To make chemotherapy drugs in direct contact with tumor cells and release them slowly, TACE treatment should be performed again at a minimum 1-mo interval.

The patients in the combination group received TACE, portal vein intracavitary therapy, and radioactive ^{125}I implantation intracavitary therapy 1 wk after the first TACE. The Beijing Kelinzon Institute of Medical Technology's radiation therapy planning system helped us make the treatment plan, determine how many particles were needed, determine how many were needed at each layer, determine the dose, and determine the radioactive activity. It also helped us predict how the particles would decay after being implanted and determine how far they could be from nearby important tissues without causing harm. We selected the appropriate body position, affixed a metal marker needle, and used a CT plain scan to determine the injection point. The puncture needle was used to drain the particles, which were then implanted. We performed a percutaneous transhepatic puncture under local anesthesia, selected the TACE embolization site to inject the needle as far as possible, and implanted radioactive particles once the needle reached the ideal location of the main PVTT. We used CT to pinpoint the optimal implantation location, modify the orientation of the needle, and distribute the implants uniformly across various layers. Following the injection, we implanted the first particle 1 cm from the distal edge of the tumor, the second particle 1 cm from the needle withdrawal site, and the final particle 1 cm from the proximal edge of the tumor. Once the operation was complete, we removed the puncture needle and applied local pressure to halt the bleeding. We conducted another CT scan to verify the absence of bleeding and the displacement of particles, among other factors. We performed a postoperative therapy planning system dose assessment and quality verification and administered hemostasis, liver protection, antiemesis, acid inhibition, anti-infection, and supportive treatments. electrocardiogram monitoring continued for 12 h.

Observation indices and detection methods

Our study evaluated clinical efficacy using the MRECIST standard. A complete response (CR) occurred when the enhancement signal in the arterial phase disappeared. Partial response (PR) occurred when the diameter of the target lesion decreased by more than 30% compared to that before treatment. Stable disease (SD) occurred when the PR or progression (PD) standards were not met. PD occurred when the diameter of the target lesion increased by more than 20% or a new tumor lesion appeared.

Evaluation of the clinical therapeutic effect of cancer suppositories

The following factors were considered when evaluating the therapeutic effect: (1) CR and enhanced CT showed that the PVTT disappeared completely; (2) PR and enhanced CT revealed that the PVTT was reduced by more than 50%; (3) SD and enhanced CT showed that the PVTT decreased by < 50% or increased by < 20%; and (4) PD and PVTT increased by

more than 20% or new PVTT appeared. The following calculations were used: Response rate = (CR + PR)/sample size × 100%; and total response rate = (CR + PR + SD)/sample size ×100%.

Testing instruments used

Our study compared the serum levels of alpha-fetoprotein (AFP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TBIL), platelet (PLT), white blood counts (WBC), and portal vein diameter between the two groups before and 8 wk after the operation. We collected fasting venous blood before and 8 wk after surgery. The Roche Cobas e601 electrochemiluminescence immunoassay and its matching kit detected AFP. A Hitachi 7060 automatic biochemical analyzer detected ALT, AST, and TBIL. We used a blood cell analyzer to detect the PLT and WBC and used color Doppler ultrasound to detect the portal vein diameter.

Statistical analysis

SPSS 23.0 statistical software was used for data analysis. Measurement data were expressed as the mean ± standard deviation, and a t test was used for comparisons between two groups. χ^2 test was used for comparisons among data groups, and $P < 0.05$ was considered to indicate statistical significance.

RESULTS

General clinical data analysis

The study included 96 patients with PHC and PVTT, with 52 patients in the combination group and 44 patients in the control group. There was no significant difference in the comparison of general data between the two groups ($P > 0.05$) (Table 1).

The efficacy of tumor lesion and PVTT treatment was compared between the two groups in the combined group

The rates of tumor lesion remission and PVTT remission were significantly greater in the combined group than in the control group ($P < 0.05$). There was no significant difference in the total tumor lesion effective rate or total PVTT effective rate between the combined group and the control group ($P > 0.05$) (Tables 2 and 3).

Analysis of portal vein diameter, liver function index, AFP, WBC, and PLT

At 8 wk after surgery, the serum AFP, portal vein main diameter, and PLT of the combined group were significantly lower than those of the control group, and the serum ALT, AST, and TBIL levels were significantly greater than those of the control group ($P < 0.05$). The serum AST, ALT, and TBIL levels in the two groups were significantly greater than those in the same group 8 wk after surgery ($P < 0.05$), and the peripheral blood PLT, AFP, and portal vein main diameter were significantly less than those in the same group before surgery ($P < 0.05$) (Table 4).

Compared complications

In the combined group, there were 29 patients with abdominal pain, 14 patients with fever, 2 patients with vomiting, 1 patient with dyspnea, and 1 patient with chest pain. In the control group, there were 18 patients with abdominal pain, 8 patients with fever, and 2 patients with vomiting. There was no significant difference in the incidence of postoperative complications between the two groups (90.38% *vs* 63.64%) ($P > 0.05$).

DISCUSSION

The onset of PHC is insidious, and most patients have no typical clinical symptoms or signs in the early stage and have reached the late stage at diagnosis[26-28]. There are many types of cancer in PHC, and it is easy for it to spread to other parts of the body. When liver cancer grows to a certain size, PVTT can easily form, which worsens portal hypertension, accelerates the spread of intrahepatic tumors, and accelerates disease progression[29]. It is also one of the main reasons PHC patients die. PVTT is an important factor in the prognosis of PHC patients. Therefore, it is very important to treat PVTT, increase portal vein blood flow, and reduce portal vein pressure[30]. TACE also works directly on the local lesion, contacts tumor cells, and slowly releases them. This approach directly targets the tumor and circumvents the detrimental side effects of chemotherapy drugs administered to the entire body[31]. However, other studies[32-34] have shown that repeated TACE treatment significantly decreases or even stops blood flow in the hepatic artery, causing the liver to develop steatosis, *etc*. The presence of a tumor thrombus will reduce the therapeutic efficacy of TACE.

PHC patients with PVTT often have a large tumor load. Conventional radiation therapy requires a large radiation dose and causes certain damage to surrounding tissues. Therefore, its use is not recommended. In recent years, with the rapid development of medical imaging technology, a large number of new treatment measures for PHC combined with PVTT have emerged[35]. Intracavitary treatment of the portal vein is one of the most widely used new methods. The portal vein cavity seals radioactive iodine particles, which do not absorb into the human body, cause little damage to normal tissues, do not participate in metabolism, do not pollute the environment, and offer high safety.

Currently, there are few reports[36-38] about the implantation of iodine particles into cancer suppositories, despite the widespread use of intracavitary implantation for the treatment of intracranial tumors, head and neck tumors, pancreatic cancer, prostate cancer, and liver cancer. The rates of tumor lesion remission and PVTT remission were much greater in

Table 1 Comparison of general information between two groups of patients

Characteristic	Joint group, *n* = 52	Control group, *n* = 44	Statistical value	*P* value
Male/female	33/19	29/15	$\chi^2 = 0.062$	0.803
Age in yr	62.5 ± 12.0	60.1 ± 13.9	$t = 0.908$	0.366
Maximum diameter of lesion in cm	7.6 ± 3.0	8.0 ± 3.4	$t = 0.612$	0.542
Child Pugh grading			$\chi^2 = 0.019$	0.890
A	30	26		
B	22	18		
PVTT position			$\chi^2 = 0.055$	0.973
Left branch of portal vein	21	17		
Right branch of portal vein	19	16		
Left and right branches of portal vein	12	11		
HBsAg positivity	35	30	$\chi^2 = 0.008$	0.927

HBsAg: Hepatitis B surface antigen; PVTT: Portal vein tumor.

Table 2 Comparison of tumor lesion efficacy between two groups of patients

Group	Cases	Curative effect				Remission rate	Total effective rate
		CR	PR	SD	PD		
Joint group	52	3	28	19	2	31 (59.62)	50 (96.15)
Control group	44	1	16	23	4	17 (38.64)	40 (90.91)
χ^2 value						4.196	1.119
P value						0.041	0.290

Date are *n* (%). CR: Complete response; PD: Progression; PR: Partial response; SD: Stable.

Table 3 Comparison of portal vein tumors efficacy between two groups of patients

Group	Cases	Therapeutic effect				Relief rate	Total effective rate
		CR	PR	SD	PD		
Joint group	52	9	33	9	1	42 (80.77)	51 (98.08)
Control group	44	4	22	15	3	26 (59.09)	41 (93.18)
χ^2 value						5.421	1.430
P value						0.020	0.232

Data are *n* (%). CR: Complete response; PD: Progression; PR: Partial response; SD: Stable.

people who were treated with TACE and portal vein ^{125}I implantation technology than in people who were only treated with TACE. At 8 wk after surgery, the serum AFP levels in patients treated with TACE and portal vein ^{125}I were lower than those in patients treated with TACE alone. The main portal vein diameter in patients treated with TACE and portal vein ^{125}I implantation was smaller than that in patients treated with TACE alone[39]. This is due to the continuous release of gamma rays by radioactive iodine particles in the portal vein cavity, which destroys the double-stranded DNA of tumor cells, directly kills tumor thrombi, produces a more accurate radiotherapy effect, relieves portal hypertension, and reduces damage to surrounding tissues[40].

In addition to particle implantation, portal vein stent implantation and portal vein particle strip implantation are relatively mature intracavity therapy techniques for PVTT[41]. Both of these methods have achieved good clinical efficacy, but there are still some problems, such as stent stenosis and occlusion, hepatic encephalopathy, a high dose of particle chain radiation, and many adverse reactions[42]. Particle implantation therapy is beneficial for the treatment of

Table 4 Comparison of portal vein diameter, liver function indicators, alpha-fetoprotein level, and platelet level between the two groups of patients before and after treatment

Time	Cases	AFP in ng/mL	ALT in U/L	AST in U/L	TBIL in μmol/L	PLT as 10^9 /L	Portal vein trunk diameter in mm	WBC as 10^9 /L
Preoperative								
Joint group	52	557.9 ± 196.4	57.2 ± 25.8	66.8 ± 29.0	20.9 ± 5.8	162.6 ± 47.2	13.90 ± 2.51	5.16 ± 1.80
Control group	44	570.2 ± 211.6	54.0 ± 19.8	61.2 ± 25.7	22.5 ± 7.5	167.0 ± 51.6	14.10 ± 2.66	5.30 ± 1.95
t value		0.288	0.651	0.964	1.154	0.426	0.369	0.357
P value		0.774	0.515	0.338	0.251	0.671	0.713	0.722
8 wk after surgery								
Joint group	52	138.2 ± 69.5	114.2 ± 47.0	123.0 ± 51.0	35.0 ± 9.4	113.0 ± 55.2	11.20 ± 2.14	3.72 ± 1.15
Control group	44	196.4 ± 73.2	82.6 ± 29.3	89.6 ± 33.7	27.1 ± 8.7	139.0 ± 50.1	12.64 ± 2.00	3.90 ± 1.24
t value		3.890	3.720	3.582	4.126	2.330	3.290	0.719
P value		< 0.001	< 0.001	< 0.001	< 0.001	0.022	0.001	0.473

AFP: Alpha-fetoprotein; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; PLT: Platelet; TBIL: Total bilirubin; WBC: White blood cells.

PVTT with few side effects and has initially achieved good clinical effects, but additional cases are needed for further confirmation[43].

This study revealed that there were no serious complications, such as severe abdominal hemorrhage or bile duct or portal vein injury, in the combined group. Other complications, such as massive abdominal hemorrhage, need further observation. This study also revealed that the serum ALT, AST, and TBIL levels in patients treated with TACE + portal vein intraventricular particle implantation were greater than those in patients treated with TACE alone, which may be related to the radioactive damage caused by radioactive iodine particles to hepatocytes, and the degree of damage can still be improved by clinical drug treatment.

CONCLUSION

TACE combined with portal vein intraventricular radioactive iodine implantation is an effective treatment, and its therapeutic effect is better than that of TACE alone in patients with PHC combined with PVTT. However, attention should be given to liver function injury caused by TACE during treatment.

FOOTNOTES

Author contributions: Meng P and Ma JP wrote the manuscript and contributed equally to this work; Huang XF collected the data; Zhang KL guided the study; All authors reviewed, edited, and approved the final manuscript and revised it critically for important intellectual content, gave final approval of the version to be published, and agreed to be accountable for all aspects of the work.

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