Postprandial Plasma Gastrin and Secretin Concentrations After a Pancreatoduodenectomy

A Comparison Between a Pylorus-Preserving Pancreatoduodenectomy and the Whipple Procedure

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Based on the observation that patients given a pylorus-preserving pancreatoduodenectomy maintain higher gut hormonal levels than do patients who have received the classic Whipple surgical procedure, which seems most likely due to a postoperative difference in the remaining digestive tract, the postprandial plasma gastrin and secretin concentrations in patients who have received either surgery have been evaluated to examine this difference more fully. The subjects were 20 patients treated by a pylolus-preserving operation and 27 patients treated by the Whipple procedure whose concentrations were compared with those of 8 healthy control patients. The postprandial plasma gastrin concentrations were found to be similar in patients given the pylorus-preserving operation and the controls and were significantly lower in patients who underwent the Whipple procedure ($p<0.05$). Similarly, the postprandial plasma secretin concentrations did not differ in these two groups, whereas patients who underwent the Whipple procedure showed significantly lower concentrations at 60, 90, and 120 minutes ($p<0.05$). The above findings, as well as supportive data in the literature, indicate that the duodenal bulb and the gastric antrum, which are resected in the Whipple procedure and are kept in the pylorus-preserving operation, seem to play important roles in the gut hormonal release and that the pylorus-preserving operation is the superior surgical technique in terms of gastrin and secretin release.

SINCE WHIPPLE AND HIS ASSOCIATES reported on a surgical operation involving a two-stage resection in 1935[1] and on a one-stage resection in 1945,[2] the Whipple operation has been generally performed for a pancreatoduodenectomy, which entails the removal of the gastric antrum, the pyloric ring, and the entire duodenum together with the head of the pancreas. Certain surgeons using this technique, however, have noted some problems they have encountered, such as postgastrectomy sequelae and a postoperative weight loss.[3,4] In 1978 a new surgical technique was documented when Travero and Longmire reported on their operational procedure in which the entire stomach and duodenal bulb are preserved.[5,6] This pylorus-preserving pancreatoduodenectomy was found to produce no sequelae associated with postgastric surgery and allows for a postoperative weight gain.[3,4,7] These advantages are considered to be caused by the fact that the whole stomach, which plays an essential role in digestion and absorption, is preserved, while it is extensively resected when using the Whipple procedure.

Thus we made an assumption that significant measurable differences in the gut hormonal levels would be found between these two surgical procedures. In other words, the difference between a Whipple resection operation and a pylorus-preserving pancreatoduodenectomy theoretically should correlate with the postoperative difference seen in the gut hormonal levels because the number of gut hormone-releasing cells depends on the number of such cells left after surgery. Gastrin-releasing cells are mainly distributed in the gastric antrum and the pyloric ring, followed by those in the duodenum and a few cells that also have been observed in the jejunum. Furthermore, the distribution of the secretin-releasing cells is highest in the duodenum, followed by other parts of the duodenum, and the jejunum. Few secretin-releasing cells, as has been reported, are distributed in the lower portion of the small intestine.[8] Should the Whipple procedure be used, most of the gastrin-releasing cells are removed, while they are preserved in the pylorus-preserving operation. Similarly, when using the Whipple procedure the secretin-releasing cells are preserved only in the upper jejunum, whereas

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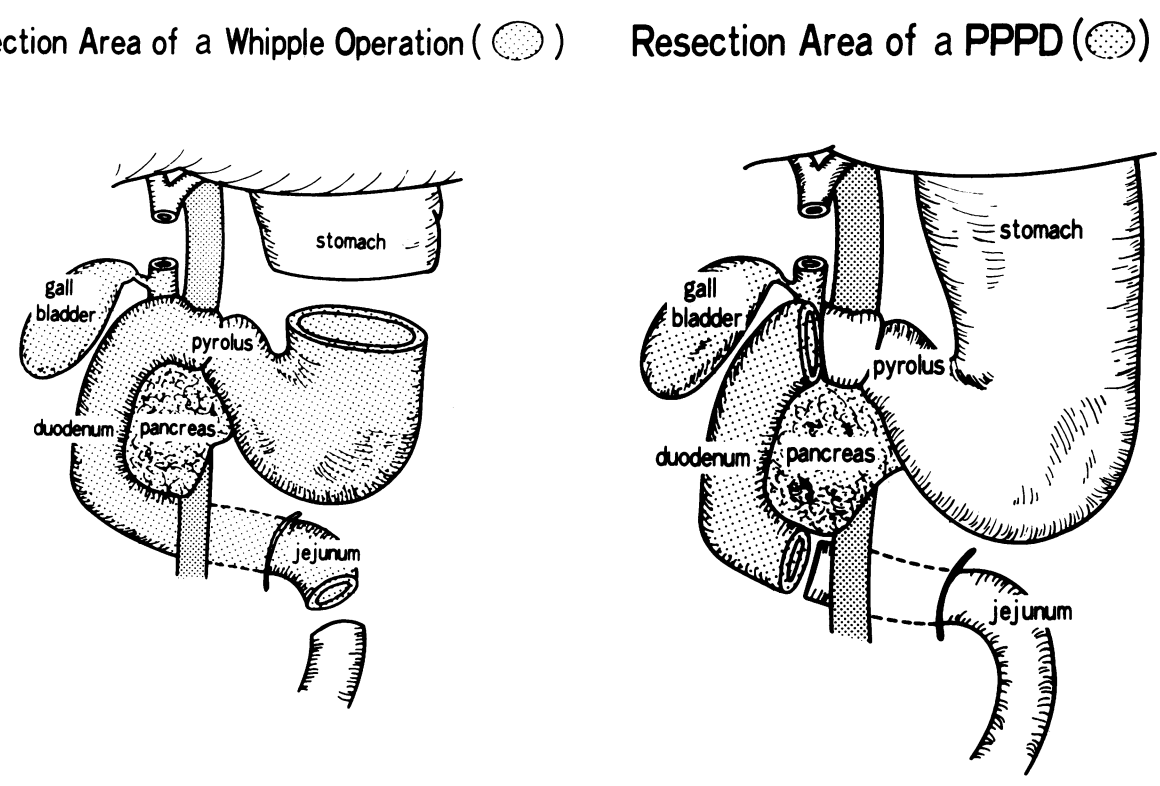

FIG. 1. Resected area of a Whipple operation and a pylorus-preserving pancreatoduodenectomy.

they are preserved in the duodenal bulb, the third and fourth portion of the duodenum, and in the jejunum with the newer surgical technique. Therefore, in order to substantiate our hypothesis, we examined and compared the postprandial plasma gastrin and secretin concentrations of patients who had been treated by either surgical procedure.

Materials and Methods

The serum gastrin and secretin levels were examined in both the fasting and postprandial state in 55 subjects: 20 patients who underwent the pylorus-preserving surgical procedure, 27 patients who underwent the Whipple procedure, and 8 healthy controls. No abnormalities were found in the routine blood biochemical examinations of these patients.

To repeat the differences between these two surgical procedures in patients who had undergone the Whipple operation, the gastric antrum, the pyloric ring, and the entire duodenum had been removed together with the head of the pancreas (Fig. 1A). In contrast, in patients who had undergone the pylorus-preserving procedure, the entire stomach, the pyloric ring, and the duodenal bulb were preserved. In this latter surgery, the duodenum was dissected about 4 cm below the pyloric ring and at the third or fourth segment from the origin of the jejunum, resulting in a resection of the second segment of the duodenum together with the head of the pancreas (Fig. 1B). The gastrointestinal tract had been reconstructed by a pancreatojejunostomy in 8 of the patients studied and by a pancreatogastrostomy in 10 other patients.

Each subject, regardless of the surgical procedure, ingested a standard meal that consisted of 2 slices of toast, 8 g of butter, 1 boiled egg, and 180 ml of soup, totaling 326 Kcal. Serial blood samples were obtained 30 minutes before the end of fasting state, and 30 minutes, 90 minutes, and 120 minutes after the meal ingestion.

Blood samples were kept in ice-cooled flasks containing heparin and were centrifuged at 3000 rpm for 15 minutes. After separation of the serum, Trasylol (500 KIU/ml) was added, and the samples kept at −20 C until measurements were conducted. Plasma gastrin concentrations were determined by radioimmunoassay (RIA). Plasma secretin concentrations also were determined by radioimmunoassay, using ethanol extraction according to Chey's method.[9-11]

Results were expressed as means ±SE and the Student's t-test was used to evaluate the statistical results.

Results

Fasting Plasma Gastrin Concentrations

Values of the fasting and postprandial plasma gastrin concentrations are shown in Table 1. No difference was

TABLE 1. *Values in the Fasting and Postprandial Plasma Gastrin Concentrations*

	Before Meal	30 min.	60 min.	90 min.	120 min.	
Control	145 ± 34	356 ± 72	274 ± 75	251 ± 65	222 ± 50	(pg/ml)
PPPD*	111 ± 21	313 ± 81	224 ± 60	202 ± 61	206 ± 65	(pg/ml)
Whipple Procedure	49 ± 5	43 ± 3	48 ± 7	33 ± 4	35 ± 4	(pg/ml)

* PPPD: Pylorus-preserving pancrestodenectomy

observed in the mean fasting plasma gastrin concentrations among the 8 controls, the 20 patients who had been treated by pylorus-preserving operation, and the 27 patients treated by the Whipple procedure.

Changes in Postprandial Plasma Gastrin Concentrations

Changes in the plasma gastrin concentration after the ingestion of the test meal are shown in Figure 2. In the controls, the gastrin concentration reached its maximum value in 30 minutes and decreased thereafter. The patients treated by the pylorus-preserving operation showed a similar result. In the patients treated by the Whipple procedure, however, the blood gastrin level did not increase postprandially because the values seen were significantly lower than those of the other two groups ($p<0.05$).

The integrated gastrin release (IGR) values at 120 minutes, reflecting the effects of the test meal on the blood gastrin release, are shown in Figure 3. No difference was observed in the mean IGR value between the controls (14,640±3844 min×pg/ml) and the patients treated by the pylorus-preserving operation (17,767±6187 min ×pg/ml). The IGR values in the Whipple-treated patients, however, were significantly lower (30±56 min×pg/ml) than that of the other two groups ($p<0.05$).

Fasting Plasma Secretin Concentrations

Values of the fasting and postprandial plasma secretin concentrations are shown in Table 2. No significant differences were observed in the mean fasting plasma secretin concentrations among the controls or either of the other two groups.

Changes in Postprandial Plasma Secretin Concentrations

Changes in the blood secretin concentrations after ingestion of the test meal are shown in Figure 4. In the controls, the postprandial plasma secretin concentrations increased until reaching a peak at 60 minutes and decreased thereafter. The patients treated by the pylorus-preserving operation showed a similar result. In the patients treated by the Whipple procedure, however, the secretin concentrations were similar to the other two groups

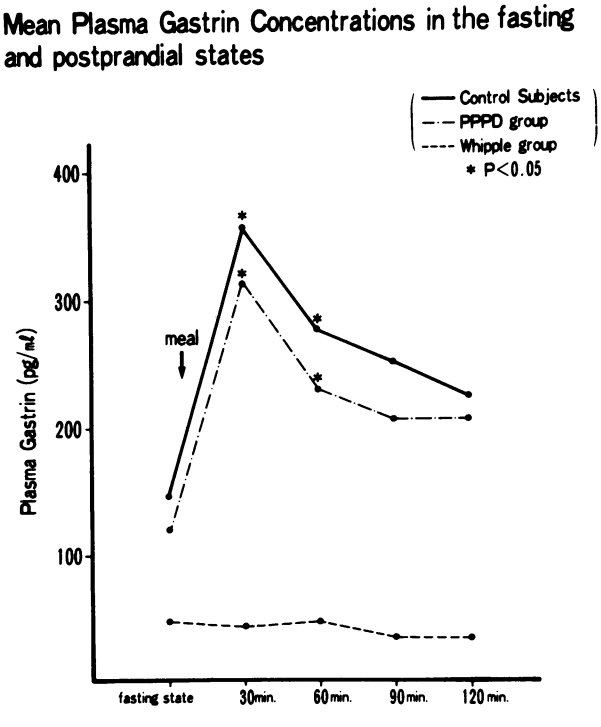

FIG. 2. Changes in the plasma gastrin concentrations after the ingestion of the test meal.

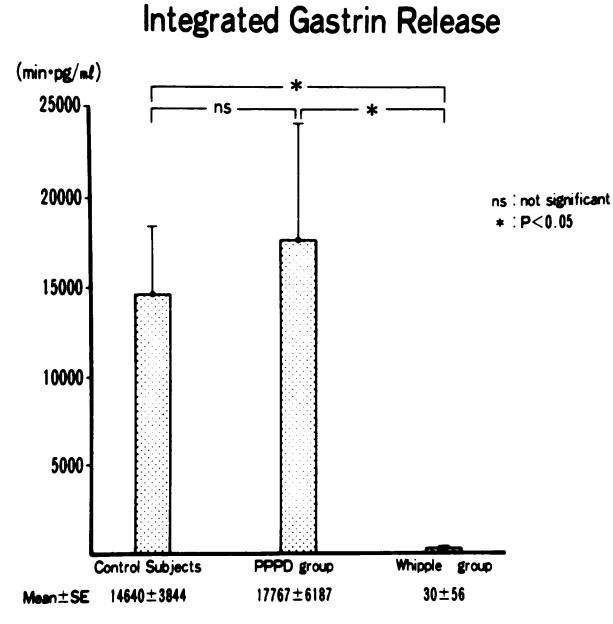

FIG. 3. Integrated gastrin release at 120 minutes.

TABLE 2. *Values in the Fasting and Postprandial Plasma Secretin Concentrations*

	Before Meal	30 min.	60 min.	90 min.	120 min.	
Control	3.5 ± 1.1	5.3 ± 1.1	8.1 ± 1.7	6.9 ± 1.6	6.5 ± 1.3	(pg/ml)
PPPD*	3.7 ± 0.8	5.2 ± 1.4	7.5 ± 1.5	6.3 ± 0.3	6.1 ± 1.1	(pg/ml)
Whipple Procedure	4.0 ± 0.7	6.1 ± 1.4	5.5 ± 0.7	5.8 ± 1.1	4.0 ± 1.3	(pg/ml)

* PPPD: Pylorus-preserving pancreatoduodenectomy

at 30 minutes, but then these values were significantly lower at 60 minutes, 90 minutes, and 120 minutes ($p<0.05$).

The integrated secretin release (ISR) values at 120 minutes, reflecting the effects of the meal on the blood secretin release, are shown in Figure 5. No difference was observed in the ISR values between the controls and the patients treated by pylorus-preserving operation. In contrast, however, the ISR values in the Whipple-treated patients were significantly lower ($p<0.05$).

Discussion

With the development of radioimmunoassay methods of high sensitivity and specificity, the physiological importance of the various gut hormones is becoming understood more clearly. Further, studies using the immunofluorescent antibody techniques are able to show the distribution of the cells secreting these hormones. Although studies of the plasma gastrin and secretin levels after a Whipple operation have been reported,[12,13] it must be emphasized that the measurements in these past studies were performed for a comparison of this conventional surgical procedure and a gastrectomy, or for a comparison between the preoperative and the postoperative state. Thus, although differences between the gut hormonal levels also were observed, two basically different operations were being compared. One was a pancreatoduodenectomy and the other was a gastrectomy. In this instance, we have compared the classic Whipple procedure and a pylorus-preserving pancreatoduodenectomy, in which the portion of the digestive tract containing abundant gut hormone-releasing cells is resected in the former surgical technique while it is preserved in the latter.

Postprandially, no increase in the plasma gastrin levels was observed in the patients who had undergone the Whipple procedure, which involves a partial gastrectomy and a total duodenectomy. This lack of increase may be caused by the resection of a region in which gastrin-releasing cells are distributed.[8] On the other hand, results showing a gastrin response similar to that of the healthy controls were obtained for patients who had undergone the alternative surgery that preserved the gastric antrum, the pyloric ring, and the duodenal bulb.

These results are bolstered by a report of Pearlmann et al.[14] that maintains that a pyloric-preserving pancreatoduodenectomy does not lead to either gastric hyperacidity

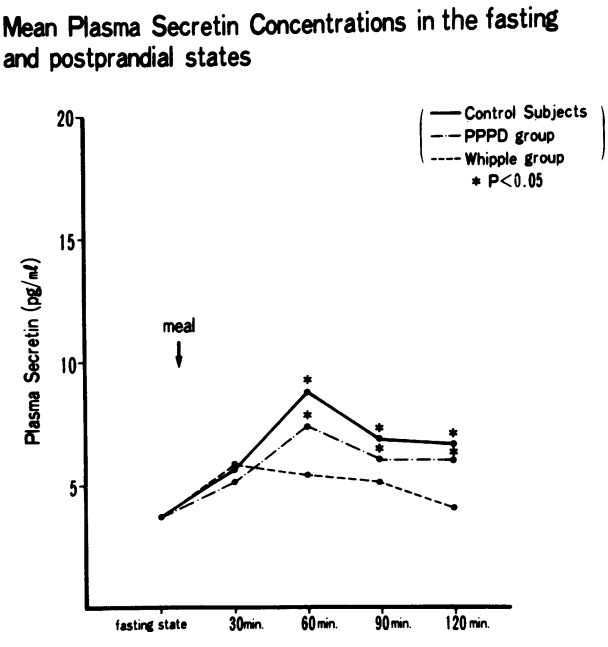

FIG. 4. Changes in the plasma secretion concentrations after the ingestion of the test meal.

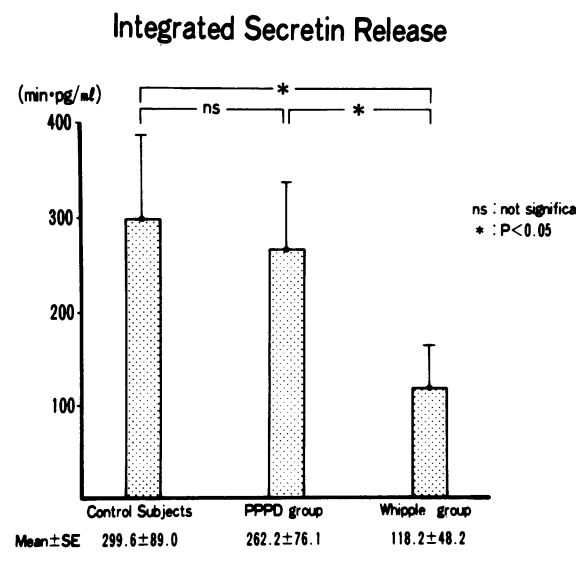

FIG. 5. Integrated secretin release at 120 minutes.

or persistant hypergastrinemia. Yamashita et al.[12] have observed that gastrin-releasing cells are mainly distributed in the gastric antrum and the duodenum, and Lechago et al.[15] have found that these cells are more frequently seen in the mucosa than in the muscular tunics. Our results also suggest that the gastric antrum and the duodenal bulb can compensate for the loss of the gastrin response capacity of the resected part of the duodenum.

The plasma secretin concentrations measured at various institutions have varied widely even among healthy subjects until the development of the plasma ethanol extraction method by Chey et al.,[9] Watanabe et al.,[10] and Shiratori et al.[11] This method and the use of a high-specificity antiserum have led to highly sensitive radioimmunoassays and far more reliable results.

In the patients treated by the Whipple procedure, the plasma secretin concentrations increased slightly at 30 minutes after the ingestion of the test meal, although this was not statistically significant. These concentrations decreased thereafter, suggesting a lack of response in the lower jejunum.

In contrast, in the healthy controls and in the patients who had undergone the pylorus-preserving operation, the postprandial plasma secretin concentrations increased at 60 minutes and then decreased. The values in these two groups at 60, 90, and 120 minutes were significantly higher than in the patients treated by the Whipple procedure. Distribution of the secretin-releasing cells was found to be highest in the duodenum, followed by those in the upper jejunum. Few secretin-releasing cells have been found distributed in the stomach.[9,12] The similarity in the secretin levels among the patients treated by pylorus-preserving operation and the controls suggests that the secretin-releasing cells considered to be present in the duodenum are concentrated on the bulb, or that the secretin-releasing capacity of the entire duodenum can be compensated by those cells on the bulb. In addition, the higher postprandial concentrations seen after the pylorus-preserving operation may be caused by a greater capacity of the duodenal bulb for releasing secretin than the jejunum.

Because the gastric antrum and the entire duodenum are resected in the Whipple procedure, the acidity of the gastric juice and gastric secretin was seen to decrease in response to the test meal. In sharp contrast, in those who had had the pylorus-preserving operation, gastric secretin was maintained at a normal level after the meal. There are other differences. As has been reported previously,[7] roughly 70% of the preoperative weight is maintained by patients given the Whipple procedure, whereas weight loss is negligible after the pylorus-preserving operation. One reason for this is that the pylorus-preserving operation allows for the ingestion of larger amounts of food. Another possible reason is that digestive function is maintained after operation, i.e., the normal acidity of the gastric juice produced by the normal gastrin response and the normal digestion time of foods in the stomach. The greater capacity for the release of secretin after the pylorus-preserving operation, in contrast to the Whipple surgical procedure, suggests a better postoperative pancreatic function.

Thus, from the above results, we conclude that the duodenal bulb and the gastric antrum, which are resected in the Whipple operation and preserved in the pylorus-preserving operation, play important roles in the gut hormonal release and that a pylorus-preserving pancreatoduodenectomy is the superior surgical technique in terms of the gastrin and secretin release.

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