Comparative Studies of Plasma Secretin Response after Reconstructive Surgery of the Stomach and Pancreas

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The postprandial plasma secretin response was examined in ten normal persons, seven patients with a Billroth I and seven with a Billroth II anastomosis after subtotal gastrectomy, seven with a Roux-en-Y anastomosis, two with an interposed jejunal anastomosis, and five with a modified Child's anastomosis after pancreatoduodenectomy. The postprandial plasma secretin response in patients with Billroth I anastomosis was better than that in patients with a Billroth II anastomosis but was less than that of normal subjects. Although no postprandial secretin response was noted in Roux-en-Y anastomosis after total gastrectomy, a response was seen in patients with the interposed jejunal anastomosis because the digested food passed through the duodenum, but it was less than that for Billroth I and II patients and normal controls. After a modified Child's reconstruction, the postprandial secretin response was similar to that of patients with the Billroth II, which preserved the duodenum. A patient with a modified Child's reconstruction was examined 12 years after surgery and had the same response as other patients with the modified Child's reconstruction and those with a Billroth II anastomosis within 2 months after surgery. After ingestion of hydrochloride solution, the plasma secretin release in patients with a Billroth I and II anastomosis after subtotal gastrectomy and Roux-en-Y anastomosis after total gastrectomy had a better response than after a meal, but this was less than in normal subjects. The authors suggest that careful selection of intestine for the gastrointestinal anastomosis, which contains many secretin secretory cells, is important to obtain endogenous secretin release. For gastrojejunostomy after pancreatoduodenectomy, a method preserving the pylorus is better than the usual gastrojejunostomy because it maintains gastric acid. The ingestion of secretin stimulants, such as hydrochloride, may help to prevent pancreatic dysfunction after gastrectomy and other surgical reconstructions.

PANCREATIC DYSFUNCTION usually occurs after various gastrointestinal reconstructions that result in abnormalities in the release of gastrointestinal hormones, such as secretin. Secretin is thought to be released mainly from the duodenum by the effect of hydrochloric acid and the potent stimulus of pancreatic secretin. After gastrectomy and subsequent procedures, factors such as reduced gastric secretion, increased emptying from the gastric remnant, alteration of pH, and the physical state of food leaving the gastric remnant may modify the response occurring in the bypassed intestine. After pancreatoduodenectomy, the duodenum is completely excised, removing the main source of secretin release.

It is important to investigate the postpradial secretin response in patients with various anatomic anastomosis following gastrectomy and pancreatoduodenectomy to understand the change in the pancreatic function.

We investigated the postprandial secretin response 2 months after the following surgical procedures: Billroth I and II anastomosis after subtotal gastrectomy, Roux-en-Y anastomosis and interposed jejunal anastomosis following total gastrectomy, and anastomosis by a modified Child's reconstruction after pancreatoduodenectomy.

Material and Methods

We examined ten normal subjects and seven patients with Billroth I and II and seven with Roux-en-Y anastomoses, two with an interposed jejunal anastomosis following gastrectomy, and five with a modified Child's reconstruction following pancreatoduodenectomy. There were 24 men and 14 women with a mean age of 56 years. At the time of gastric surgery there was no metastasis or pancreatic involvement. Pancreatoduodenectomy was performed on patients with carcinoma of the ampulla of Vater and carcinoma of the head of the pancreas. The test meal was given 2 months after operation, except in one patient, who received it 12 years after pancreatoduodenectomy. After 12 hours of

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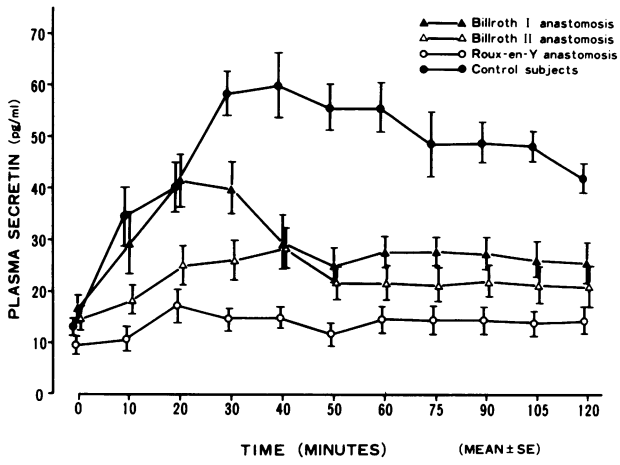

FIG. 1. Postprandial plasma secretin response in control subjects and in patients with Billroth I and II and Roux-en-Y anastomoses after gastrectomy.

fasting, a glass electrode for recording luminal pH was inserted nasally into the duodenum or the jejunum at the anastomotic site and luminal pH was continuously recorded for 2 hours after ingestion of the meal, which consisted of 150 g of cooked beef, a slice of bread, and 100 ml of milk.

Blood samples were drawn from a peripheral vein for plasma secretin assay at 10-minute intervals for 120 minutes.

Five patients in each of the groups, Billroth I, Billroth II, and Roux-en-Y, received 60 ml of a mixture of 10 ml of 0.03 N hydrochloric acid, 7 ml of saccharin, and 83 ml of water (pH 1.0), which is often used postoperatively to stimulate appetite, and plasma secretin response was examined every 10 minutes for 40 minutes.

Heparinized venous blood samples were kept on ice and separated by refrigerated centrifugation at 4 C at 2600 rpm for 10 minutes. Plasma, treated with aprotinin, was stored at −20 C until assay. The plasma concentration of secretin was determined by the radioimmunoassay method of Chang and Chey.[1]

The results were expressed as mean ± standard error, and the Student's *t*-test was used for statistical significance. A p value of <0.05 was considered a significant difference.

Results

Comparative results of the postprandial plasma secretin response in control subjects and in patients with Billroth I and II and Roux-en-Y anastomoses after gastrectomy are shown in Figure 1.

In control subjects, the postprandial plasma secretin response increased significantly from a mean fasting value of 13.0 pg/ml (±1.8 SE) to a mean peak of 60.1 pg/ml (±6.4 SE) at 40 minutes. Mean plasma secretin concentrations from 34.6 pg/ml (±5.7 SE) to 42.2 pg/ml (± 2.9 SE) were maintained throughout the experiments, which were significantly higher than the fasting measurement ($p < 0.05$) and were accompanied by a decreased luminal pH of 4.0–5.0, although duodenal pH frequently fluctuated.

In Billroth I patients, the fasting duodenal pH ranged from 6.0 to 7.0 and decreased to about 4.5 within 20 minutes before gradually returning to 5.5–6.5. The mean fasting plasma secretin concentration in these patients was 14.6 pg/ml (±2.6 SE), which was similar to that of normal subjects. Postprandial mean peak plasma secretin concentrations of 41.6 pg/ml (±4.8 SE) were observed as early as 20 minutes; these returned to near fasting values within 20–120 minutes.

The fasting jejunal pH after Billroth II was 7.0–8.0 but declined to 4.0–5.0 within 35 minutes and fluctuated between 6.0 and 7.0 during the last 60 minutes postprandially. Although the mean fasting plasma secretin (14.6 ± 2.6 pg/ml) was similar in Billroth I patients and normal subjects, the postprandial secretin in these patients was much lower than that observed for Billroth I patients. Mean peak levels of 28.5 pg/ml (±3.7 SE) were observed at 40 minutes.

In patients with Roux-en-Y anastomoses after total gastrectomy, the jejunal pH of 6.5 changed little for 120 minutes postprandially, and there was no increase in plasma secretin from the mean fasting value of 9.5 pg/ml (±1.6 SE).

Although only two patients were studied, the postprandial secretin response in patients with an interposed jejunal anastomosis after total gastrectomy was different from that of patients with Roux-en-Y anastomoses because secretin increased from the fasting value of 9.8

TABLE 1. *Postprandial Plasma Secretin Response in Patients with an Interposed Jejunal Anastomosis*

	Time										
	Before	10	20	30	40	50	60	75	90	105	120
1	8.6	19.9	25.9	15.4	8.1	12.7	11.2	12.6	10.9	12.5	9.8
2	11.0	26.3	33.1	30.2	27.9	18.5	20.2	16.4	19.1	15.7	14.8
Mean	9.8	23.1	29.5	22.8	18.0	15.6	15.7	14.5	15.0	14.1	12.3

and 10.0 pg/ml to peaks of 29.5 and 29.0 pg/ml at 20 minutes. Throughout the experiment, it was slightly higher than in the fasting state (Table 1).

The results of postprandial plasma secretin response in patients with pancreatoduodenectomy, patients with Billroth II, which has the same anastomosis with stomach and jejunum, and control subjects are compared in Figure 2.

In four patients with pancreatoduodenectomy, the jujunal pH and plasma secretin response were not different from those of Billroth II patients. Postprandial secretin increased from a mean fasting value of 6.0 pg/ml (±1.3 SE) to a mean peak of 25.6 pg/ml (±2.2 SE) at 50 minutes. The mean postprandial plasma secretin concentration was higher than the mean fasting measurement throughout the experiment. A patient who was examined 12 years after pancreatoduodenectomy showed almost the same postprandial secretin response as other patients with a pancreatoduodenectomy (Table 2).

The mean plasma secretin response in patients with Billroth I and II and Roux-en-Y anastomoses after ingestion of hydrochloride solution is shown in Figure 3.

After ingestion of this solution (pH 1.0), duodenal and jejunal pH decreased from the fasting value of 6.0 to less than 3.0 within a few minutes and then increased gradually, returning to the pretest value at 20 minutes. Mean plasma secretin increased from the mean fasting concentrations 15.0 pg/ml (±3.0 SE) in patients with Billroth I, 14.0 pg/ml (±2.0 SE) in patients with Billroth II, and 10.0 pg/ml (±2.0 SE) in patients with Roux-en-Y anastomoses to mean peak values of 52.0 pg/ml (±7.0 SE), 36.0 pg/ml (±5.0 SE), and 29.0 pg/ml (±6.0 SE), respectively, at 5 minutes. They all declined gradually to the pretest values at 40 minutes.

Discussion

Although there were no measurements of endogenous secretin release after a test meal, it has been suggested that impairment of endogenous secretin release following a meal may be related to the decreased pancreatic secretion after Billroth I.[2,3]

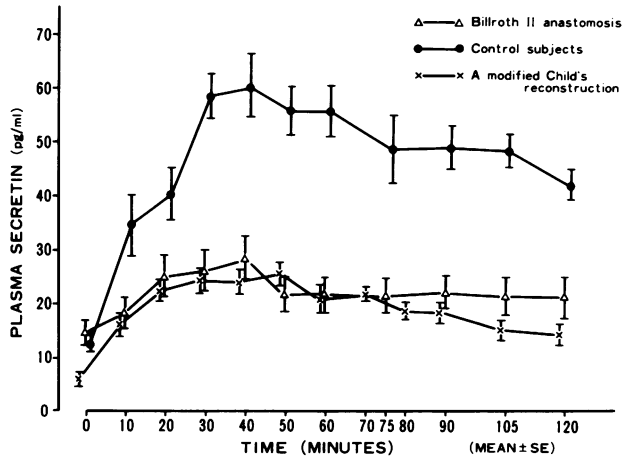

FIG. 2. Postprandial plasma secretin response in control subjects and in patients with Billroth II anastomosis after gastrectomy and a modified Child's reconstruction after pancreatoduodenectomy.

Plasma secretin response after Billroth I anastomosis increased significantly when the duodenal pH was less than 4.5, although the response was lower than normal and the duration was shorter. This may be related to the decrease in duodenal acid and rapid gastric emptying, which are usually observed after gastrectomy.

In patients with Billroth II anastomosis although the jejunal pH decreased to less than 5.0 as for Billroth I anastomosis, the plasma secretin response after the meal increased slightly and was lower than that observed after Billroth I. This difference between Billroth I and II anastomoses may be related to food bypassing the duodenum.

Secretin secretory cells are most abundant in the duodenum, with a decreasing density from the duodenum to the ileum.[4,5] This distribution may alter the postprandial secretin response in patients with the Billroth I and II anastomoses. Similar results were found in studies of exocrine pancreatic secretion, in which the pancreatic volume output decreased in 30% of the patients with Billroth I and was much lower in those with Billroth II.[2]

In the Roux-en-Y anastomosis after total gastrectomy, no secretin response was observed in the postprandial state, and the jejunal pH was 6.0–7.0 throughout because

TABLE 2. *Postprandial Plasma Secretin Response in a Patient 12 Years after Pancreatoduodenectomy*

	Time										
Case	Before Meal	10	20	30	40	50	60	70	80	90	105	120
1	4.1	9.8	16.9	18.1	24.1	23.9	22.3	18.7	14.4	11.6	8.5	7.8

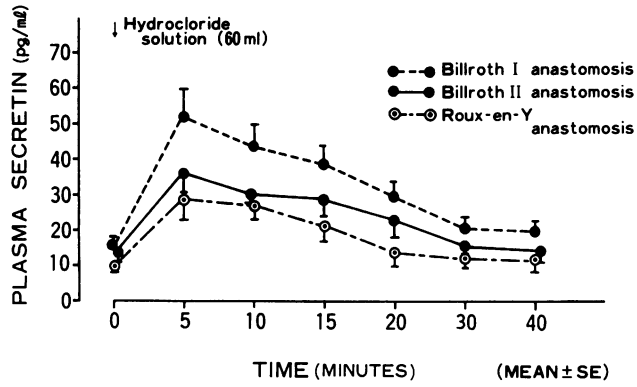

FIG. 3. Mean plasma secretin response in patients with Billroth I and II and Roux-en-Y anastomoses after ingestion of hydrochloride solution.

of the lack of gastric acid and the effect of the duodenal bypass on food digestion after total gastrectomy. In interposed jejunal anastomosis after total gastrectomy, even though the jejunal pH was similar to that in Roux-en-Y anastomosis, plasma secretin increased at 20 minutes, which suggests that a secretin releasing factor other than gastric acid existed and that the passage of food through the duodenum is important for the release of secretin.

In patients with a modified Child's reconstruction after pancreatoduodenectomy, although the duodenum, which is thought to be a main source of secretin, is completely removed, the increase plasma secretin response after a meal was similar to that after Billroth II. A patient who was examined 12 years after pancreatoduodenectomy showed the same plasma secretin response as other patients who had had pancreatoduodenectomy and Billroth II. Thus, the plasma secretin response after a meal was related to the anastomotic region and was not affected by the absence of the duodenum.

It has been reported that after pancreatoduodenectomy, blood secretin levels were high in the preoperative group with occlusion of the biliary tract and remained so after operation after hydrochloride loading.[6] The same report suggests that the high secretin before operation was due to a metabolic disturbance of secretin and not to increased secretion. Secretin concentrations were almost normal 1 month postoperatively.

Although we did not examine preoperative secretin in patients with obstructive jaundice who had subsequently undergone pancreatoduodenectomy, our results showed that the postprandial secretin response was not high compared with the controls and that the mean fasting secretin returned to normal within 2 months. The discrepancies between the results may be due to either the difference in the method for plasma secretin measurement or the different stimulation from either the meat meal or hydrochloride ingestion. However, the latter can be rejected because we showed that the plasma secretin response after hydrochloride loading in patients with Billroth I and II and Roux-en-Y anastomoses was greater than that after the meat meal but was less than that after a meal in normal subjects. The high plasma secretin found may be because plasma interfered with the assay, giving spuriously high secretin values.[7]

We have reported that the infusion of bile into the duodenum released secretin.[8] This suggests that when gastric acid is decreased or absent from the duodenum after gastrectomy, bile, which is a weak stimulant, passes into the duodenum and releases endogenous secretin. However, the postprandial plasma secretin response in Billroth II anastomosis, in which bile drained into the duodenum, was similar to that in patients with a modified Child's anastomosis after pancreatoduodenectomy, in which bile drained into the jejunum. Thus, bile alone seems to be too weak to stimulate endogenous secretin release.

Although it has been suggested that the upper jejunum, less than 10 cm below the ligament of Treitz, should be preserved for plasma secretin release after pancreatoduodenectomy,[6] there were no differences in postprandial plasma secretin response between the patients with Billroth II and the modified Child's reconstruction. Here, the jejunum, 20 cm below the ligament of Treitz, was used for gastrointestinal anastomosis. With the modified Child's anastomosis, the jejunum, 40 cm below the ligament of Treitz, was used, while in Billroth II, the duodenum is preserved. These results indicate that the duodenum played no role in releasing secretin unless digested food or gastric acid passed through it. When surgical reconstruction is performed, it is important to select the adequate portion of intestine for anastomosis, which contains high-density secretin secretory cells.

It is clear that the Billroth I anastomosis after subtotal gastrectomy and the interposed jejunal anastomosis after total gastrectomy, by which digested food can pass through the duodenum, are better methods than the Billroth II and Roux-en-Y anastomoses for obtaining postprandial secretin release.

When gastrojejunal anastomosis after pancreatoduodenectomy, using either Whipple's or Child's operation, is performed, preservation of the pylorus is better than the usual gastrojejunostomy for obtaining pastprandial secretin release because gastric acid secretion is maintained.

The impairment of secretin release observed after gastrectomy and other surgical reconstructions may be important for postoperative pancreatic dysfunction.

Our experimental results show that endogenous secretin release in patients with Billroth I and II and Roux-en-Y anastomoses after ingestion of hydrochloride solution was better than that after a meat meal, although concentrations were lower than in normal subjects. We suggest that secretin stimulants, such as hydrochloride and oleate,[9] be given to patients after gastric surgery to prevent pancreatic dysfunction related to secretin release.

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