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# COMBINATION OF CHOLECYSTOJEJUNOSTOMY OR CHOLEDOCHJEJUNOSTOMY PERFUSION CHEMOTHERAPY AND RADIOTHERAPY FOR CANCER OF THE PANCREATIC HEAD

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**64 patients with unresectable cancer of the pancreatic head were admitted in our hospital form 1989 to 1995. 21 cases were treated by radiotherapy (Group A). 23 cases were treated by cholecystojejunostomy or choledojejunostomy (Group B). 20 cases were treated by cholecystojejunostomy or cholecystojejunostomy combined with superior panreatocoduodenal artery ADM, 5-Fu perfusion with multifunctional implantable drug-delivery system and radiotherapy (Group C). The 1-year survival rates of these three groups were 0%, 0% and 4% respectively. The authors believe that combined treatment of Group C is recommended for unresectable cancer of the pancreatic head.**

**Key words: Pancreatoncus, Operation, Perfusion chemotherapy, radiotherapy.**

23 cases of unresectable cancer of pancreatic head were performed cholecystojejunostomy (Group B), another 21 cases of unresectable cancer diagnosed with CT received radiotherapy (Group A) in our hospital from June, 1989 to March, 1993. Since April 1993, another 20 cases were treated bycholecystojejunostomy or choledochojejunostomy combined with superior pancreatocoduodnal artery ADM, 5-Fu perfusion with multifunctional implantable drug delivery system and radiotherapy (Group C). All these 64 cases were followed up for over 1 year.

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## MATERIALS AND METHODS

Of these 64 cases, 51 were male and 13 were female aged from 40 to 71 years. All cases in Group A were diagnosed unresectable cancer of pancreatic head with CT, which were proved ductal adenocarcinoma of pancreas by fineneedle puncture pathological examination under B ultrasound. The other 43 cases were proved unresectable by exploratory laparotomy, and proved ductal adenocarcinoma of pancreas by biopsy. No malignant metastasis occurred to liver or other distant part in these 3 groups. In Group A, with location by B ultrasonography 2Gy/time $^{60}Co$ irradiation was undertaken at anterovertical area and dextral area for twice a week with total dose of DT 60 Gy.

In Group B, cholecystojejunostomy was performed on those of unobstructed cystic duct proved by exploratory laparotomy. Choledochoje-junostomy and cholecystectomy were performed on those of poor unobstructed cystic duct.

In Group C, the same cholecystojejunostomy and choledochojejunostomy in Group B was

performed. Gastroduodenal artery near common hepatic artery was ligated in operation through a small resection far away from ligature, the catheter of multifunctional implantable, the catheter of multifunctional implantable drug delivery system made in USA was inserted to superior pancreaticoduodental artery. Meanwhile right gastro-epiploic artery was ligates. Methylene blue was injected into drug delivery pocket which was implanted in subcutaneous tissue for tumor staining. 10 mg of ADM and 1.0g of 5-Fu were injected through drug delivery system in operation and one week later, the same dose was administered once a week with the total 5-Fu amount of 10g. Another 2 weeks later, with location by B ultrasound, 1.5 Gy/time of $^{60}Co$ was irradiated at anterovertical area with the total dose of DT 60 Gy, 3 weeks after one therapeutic course, 10 mg of ADM and 0.5g of 5-Fu were injected through drug delivery system in every 2 weeks for 2 months.

Sex proportion, average age and preoperative total bilirubin level had no obvious difference among these 3 groups.

## RESULTS

Short-term tumor retraction rate was studied when total therapeutic course had completed (10 weeks after operation in Group B) on basis of tumor retraction degree before and after CT and B-ultrasound test (Table 1). It was divided into 3-month, 6-month and 12-month survivorship according to survival time (Table 1). Symptoms improvement and laboratory examination changes were compared among these 3 groups (Table 2).

*Table 1. Results of cancer of pancreatic head in 64 cases*

| Results | Group | | |
|---|---|---|---|
| | A | B | C |
| Tumor retraction mostly (%) | 0 | 0 | 2/20 (10) |
| Tumor retraction partially (%) | 5/21(23.8)* | 0 | 14/20(70)** |
| No effect | 16/21(76.2)* | 23/23(100)* | 4/20(20)** |
| 3-month survival rate | 18/21(85.7) | 20/23(87) | 20/20(100) |
| 6-month survival rate | 15/21(71.4) | 16/23(69.6) | 16/20(80) |
| 12-month survival rate | 0 | 0 | 8/20(40)*** |
| Median survival rate | 26.5 | 25.5 | 58.5*** |

Notes: * $P<0.025$ compared with Group B.
** $P<0.01$ compared with Group A. $P<0.005$ compared with Group B.
*** $P<0.005$ compared with Group A,B

*Table 2. Symptoms improvement and laboratory changes among these 3 groups*

| Studied item | Groups | | |
|---|---|---|---|
| | A | B | C |
| Weight increase | 2/21* | 11/23 | 14/20 |
| Appetite stimulation | 3/21* | 18/23 | 17/20 |
| Pain relieve | 15/21** | 0 | 19/20 |
| Decreased total bilirubin level | 5/21 | 5/23 | 1/20 |
| Normal total biliubineves | 0* | 18/23 | 19/20 |

Notes: * $P<0.005$ compared with Group B,C
** $P<0.005$ compared with Group B

## DISCUSSION

### Value of Combination Treatment for Cancer of Pancreatic Head

Cancer of pancreatic head is not specific in early stage. When it has been diagnosed, it is unresectable and the palliative treatment is the main way to prolong patient's life. Any of the palliative treatment methods has no satisfactory result. It was reported simple exploratory laparatomy without treatment could prolong for average of 4.6 months, operation for 8 months radiotherapy for 9 months and general chemotherapy for 8 months.[1-3] Singh, et al.[1] reported that patients with cancer of pancreatic head only with exploratory laparatomy but no treatment usually died of hepatic complications. Long-time icterus was the main cause of hepatic failure by injuring hepatic function.

Therefore, how to eliminate jaundice as soon as possible is the principle for treating cancer of pancreatic head. In our study, the survival time of

Group C was the longest, its jaundice elimination was better than Group A and tumor retraction and pain relieve effects were better than Group B. It is indicated that the combination method which comforms to the treatment principle is the satisfactory palliative treatment for cancer of pancreatic head because it can make up each other's deficiencies. It has many advantages as the following, 1) The patients with unresectable cancer of pancreatic head usually show high total bilirubin level, obvious intrahepatic cholestatic jaundice, poor appetite and bad systemic function. And the side-effects of radiotherapy would make the above symptoms more serious. And some patients died of hepatic or systemic function failure before jaundice had been eliminated. With the combination method, cholecystojejunostomy or choledochojejunostomy could eliminate jaundice immediately, stimulate the appetite and improve hepatic and improve hepatic and systemic function, with provided a good foundation for radiotherapy and chemotherapy; 2) Radiotherapy or chemotherapy would kill cancer cells to inhibit the growth of cancer and relieve pain; 3) Ligating gastroduodenal artery to reduce blood supply to cancer also could inhibit the growth of cancer.

**Applications of Multifunctional Implantable Drug delivery System**

Blood supply in pancreas is very sufficient with the main source of superior pancreatoduodenal artery at pancreatic head. Rationable perfusion with drug delivery system is performed through this artery. The advantages are as the following, 1) Local administration with high concentration has less side-effects than general administration; 2) A large amount of drug can be directly injected into tumor through catheter in drug delivery system for the catheter can exactly get into superior pancreatoduodenal artery; 3) Gastric system has slight reaction since gastro-duodenal artery and right gastro-epiploic artery have been ligated so the drug can't reach gastric wall; 4) Drug is delivered as simply as intramuscular injection and this method is easy to be accepted by patients.

**Combination of Radiotherapy and Chemotherapy for Cancer of Pancreatic Head**

Shibamoto, et al.[2] suggested irradiation dose for unresectable pancreatic cancer should be 55-60Gy, and pointed out the combination of radiotherapy and chemotherapy and the application of radiosensitivity enhance were the hopeful way to improve therapeutic effect. In Group C, at the intermission in every week of irradiation with small dose, delivering small amount of ADM and 5-Fu achieved a better result than Group A. Its mechanism would be,[4] 1) When DNA is reproducing in cancer, ADM and 5-Fu could get into DNA molecular structure to inhibit DNA synthesis and enhance radiosensitivity; 2) ADM and 5-Fu could interfere cytokinetics and increase the proportion of sensitive cells and proliferative cells. Some researchers believed small amount of ADM or continuous irradiation with small dose could enhance radiosensitivity of the tumor cells which had been in $G_2$ and M stage; 3) radiotherapy and chemotherapy make up each other's deficiencies to kill more drug-resistant and irradiation-resistant tumor cells.

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