Influence of In Situ Neural Isolation of Jejunoileum on Postprandial Pancreatobiliary Secretion and Gastric Emptying

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Our aims were to examine the influence of neural isolation of the jejunoileum on postprandial pancreatobiliary secretion. In four dogs, duodenal perfusion and aspiration catheters were implanted, and serosal electrodes were placed along the proximal small bowel. Control studies of gastric emptying, output of bile acids and amylase, and plasma concentrations of peptide YY and neurotensin were performed on three occasions following ingestion of a 340-kcal mixed-nutrient liquid meal. The dogs then underwent our model of in situ jejunoileal neural isolation, and the meal studies were repeated. Neural isolation, when compared to control, did not affect either postprandial conversion of intestinal myoelectric activity to the "fed" pattern, gastric emptying (T1/2,X \pm SE of the liquid meal (74 \pm 6 vs 79 \pm 7 min; P > 0.05), or cumulative amylase output (373 \pm 59 vs 305 \pm 66 kU; P > 0.05). Neural isolation decreased cumulative postprandial bile acid output from 6.6 \pm 0.9 mM to 3.4 \pm 1.1 mM (P < 0.05) and increased postprandial plasma concentrations of peptide YY and neurotensin. Our findings suggest that the jejunoileal denervation that accompanies the in situ neural isolation of the jejunoileum is not associated with changes in postprandial motility patterns, gastric emptying, or pancreatic amylase secretion. Loss of this innervation, however, may decrease postprandial output of bile acids and lead to a compensatory increase in the postprandial release of neurotensin and peptide YY.

KEY WORDS: extrinsic denervation; intestinal transplantation; pancreatic secretion; gastric emptying; bile acid output; peptide YY; neurotensin.

Intestinal transplantation will likely become a clinical reality in the near future (1). To begin investigating the effects of intestinal transplantation upon a variety of gastrointestinal functions, we have established a canine model of in situ neural isolation of the entire jejunoileum (2-4). By using this model, immunologic effects are eliminated as are any effects of ischemia that would occur during harvest of a jejunoileal graft for transplantation. Consequently, physiologic effects secondary to extrinsic denervation are eliminated. In this study, we have investigated the effect of neural isolation on postprandial motility, gastric emptying, and secretion of bile acids and amylase.
denervation of the transplanted intestine can be investigated independently from immunologic or ischemic effects that might affect physiologic functions. We have confirmed that the entire jejunooileum in our model is extrinsically denervated by demonstrating that tissue concentrations of catecholamines in the jejunum and ileum are markedly decreased and remain so for greater than three months (3, 4).

Our knowledge of the effects of intestinal transplantation on physiologic enteric functions is limited. Basic studies are needed that assess the physiology of the transplanted gut and the effects of the transplanted intestine on other nontransplanted but related organ systems of the gut. Under normal postprandial conditions, nutrients increase both exocrine pancreatic secretion and bile acid delivery into the small intestine by releasing enteric hormones and/or by stimulating intestinopancreatic and intestinobiliary reflexes (5). In the present study, we sought to determine the effects of complete in vivo neural isolation of the entire canine jejunooileum on gastric emptying, secretion of amy- lase and bile acids, postprandial myoelectric activity of the small intestine, and plasma concentrations of peptide YY and neurotensin in the early period following oral ingestion of a mixed-nutrient, liquid meal. Our hypotheses were that in vivo neural isolation of the entire jejunooileum might lead to a decrease in pancreatic exocrine secretion but would have no effect on gastric emptying or on delivery of bile acids into the duodenum. We chose to study peptide YY and neurotensin because of their distribution in the jejunooileum and their potential role as putative regulatory peptides in pancreatic secretion.

MATERIALS AND METHODS

Experimental Preparation. Surgical procedures and subsequent care and conduct of experiments were performed according to criteria set forth by the Animal Care and Use Committee of the Mayo Foundation in accordance with the guidelines of the National Institutes of Health and the Public Health Service Policy on the Humane Use and Care of Laboratory Animals. Four healthy, female, mongrel dogs ranging in weight from 13.0 to 19.5 kg were subjected to celiotomy using intravenous pentothal sodium (25 mg/kg) and inhaled halothane for anesthesia. Two catheters were inserted through a proximal duodenotomy. The tip of the infusion catheter (OD, 2 mm) was positioned near the entrance of the main pancreatic duct and the tip of the aspiration catheter (OD, 3 mm) was placed 18 cm distally (Figure 1A). By infusing a nonabsorbable marker through the proximal catheter and aspirating duodenal contents through the distal catheter, we could measure duodenal flow (via marker dilution) and thereby quantitate recovery of gastric marker (gastric emptying) and biliopancreatic secretion. Eight unipolar Ag-AgCl serosal electrodes were implanted along the duodenum and jejunum. The electrodes were connected by insulated copper wires to a multipinned socket within a flanged stainless-steel cannula that was fixed within the abdominal wall. The animals were allowed to recover for a two-week period prior to beginning control studies.

After completion of these control experiments, the same dogs underwent our model of in situ neural isolation of the entire jejunooileum. During this procedure, we divide all neural, myogenic, lymphatic, and connective tissue continuity with the jejunooileum except for the superior mesenteric artery and vein (3). After transecting the ligament of Treitz, the duodenum is fully mobilized and divided just distal to the region supplied by the inferior pancreatoduodenal artery (Figure 1B), thereby interrupting intrinsic myoneural continuity with the proximal, innervated duodenum and any extrinsic nerves traveling distally within the wall of the bowel or its mesentery. The mesentery is then transected in radial fashion back to the upper mesenteric artery and vein just distal to the inferior pancreatoduodenal vessels at the base of the small bowel mesentery. Similarly, the terminal ileum is transected and its mesentery divided in radial fashion back to the same region of the superior mesenteric vessels. Next, all extrinsic nerves, lymphatics, and connective tissues at the base of the mesentery are ligated. During this step, optical magnification is used to isolate and meticulously excise the investing adventitia of the superior mesenteric artery and vein for a length of 2 cm. At this point, the distal duodenum, the entire jeju-