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Changes of the Pancreatic Exocrine Function in New Canine Model of Pancreaticoduodenectomy by BTPABA Test*)

Tsuneo TANAKA, Yasuyuki ICHIBA, Osamu KODAMA and Haruo EZAKI

The Second Department of Surgery, Hiroshima University School of Medicine, 1-2-3, Kasumi, Minami-ku, Hiroshima 734, Japan

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ABSTRACT

An experimental study on the changes in the pancreatic exocrine functions before and after pancreaticoduodenectomy (PD) for the treatment of periampullary carcinoma was performed. Pancreatic insufficiency models with pancreatic duct stenosis was prepared with dogs by giving them complete ligation of the minor pancreatic duct and intubation into the major pancreatic duct. After 3 months of pancreatic duct stenosis, intubation placed into the major pancreatic duct was withdrawn to drain the pancreatic juice. At the same time, approximately 50% pancreatectomy, with approximately 50 cm duodenojejunectomy, was performed to prepare a PD model. The results of the N-benzoyl-L-tyrosyl-p-aminobenzoic acid test (BTPABA test) showed reduction in what during stenosis of the pancreatic duct. Although the results of the BTPABA test shortly after reoperation showed reduction, a gradual recovery was noted, returning in 4-5 months to almost the same level as before the operation. The findings of the present study indicate that pancreatic exocrine insufficiency in periampullary carcinoma is due to pancreatic duct obstruction, and that the post-PD pancreatic exocrine function can be successfully maintained at the level close to that in normal sujects if drainage of the pancreatic duct functions effectively.

INTRODUCTION

The authors[2,3] have been using the BTPABA test to determine the pancreatic exocrine function before and after PD for periampullary carcinoma. As the results, the following five points are suggested: 1) The low levels of the results of the preoperative BTPABA test were mainly due to the disturbance of the outflow of pancreatic juice, rather than due to the impairment on the pancreatic parenchyma by obstructive pancreatitis. 2) The reduction in the results of the BTPABA test at an early stage after operation was due to the impairment on the pancreatic exocrine function caused by maldigestion and malabsorption, and by the changes in gut hormones and in innervation. 3) The fact that the results of the BTPABA test for over 1 year after PD were improved to the level nearly those in the control, meant the improvement of the condition at an early stage after operation as well as a good maintenance of pancreatic juice drainage. 4) In view of the fact that about 50% of the pancreas was resected at PD, the reserve capacity of pancreatic exocrine secretion was quite considerable. 5) The impairment on pancreatic exocrine function due to preperative obsturctive pancreatitis was reversible. The authors therefore took note of these points, and prepared new PD models with dogs, and the changes in the pancreatic exocrine function before and after

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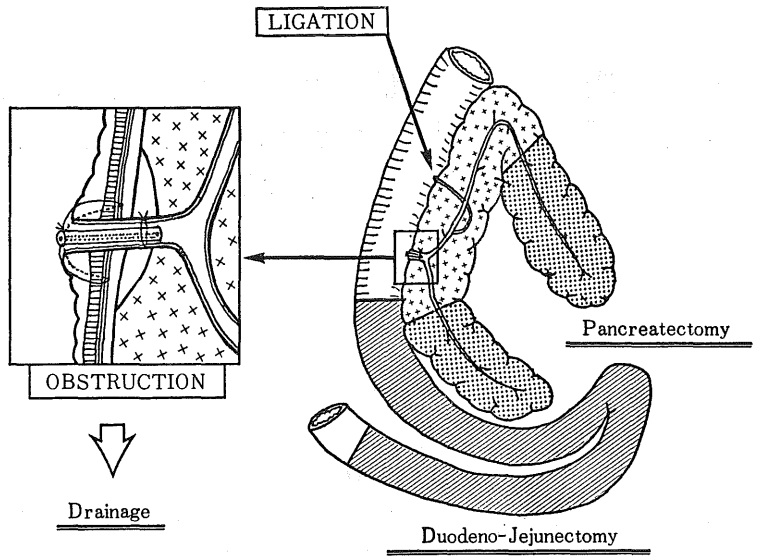

Figure The canine model of pancreaticoduodenectomy

PD were studied.

MATERIALS AND METHODS

Adult mongrel dogs of both sexes weighing 10.0–13.0 kg were used to prepare the PD models. The animals were anesthetized with 20 mg/kg sodium pentobarbital (Nembtal), and were laparotomized asceptically. Then the minor pancreatic duct (the duct of Wirsung) was ligated and separated, and transverse duodenotomy was given. A polyethylene tube with the outer diameter of 1.7 mm and the inner diameter of 0.4 mm was inserted into the major pancreatic duct (the duct of Santorini), and it was fixed with the 5-0 Nylon yarn at two points (Figure). In 3 months after the obstruction of the pancreatic duct with these methods, the animals were relaparotomized, and then pancreatic drainage was given by taking out the tube inserted into the major pancreatic duct. Simultaneously, about 50% of the pancreas as well as the second part of the duodenum and the upper portion to the jejunum (about 50 cm in length) was resected. The animals on which these operations were given were made the PD model group (n=5).

The methods for observation included macroscopic findings, the BTPABA test, histopathological observations, and pancreatography. The method for the BTPABA test was as follows: the animals were fasted for 24 hr, and then a mixture of the test solution (169 mg PABA) in 1 ampule and about 5 g skim milk dissolved in about 200 ml water, was administered. Then the animals were put into a cage for urine collection, and the whole urine during 24 hr was collected. PABA in the urine was determined with the DACA method[5], and the rate of collection of urinary PABA was calculated. Histopathological findings were recorded as follows: histopathological samples were collected from the right and left lobes, and the samples were stained with hematoxylin-eosin, and with Azan-Mallory's method, and were examined microscopically. After resecting the pancreas and the duodenum in a mass, pancreatography was performed immediately by inserting a catheter into the major pancreatic duct and the duct was photographed after infusing microbarium. X-ray pictures were taken by placing the extracted pancreas onto the X-Omat TL film (Kodak) under the condition of 300 mA, 26 kVp, 1.0 sec, FFD 88 cm. When the contrast medium was infused, a method whereby the medium might drop naturally from a height of about 10 cm was adopted so that the pressure might be as uniform as possible.

RESULTS

In the PD models, when the pancreatic duct was narrowing, the results of the BTPABA test (Table) showed reduction ($p<0.01$). Al-

Table Change of the pancreatic exocrine function in canine model of pancreaticoduodenectomy by BTPABA test

	Urinary excretion of PABA (mean±S. D., %)
Before operation	87.1± 7.3
2 wk. after operation	67.2± 8.0**
4 wk.	67.8± 8.9*
6 wk.	69.4± 7.8*
8 wk.	68.2±10.5*
10 wk.	69.0±10.1*
12 wk.	70.0±10.4*
2 wk. after reoperation	67.0±12.8*
4 wk.	67.9±11.6*
6 wk.	69.6±10.5*
8 wk.	72.3± 8.6*
10 wk.	74.4± 9.2
12 wk.	72.5±11.4
14 wk.	78.4± 8.0
16 wk.	78.0± 9.0
18 wk.	82.4± 8.4
20 wk.	81.0± 9.1

Significant difference: * $p<0.05$
** $p<0.01$

though the results of the BTPABA test at an early stage after re-operation showed reduction ($p<0.05$), as compared before operation, a gradual recovery was noted, restoring almost to the same level before operation in 4–5 months after operation.

Histopathological study after the narrowing of the pancreatic duct for 3 months detected fibrosis surrounding the pancreatic duct. However, inflammatory cell infiltrations were mild, and the finding of acute pancreatitis was not obtainable. Inspection in 5 months after pancreatic juice drainage found that the extent of pancreatic fibrosis became milder without showing the worsening of the lesion.

Pancreatography performed after the narrowing of the pancreatic duct for 3 months recoogized the dilatation and meandering of the main pancreatic duct, together with the pictures of poor secondary and tertiary bifurcations of the duct. In the pancreatography of the PD model, however, the dilatation and meadering of the main pancreatic duct were no more noticed, and the secondary and tertiary bifurcations of the duct were well reproduced. Macroscopically, the cicatricial narrowing of the major pancreatic duct and the papilla was not observed, suggesting an effective function of pancreatic juice drainage.

DISCUSSION

From the results using the canine PD moddel, the following points were clarified. The BTPABA test showed reduction during stenosis of the pancreatic duct. Although the outcome of the BTPABA test shortly after reoperation showed reduction, a gradul recovery was noted, returning in 4–5 months to almost the same level as before the operation. Histopathological study revealed that pancreatic juice drainage inhibited the worsening of the lesion, which even induced improvement in some parts, even after the narrowing of the pancreatic duct was induced in 3 months.

Thus, the findings presumed from clinical results were supported by these of the experiment. It was necessary, however, to recognize the different points in the PD for clinical cases and in the canine PD model used by the authors: in the canine PD model, hemigastrectomy and truncal vagotomy were not performed, the duodenum was resected partially, and the reconstruction of the digestive tract was made with the Billroth type I. Consequently, the changes in gut hormones and the influence on the pancreatic exocrine function due to the changes in innervation, had not been clarified with the present experiment.

Experimental impairment of the pancreas has long been attempted in animals. Tiscornia[4] reported that pancreatic impairment caused by the ligation of the major pancreatic duct could be restored by anastomosing the major pancreatic duct with the microsurgical technique in 7–46 days. Whereas Carnevali et al.[1] stated that they produced pancreatic impairment by inserting a PVC tube into the major pancreatic duct, and then the side-to-side anastomosis anastomosis of the pancreatic duct and the jejunum was made, and that as a result the progress of pancreatic fibrosis was suspended, and inflammatory cell infiltrations disappeared.

All thoese reports pointed to the importance of pancreatic juice drainage, and the fact that the postoperative pancreatic function was largely influenced by pancreatic drainage, agreed with the outcome obtained by the authors. The

difference between these studies and the present experimental models was that in our models, pancreatic resection was performed additionally after the recovery from pancreatic duct impairment.

The authors clarified that when there was mild impairment on the pancreas due to obstructive pancreatitis, the postorerative pancreatic exocrine function was well maintained to the level near that in the control, if we would give effective pancreatic juice drainage, even after about 50% resection of the pancreas.

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