

Catheterization-associated complications of intraperitoneal chemotherapy in advanced gastric cancer

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Abstract

AIM: To assess the catheterization-associated complications during intraperitoneal chemotherapy (IPCT) for advanced gastric cancer.

METHODS: From 1998 to 2002, 80 patients with advanced gastric cancer received a total of 320 courses of IPCT using a large bore central venous catheter and associated complications were analyzed.

RESULTS: Catheterization-associated complications occurred in 11 of the 80 patients (13.8%), including abdominal pain caused by catheter in 2 cases (0.63%), insertion failure in 2 cases (0.63%), bowel perforation in 1 case (0.31%) and abdominal pain during chemotherapy in 6 cases (1.88%). No serious complications required surgical intervention.

CONCLUSION: IPCT using central venous catheters can be performed safely and simply without severe associated complications.

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INTRODUCTION

Gastrointestinal tumor is quite common. In China, the morbidity of gastric cancer is the leading cause of malignant tumors. For non-advanced gastric cancer, surgical removal is the first choice, but for advanced gastric cancer, the outcome of surgical resection remains unsatisfactory. Fifty percent of gastric cancer patients have local recurrence or long distance metastasis after radical surgery within 5 years. The common sites of gastric cancer recurrence or metastasis are the resection site, liver and peritoneal surfaces^[1-4]. It was reported that intraperitoneal chemotherapy could result in markedly increased local drug concentration, and had favorable clinical results in preventing recurrence and metastasis of gastric cancer after surgical treatment, but some complications were reported by using Tenckhoff catheter in IPCT^[5-7]. From March 1998 to June 2002, 80 patients with advanced gastric cancer were treated by central venous catheterization during intraperitoneal chemotherapy (IPCT) after radical gastrectomy in SRRSH Cancer Center. The

main purpose of this study was to analyze the complications of central venous catheterization during IPCT.

MATERIALS AND METHODS

Patients

Between March 1998 and June 2002, 80 patients with advanced gastric cancer were treated in SRRSH Cancer Center. Forty-eight cases were males and 31 females aged 29 to 71 years (median 43.5 years). Patients in stage III_A were 18 cases, stage III_B 29 cases, stage IV 33 cases. The patients were treated with a total of 320 courses of IPCT. Each patient received at least 3 courses of IPCT (mean 4 courses for each patient).

Peritoneal catheters and methods

Single cavity central venous catheters were produced by Arrow Raulerson Syring Ltd, USA. Transparent protecting patches and heparin caps were produced by 3 mol/L Health Care Ltd, USA. As there are no large vessels in this site, puncture site is usually chosen at the cross-point of left midclavicular line and navel line, which is located at outer edge of rectus abdominis muscle. Two percent lidocaine was used for local anesthesia, then a conducting needle was put into the peritoneal cavity, after a steel string was put into peritoneal cavity though the conducting needle. The needle was taken out and the central venous catheter was put into the peritoneal cavity following the steel string after the abdominal wall was dilated. Then 100 mL normal saline was administrated though the catheter, if nothing abnormal was observed, and a heparin cap was put on the top of the catheter and the catheter was fixed to the abdominal wall.

The regimen of intraperitoneal chemotherapy was HCPT+5-FU+CF+VP-16, the dose of chemotherapeutic agents was 8 mg/m² for HCPT, 375 mg/m² for 5-FU, 100 mg for leucovorin (CF), 80 mg/m² for etoposide (VP-16) for three days. HCPT was administrated though peritoneal cavity, other agents were administrated though peripheral vein. Before chemotherapy started, 1 000 mL warm (42 °C) normal saline was administrated into the peritoneal cavity together with 10 mg DXM and 20 mL 20 g/L lidocaine. HCPT was dissolved in 500 mL of normal saline and instilled in the peritoneal cavity though the implanted catheter. Then 42 °C normal saline was instilled to the peritoneal cavity again, until the total volume reached 1 500 mL/m². Patients were asked to change their position every 15 min for 2 h after drug administration. Chemotherapy was given 2 wk after surgery, and repeated every 3 wk with the same regimen. The central venous catheter was taken out after each cycle of chemotherapy, a new catheter was put into peritoneal cavity just before the next cycle of IPCT started.

RESULTS

The complications associated with catheterization during IPCT in this series were common and mild. Moderate to severe pain induced by catheterization occurred in 2 cases (0.63%). Failure in catheterization because of intraabdominal adhesion occurred in 2 cases (0.63%), but the catheter was successfully put into peritoneal cavity through the other side of abdominal wall. Bowel perforation occurred in one case (0.31%) possibly due

to severe intraabdominal adhesion after surgery, and the catheter was put into bowel cavity. This patient received systemic chemotherapy instead of IPCT afterwards, and antibiotics were given to him. He had no signs of peritonitis during the procedure. Moderate pain during chemotherapy occurred in 6 cases (1.88%). There was no incidence of severe complications such as intestinal obstruction, peritonitis, intestinal hemorrhage, leakage of peritoneal fluid and anastomotic stoma fistula (Table 1).

Table 1 Catheterization-associated complications

Complications	Cases (n=320, %)
Pain by catheterization	2 (0.63)
Insertion failure	2 (0.63)
Bowel perforation	1 (0.31)
Pain during chemotherapy	6 (1.88)

DISCUSSION

Postoperative IPCT should be started early^[18-11]. Because surgery for gastrointestinal cancer is associated with an extremely high rate of dissemination within the peritoneal cavity and seeding on peritoneum, the resection site and abraded peritoneal surfaces are common sites of tumor cell seeding, early postoperative IPCT lets all intraabdominal surfaces expose to intraperitoneal chemotherapy agents. Because all adhesions are lysed at this time, the response rate of minor metastatic lesions on peritoneal surface to the chemotherapy agents can be 100%. Besides, tumor burden is light at this time according to tumor cell proliferative kinetics, chemotherapy agents can not only kill dissociative tumor cells in peritoneal cavity, but also kill inflammatory cells in peritoneal cavity, thus decreasing the releasing of cellular factors and preventing their effect on tumor cell proliferation. Regional chemotherapy could result in markedly increased local responses without compromising systemic effects^[12-14]. Studies of pharmacokinetics of IPCT also showed advantages. Sugarbaker^[15] summarized the pharmacokinetics of 4 kinds of chemotherapy agents often used in IPCT, the area under the curve (AUC) within peritoneal fluid compared with plasma of these agents was as follows, 5-FU 150/1, MMC 72/1, ADM 205/1, and DDP 20/1. There was an obvious difference between AUC within peritoneal fluid and AUC within plasma.

Several methods could be used in IPCT^[7,16]. The catheters commonly used are Tenckhoff catheter and single peritoneal cavity catheter. Tenckhoff catheter is popular in Western countries. After completing the surgical procedure and prior to closing the abdominal wall, Tenckhoff catheter is placed through the abdominal wall and then a Dacron cuff is fixed subcutaneously. A needle is inserted into the Dacron cuff during chemotherapy. The disadvantage of this method is that the catheter is left in the peritoneal cavity for a long period, and there are some complications. Esquivel *et al.*^[17] reported that in 44 patients who received IPCT during the first day to fifth day after surgery, 13% of the patients had pneumonia, 9% bleeding after surgery, 9% intestinal fistula, 7% a prolonged duration of intubation, 2% biliary fistula, 2% anastomotic stoma fistula, and 2% pancreatitis. The total complication morbidity was 37%, 17% of the complications were related to bowel function. Topuz *et al.*^[18] also reported that there were 39 patients in 205 cycles of intraperitoneal chemotherapy, severe abdominal pain was in 4 patients (10.3%), peritonitis and coloperitoneal fistula each in 1 patient (2.6%), catheter obstruction in 3 patients (7.7%) and colon puncture in 4 patients (10.3%). Sakuragi *et al.*^[19] did IPCT in 78 patients using Tenckhoff catheter, the total cycles were 365. Among them, 27 (34.6%) experienced IPCT related complications, 17 (21.8%) had extensive intraabdominal

adhesion, 13 (16.7%) had local infection around the reservoir, 3 (3.8%) had an abscess at the site of the implanted port of the catheter, 3 (3.8%) had catheter obstruction, one (1.3%) had ileus, one (1.3%) had perforation of small intestine, one (1.3%) underwent opening of the wound at the site of catheter implantation due to bleeding.

We used central venous catheter in IPCT, the procedure of catheterization was easy to master. Meanwhile it was not necessary to leave the catheter for a long time, the catheter could be taken out 2-3 d after chemotherapy, which could improve the life quality of patients. Moreover, central venous catheter was used only one time with few complications. In fact, our patients had no severe complications such as intestinal perforation, intestinal bleeding, peritonitis, anastomotic stoma fistula and implantation site infection. The morbidity of complications in our group was 13.75%, much lower than reported in other documents. Pain after catheterization was due to the length of catheter into the peritoneal cavity, and the pain could be relieved after pulling out the catheter. The pain during chemotherapy could be relieved by administering lidocaine and DXM into peritoneal cavity.

The reasons why our group has a low morbidity of complications are as follows. Chemotherapy was started two weeks after surgery instead of 5 d after surgery. Since surgical incision was healed 2 wk after surgery, many complications of IPCT were avoided by starting chemotherapy 2 wk after surgery. Besides, statistical analysis showed that there was no difference in response rate (data not shown). Tenckhoff catheter used by Sakuragi *et al.*^[19] had to put in the peritoneal cavity for a long period and there also must be a drainage system or an outflow tube. But we used central venous catheter only one time and did not need an outflow tube and the chemotherapy agents of IPCT were spontaneously absorbed by peritoneum. Clinical observation revealed that intraperitoneal fluid could be absorbed spontaneously 2 or 3 d after chemotherapy. Radical gastrectomy has a great surgical scope and can cause severe intraabdominal adhesion which can limit intraperitoneal fluid to flow freely. Sugarbaker *et al.*^[15] thought this would affect the distribution of chemotherapy agents in peritoneal cavity, and would affect chemotherapy agents to contact with peritoneum. If there was not enough fluid in the peritoneal cavity, the fluid could not flow freely in peritoneal cavity because of resistance. Though patients changed their position frequently, chemotherapy agents could not distribute to the whole peritoneal cavity, thus decreasing the response rate. Only a large volume of fluid causing abdominal distension could make chemotherapy agents distribute evenly in peritoneal cavity^[20]. Therefore, 1 500-2 000 mL fluid should be given to patients every time during chemotherapy, and the patients should change their position frequently in order to achieve chemotherapeutic effect. Besides, a large volume of fluid can decrease the incidence of complications such as abdominal pain, intestinal perforation, intestinal bleeding, ileus, peritonitis and anastomotic stoma fistula.

In conclusion, it is safe and convenient to use central venous catheters in intraperitoneal chemotherapy and it also has less side effects and fewer complications.

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