Effect of long-term parenteral feeding on gastric secretion in dogs

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Thor, Piotr J., Edward M. Copeland, Stanley J. Dudrick, and Leonard R. Johnson. Effect of long-term parenteral feeding on gastric secretion in dogs. Am. J. Physiol. 232(1): E39-E43, 1977. -Three dogs were surgically prepared with gastric fistulas and Heidenhain (vagally denervated) pouches. Acid and pepsin responses to pentagastrin and food were determined before, at the end of a 1-mo period of total parenteral feeding, and 1 mo after the resumption of a normal oral diet. Acid and pepsin output from the denervated pouch in response to pentagastrin and food decreased significantly (P < 0.001) after parenteral feeding and returned to control levels after the dogs resumed a normal diet. Secretory outputs from the gastric fistula in response to pentagastrin remained unchanged throughout the experiment. Basal serum gastrin levels decreased 50% during the period of intravenous feeding and returned to levels approximately twice the control levels following resumption of normal oral food intake. Serum gastrin responses to meals also decreased during intravenous alimentation and returned to higher than normal levels following a 1-mo period of oral intake. These studies indicate that the absence of oral food intake in the dog does not result in decreased acid secretion from the innervated stomach. Vagal innervation in some way is responsible for the preservation of normal secretion during the absence of food from the gastrointestinal tract of the dog.

Parenteral nutrition; acid; pepsin; gastrin

Intravenous alimentation or parenteral nutrition has become a widely used clinical technique since its description in 1968 (5). One benefit of this procedure is the reduction of drainage from high enteroenteric fistulas and subsequent fistula closure (4). The mechanism involved in this decreased fluid output is presumed to be decreased gastric and pancreatic secretion due to the lack of normal stimuli created by the ingestion and presence of food within the gastrointestinal tract. Whether the long-term absence of oral food intake results in decreased secretory capacities has not been investigated.

Our laboratory has used total parenteral nutrition as a tool to study the effects of food on the gut. In the rat, a 2-wk absence of oral food ingestion results in significant decreases in the weights of the oxyntic gland area of the stomach, small intestine, and pancreas. Disaccharidase levels drop significantly, and antral and serum gastrin levels are considerably lower (8). The changes in tissue weights and enzyme activity are largely prevented by the addition of a low dose of pentagastrin to the intravenous nutrient solution (9). This is the first study which examines gastric secretion following the long-term absence of food from the gut.

Methods

Experiments were performed on three male dogs weighing 15-19 kg. Each dog was anesthetized with thiopental sodium, 20 mg/kg, and methoxyflurane. A laparotomy was performed under aseptic conditions and a vagally denervated pouch (Heidenhain type) was constructed from the oxyntic gland area of the stomach. The pouch was drained to the outside through a Gregory cannula. A gastric fistula was created by inserting a Thomas cannula in the most dependent portion of the gastric remnant.

The animals were supported by slings and trained to stand quietly on tables. Experiments began 3 wk following surgery. A peripheral leg vein was cannulated and saline infused via a Harvard peristaltic pump at a rate of 1 ml/min. The gastric fistula was opened and both the main stomach and denervated pouch were washed gently with distilled water and allowed to drain. Basal secretion from both the Heidenhain pouch and gastric fistula was collected for two 15-min periods.

Two types of studies were performed. In one series, pentagastrin (Imperial Chemical Industries) was infused in doses increasing in a stepwise manner of 0.5, 1.0, 2.0, and 4.0 μg/kg per h. Each dose was infused for three 15-min collection periods. In the other study, one can of dog food (Prescription Diet Riviano Foods, Hill’s Division, Topeka, Kans.) was fed following the collection of basal secretion. Gastric juice was collected at 15-min intervals for 3 h following feeding. The food was entirely consumed in each instance within a few minutes of presentation. Blood samples for serum gastrin assays were collected at the end of the basal period and at 30 and 60 min following eating. Two experiments of each type were run on each of the three dogs, so all mean values reported are from six observations.

The volume of each secretory sample was measured...
and aliquots were taken for determination of acid and pepsin concentrations. Acid content was determined by titration with 0.2 N NaOH to pH 7.0 using an automatic titrator and pH meter (Autoburette, Radiometer, Copenhagen, Denmark). Pepsin concentrations were measured using a modification (11) of the Anson (1) hemoglobin method and were expressed as milligrams pepsin per milliliter by reading the trichloroacetic acid supernatant at 280 nm and comparing it with solutions incubated with different amounts of pepsin standard (hog pepsin, Pentex Biochemicals). Pepsin outputs were calculated and expressed as milligrams pepsin per 15 min. Results for the pentagastrin studies were expressed as acid and pepsin outputs for the last 30 min of infusion of each dose. For the feeding studies, two consecutive 15-min periods were combined and outputs were expressed per 30 min. Serum was collected from each of the 5-ml blood samples and frozen for gastrin radioimmunoassay. The gastrin assays were done in one batch at the end of the entire study according to the method described by Yalow and Berson (15) and using an antibody characterized by Dockray and Walsh (3). Synthetic human gastrin I. 1-17, obtained from Imperial Chemical Industries, Ltd., England, was used as a standard. Gastrin levels are expressed as picograms of G-17 equivalents per milliliter serum. Experiments were carried out on alternate days and not more frequently than 3 times per week. The order of experiments was randomly assigned.

Following the completion of both studies, an intravenous catheter was inserted through a superficial neck vein and advanced into the vena cava. The dogs were placed in metabolic cages and the catheter was inserted through a swivel apparatus, Harvard peristaltic pump, and connected to a reservoir containing the intravenous nutrient solution. This arrangement allowed for complete mobility of the dogs within the cages without twisting or cramping the catheter (5).

Infusion of the alimentation solution began immediately and was gradually increased to 1,200 ml/day. The nutrient solution consisted of 4.25% Freemine (solution of essential free amino acids) and 25% dextrose. Salts were added so that each liter contained 50 meq NaCl, 50 meq Na acetate, 40 meq K acetate, 15 meq K2HPO4, 15 meq Na2SO4, and 1 g Ca gluconate. Solutions were passed through a 0.22-μm membrane filter. The animals were fed totally by vein for 1 mo during which they returned to normal levels after the animals were placed back on oral diets (Table 1). Serum gastrin increased 30 min following the 1 mo absence of food from the gut. The percent increase in serum gastrin over basal levels, however, was actually higher at this time, indicating that the absence of food from the gut did not alter either acid (Fig. 5) or pepsin (Fig. 6) output significantly lower following the 1 mo absence of food from the gut than normal oral food intake (Figs. 1 and 2). Heidenhain pouch acid and pepsin outputs in response to pentagastrin also declined significantly after the absence of food from the gut for 1 mo (Figs. 3 and 4). Although the decreased response to pentagastrin was not as great as it was to a meal, outputs were significantly lower at each dose of pentagastrin (P < 0.05). Both acid and pepsin outputs in response to pentagastrin had returned to control levels 1 mo after the resumption of normal oral food intake (Figs. 3 and 4).

The absence of food from the gastrointestinal tract did not alter either acid (Fig. 5) or pepsin (Fig. 6) output from the vagally innervated stomach in response to pentagastrin. Basal serum gastrin levels decreased approximately 50% during the period of total parenteral feeding and returned to normal levels after the animals were placed back on oral diets (Table 1). Serum gastrin increased 30 and 60 min after a meal regardless of the diet regimen. Absolute gastrin levels 60 min after eating were significantly lower following the 1 mo absence of food from the gut. The percent increase in serum gastrin over basal levels, however, was actually higher at this time, indicating that the absence of receptor stimulation for the release of gastrin during the period of parenteral nutrition did not impair the gastrin release mechanism. Gastrin outputs in response to a meal were significantly lower at each dose of pentagastrin (P < 0.05). Both acid and pepsin outputs in response to pentagastrin had returned to control levels 1 mo after the resumption of normal oral food intake (Figs. 3 and 4).

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<th>Table 1. Serum gastrin before, 30, and 60 min after a meal</th>
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Values are in picograms per milliliter. Experiments were done before, 1 mo after the start of total parenteral feeding, and 1 mo following return to normal oral food intake. *P < 0.001, +P < 0.005, $P < 0.05, # P < 0.05.
FIG. 1. Acid secretion from vagally denervated Heidenhain pouch following a meal. Before, before intravenous alimentation. During, at end of a 30-day period of total parenteral feeding. After, 1 mo after dogs had resumed normal food intake. Means and standard errors of means of two observations in each of three dogs.

FIG. 2. Same as Fig. 1, except pepsin output was measured.

higher than control levels after the dogs had been feeding normally for 1 mo (Table 1)

DISCUSSION

This is the first study to examine the effects of the long-term absence of food from the gut on gastric secretion. There have been several studies from the surgical literature concerning the mechanism by which total
oral water intake was given intravenously. The animals
nerated canine pouches during periods when normal
osmotic diuresis occurred in all experiments. Changes in plasma osmolarity could explain findings.

First, the studies were not controlled for
error. First, the studies were such that possible mechanisms behind the changes were not revealed. The current study operates from a completely different premise, namely, that secretory changes might occur from the chronic absence of stimulation normally provided by the oral ingestion and presence of food within the digestive tract.

Experiments involving parenteral alimentation in rats support this contention. The weights of the oxyntic gland area of the stomach, the small intestine, and pancreas from rats fed intravenously for 10 days were significantly lower than corresponding values from sham-operated orally fed controls (8). The body weights and weights of other organs did not change. Antral and serum gastrin levels were also significantly lower in the parenterally fed rats (8, 9). The addition of a low dose of pentagastrin to the intravenous nutrient solution prevented most gastrointestinal tract weight loss as well as the decreases in disaccharidase activity which occur in these animals (2, 9). On the basis of the rat data one might have expected canine gastric secretion in response to pentagastrin to be decreased because of decreased mass of secretory mucosa and the response to a meal to be decreased for the same reason and because of lower endogenous gastrin levels. This clearly was not the case for the vagally innervated stomach.

Even though basal serum gastrin levels decreased 50% as a result of parenteral feeding, the serum gastrin response to the meal was unchanged at 30 min and only slightly lower than control levels 60 min after feeding. In fact, the percentage change in serum gastrin level in response to a meal was greater following the period of intravenous feeding than it was during the control period 1 mo earlier. The fact that both acid and pepsin outputs from the main stomach were unchanged during the course of the experiment indicates that neither the parietal cell mass nor the sensitivity of the parietal cells to gastrin changed during the prolonged absence of food from the stomach.

Acid and pepsin output from the vagally denervated Heidenhain pouch, however, decreased significantly in response to both pentagastrin and food. The calculated maximal output of the Heidenhain pouch in response to pentagastrin decreased from the control value of 1.163 meq H+/30 min to 0.683 meq H+/30 min after 1 mo of intravenous feeding. During the same period the Km or D50 for acid secretin increased from 1.37 to 2.62. These changes imply that both the secretory mass (or individual parietal cell response) and parietal cell sensitivity to pentagastrin decreased during this period of time. This
accounts for the large decrease in acid secretion. That these changes were not permanent is evidenced by the total recovery of secretory capacity after the animals resumed normal oral feeding. The pouch response to food was depressed even more than the response to pentagastrin. The factors, mentioned above, responsible for the decrease to pentagastrin stimulation are, in part, responsible for the decreased secretion in response to a meal. To these must be added the significantly decreased serum gastrin response which was evident 60 min after eating.

This is the first study examining the effects of long-term absence of an oral food intake on the dog stomach. Numerous species differences are evident when compared to the rat. After 10 days of parenteral nutrition, rat serum gastrin decreased to one-eighth control levels (9) compared to one-half in the current study. Food deprivation for a period of 4 days in the rat resulted in a drop in serum gastrin levels to one-seventh the normal level (1). Thus, maintenance of rat gastrin levels seems dependent on the trophic hormone (7). Gastrin is also a trophic hormone for the dog oxyntic gland mucosa (13), and there appears to be no difference between the two species. Therefore, since acid secretion did not change, one must conclude in the current studies that either endogenous gastrin levels did not drop sufficiently to cause atrophy of the inner-vated gastric mucosa or other trophic factors canceled the effects of changes in gastrin levels. Although the secretory capacity of the Heidenhain pouch decreased, the reason for this is not apparent. There is no evidence on the question of whether gastrin is a more potent growth hormone in vagally denervated mucosa. The in vivo experiments demonstrating trophic effects of gastrin, to our knowledge, have all been performed with innervated tissues (7).

The fact remains that the vagally innervated main stomach was immune to the factor which decreased the sensitivity and secretory mass of the Heidenhain pouch parietal cells. The only explanation for this phenomenon is the obvious one, that in some way vagal innervation maintained the sensitivity of the oxyntic gland mucosa to various secretory stimuli and, at the same time, compensated for slightly decreased serum gastrin levels.

Assuming that the human stomach more closely resembles the canine mucosa, the absence of food for periods of time during intravenous feeding is not likely to decrease gastric secretory capacity in the intact stomach of man.

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REFERENCES