Comparison of Somatostatin and Pancreastatin on Secretion of Gastrin, Pancreatic Polypeptide, and Peptide YY

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Abstract. **The purpose of this study was to compare the effects of pancreastatin (PST) (400 pmol/kg/hr) and somatostatin (SRIF) (400 pmol/kg/hr) on food-induced release of gastrin, pancreatic polypeptide (PP), and peptide YY (PYY) in conscious dogs. The present findings indicate that SRIF is more potent than PST on the inhibition of food-induced release of PP; that SRIF and PST do not influence food-induced release of gastrin; and that PST cannot inhibit food-induced release of PYY, whereas SRIF inhibits PYY release in a potent fashion.** [P.S.E.B.M. 1997, Vol 215]

Pancreastatin (PST) is a recently discovered peptide from porcine duodenal extracts (1). The name, pancreastatin, was derived from its inhibitory action on release of insulin by the endocrine pancreas (1, 2). PST also exerts an inhibitory action at other target tissues. For instance, PST has been shown to inhibit pancreatic exocrine secretion and parathyroid hormone secretion (3, 4). Immunoreactive pancreastatin is found throughout the gastrointestinal tract, as well as in the pancreas (5–7). Whether PST can inhibit food-induced release of other gastrointestinal and pancreatic hormones is not known. The purpose of this study, therefore, was to compare the effects of PST with those of a peptide that has multiple inhibitory actions in the gut, somatostatin (SRIF) (8), on nutrient-induced release of gastrin, PP, and PYY in the conscious dog.

Methods and Materials

Experimental Design. After an 18- to 24-hr fast, six mongrel male and female dogs (18–22 kg) were given one of two types of oral meals on separate occasions alone or in combination with iv saline, PST (400 pmol/kg/hr), or SRIF (400 pmol/kg/hr). For stimulation of PYY release, dogs were given a mixture of one can of dog food, one sausage, two eggs, 30 g of glucose, and 100 cc of water. For stimulation of gastrin and PP release, fasted dogs were given the above-described meal containing 3.5 g of tryptophan and 10 g of peptone. Tryptophan and peptone are potent secretagogs for release of gastrin. The meals were given at 9–10 AM and the meals were consumed fully within 5 min. The PST and SRIF infusions were started 15 min before basal blood samples were collected and continued for 60 min. Synthetic porcine PST (1–49) and cyclic SRIF (1–14) (Peninsula Laboratories, Belmont, CA) were prepared in 0.1% bovine serum albumin containing saline.

Blood specimens for measurement of serum gastrin and plasma PP and PYY levels were collected before and at frequent intervals after the oral meals. Blood samples were collected into chilled empty glass tubes or into chilled glass tubes containing sodium heparin (15 U/ml) and aprotinin (100 U/ml; Novo Research Institute, Bagsvaerd, Denmark). Serum and plasma samples were stored at −20°C until assayed.

Gastrin, PP, and PYY Radioimmunoassays. Serum gastrin and plasma PP and PYY levels were measured using double antibody radioimmunoassay (RIA) methods as described previously (9–11). The ID_{50}'s (50% inhibition of bound radioligand) and sensitivities for the gastrin, PP, and PYY RIAs were 0.025 and 0.006 pg/tube, 0.016 and 0.006 pg/tube, and 0.05 and 0.005 pg/tube, respectively.

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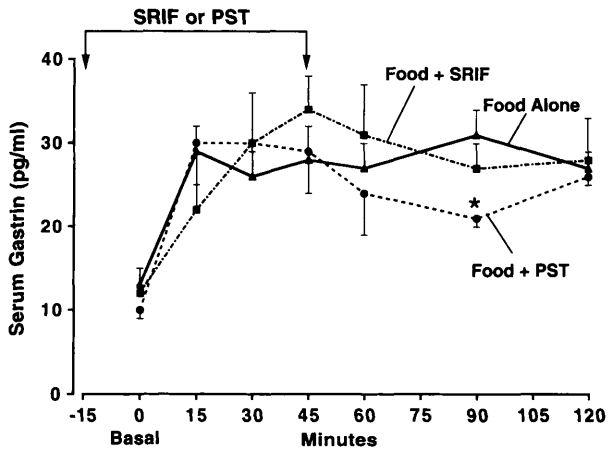

Figure 1. Serum gastrin levels in response to an oral meal alone or in combination with iv SRIF or PST. *$P < 0.05$ versus food alone.

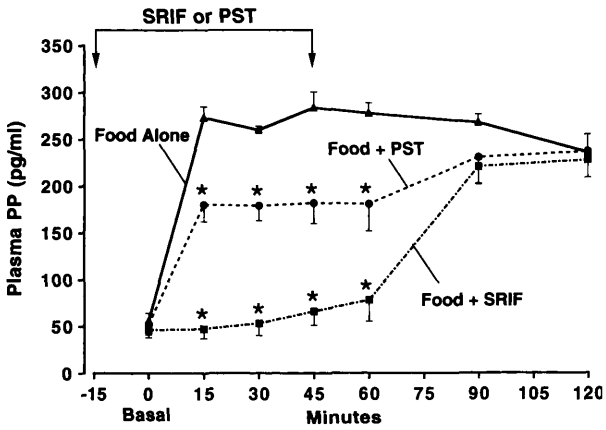

Figure 3. Plasma PP levels in response to an oral meal alone or in combination with iv SRIF or PST. *$P < 0.05$ versus food alone; †$P < 0.05$ versus food alone and food plus SRIF.

Data Analysis. Multiple comparisons were made with the two-way analysis of variance with repeated measures followed by Newman-Keuls test. The integrated release of gastrin and PYY were calculated according to a method described previously (12). Differences with $P < 0.05$ were considered statistically significant.

Results

Oral ingestion of a mixed meal in the control group resulted in a significant elevation of serum gastrin levels when compared with basal gastrin levels (Fig. 1). Basal serum gastrin levels increased nearly three-fold from a mean of 13 pg/ml to approximately 29 pg/ml. Intravenous administration of PST or SRIF with the oral meal did not affect the serum gastrin response, with one exception. At 90 min, the serum gastrin levels were significantly lower in the food plus PST group when compared with those of the food alone group. Integrated gastrin release in response to the oral meal did not differ significantly ($P > 0.05$) when compared with the integrated gastrin release in dogs given the oral meal plus iv SRIF or PST (Fig. 2). Plasma PP levels increased significantly in response to oral ingestion of a meal (Fig. 3). The plasma PP levels to oral food were significantly lower at 15–60 min in the food plus iv SRIF and PST groups. SRIF inhibited food-induced PP release more potently than PST (15- to 60-min values). Integrated PP release in response to the oral meal alone and to the oral meal plus iv PST was significantly higher than the integrated PP release in response to the oral meal plus iv SRIF (Fig. 2). Oral ingestion of a mixed meal also resulted in a significant elevation of plasma PYY levels when compared with basal PYY levels (Fig. 4). Intravenous administration of SRIF with the oral meal decreased the plasma PYY response (15- to 45-min values) to oral food, whereas iv administration of PST did not inhibit food-induced release of PYY. Plasma levels of PYY and PP increased significantly after the iv infusion of SRIF ceased. Integrated PYY release in response to the oral meal alone is significantly higher when compared with dogs given the oral meal plus iv SRIF.

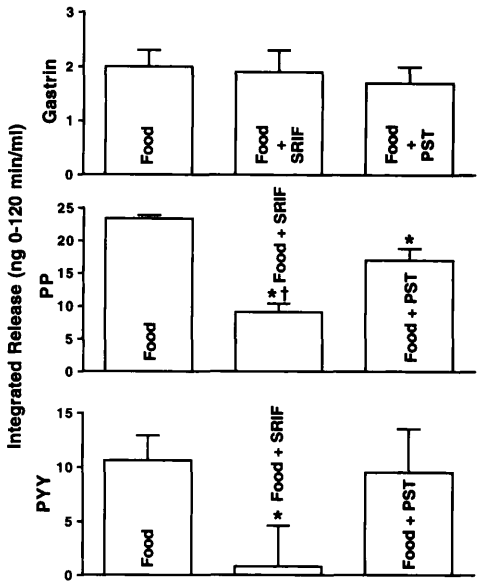

Figure 2. Integrated gastrin, PP, and PYY release in response to an oral meal alone or in combination with iv SRIF or PST. *$P < 0.05$ versus food alone; †$P < 0.05$ versus food plus PST.

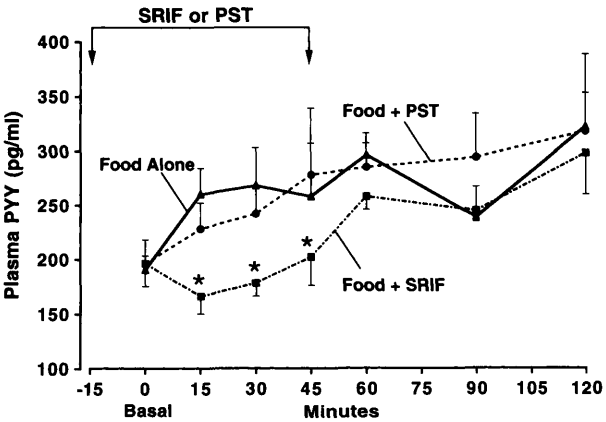

Figure 4. Plasma PYY levels in response to an oral meal alone or in combination with to iv SRIF or PST. *$P < 0.05$ versus food alone.

Discussion

The present report indicates that SRIF and PST, at 400 pmol/kg/hr, can inhibit food-induced release of PP; however, only SRIF can inhibit food-induced PYY release. Both SRIF and PST did not inhibit food-induced release of gastrin. Additionally, the inhibitory action of SRIF on food-induced PP release is more potent when compared with the inhibitory action of PST. Earlier reports indicate that SRIF can inhibit secretion of gastrin and PP, as well as other gut peptide hormones (8); however, whether PST can influence gastrin, PP, and PYY release has not been described. Additionally, the relative potencies of SRIF and PST on food-induced gut hormone secretion have not been reported. SRIF has been described previously to inhibit gastrin release (13,14). Although speculative, the finding that SRIF failed to inhibit food-induced release of gastrin may be explained, in part, by the simultaneous SRIF-induced reduction in food-induced release of gastric acid. SRIF can inhibit gastric acid secretion (15–17), and a reduction in gastric acid secretion can result in a reciprocal increase in serum gastrin levels. It is also possible that the dose of SRIF used in this study was inadequate to inhibit the potent stimulatory actions of tryptophan and peptone on release of gastrin, although SRIF did inhibit tryptophan and peptone-induced release of PP. Interestingly, PST has been shown to stimulate gastric acid secretion in conscious dogs (18). Therefore, in the present study, a stimulation of acid secretion by PST is expected to enhance the gastrin response to a meal. However, such an enhancement did not occur. We cannot offer an explanation for the absence of an enhanced elevation of serum gastrin levels in response to the oral meal plus PST.

Immunoreactive PST is found in the stomach, in the pancreas, and in the large intestine (5–7). PST is derived posttranslationally from a larger precursor protein called chromogranin A (CGA), which is found in all enteroendocrine cells (19–21). The finding that PST inhibits only PP and not gastrin and PYY release suggests that PST receptors are not present on stomach "G" cells or intestinal "L" cells. PST receptors may exist only in the endocrine pancreas since PST can inhibit insulin secretion from the endocrine pancreas as well as exocrine secretion (1–3). PST, in the pancreas, may have a physiological role in the regulation of PP secretion.

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