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Effect of Sham Feeding on Gastric Emptying of Liquids in Dogs

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The effects of sham feeding and of cimetidine, an inhibitor of gastric acid secretion, used alone or in combination on the gastric emptying of liquids were studied in four dogs fitted with a gastric fistula and a Komarov esophagostomy. Gastric emptying of a 290-ml water meal was slowed by sham feeding but not by cimetidine. Our experiments indicate that, in dogs, sham feeding slows gastric emptying of liquids by a mechanism independent of the acid secretion induced by vagal stimulation.

The role played by the vagus nerve in the control of acid secretion is well established; however, its influence on gastric emptying is still poorly understood. The presence of vagal pathways stimulating and inhibiting the motor activity of the proximal stomach have been demonstrated (1). Cholinergic and noncholinergic neurotransmitters are involved in these actions (1). Some of these inhibitory pathways are brought into play by sham feeding, deglutition, or distension of the stomach; the proximal stomach relaxes to receive food (1, 2). Since gastric emptying of liquids depends mainly on the extent of this relaxation (1), it has been assumed that vagal stimulation slows gastric emptying of liquids. However, only Schiller et al (3) have studied in a direct way the effects of a physiological vagal stimulation (sham feeding) on gastric emptying. Studies were performed in humans with the modified sham-feeding method. No change of the emptying rate of water and a slight acceleration of that of a homogenized meal was observed.

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The fact that vagal stimulation increases acid secretion and that acidification of the duodenum slows gastric emptying make the interpretation of some of the above-mentioned studies difficult (1, 2).

The purpose of the present work is to study the effect of sham feeding on the gastric emptying of liquids in dogs and to examine if this effect depends on the acid secretion induced by vagal stimulation.

MATERIALS AND METHODS

Four dogs (12–18 kg) were prepared with a gastric canula and a Komarov esophagostomy (4). The experiments were started at least two months after surgery, and no dog was used more than twice a week with an interval of at least 48 hr between each experiment.

After a 18-hr fast, the dogs were placed on a Pavlov stand. The gastric canula was opened and gastric juice collected during 30 min in order to evaluate basal acid secretion. In case food was present or if the basal acid secretion exceeded 1 meq/hr, the experiment was postponed. Water, 290 ml, containing [^{125}I]polyvinylpyrrolidone (PVP) ($\pm$5000 cpm/ml) and phenol red (0.5 mg/ml) as tracers were then introduced into the stomach through the gastric canula over a 2-min period with a peristaltic pump. Serial gastric volumes were estimated by the double sampling indicator dilution method of George (5). At 5, 15, 25, and 35 min, after introduction of the meal, the gastric content was mixed through the gastric fistula with a 50-ml syringe and 5 ml was sampled. Water, 10 ml, containing $\pm$150.000 cpm/ml [^{125}I]PVP and 1 mg/ml cold PVP (to avoid adsorption to the gastric walls) was then infused into the stomach, thoroughly

TABLE 1. EFFECT OF SHAM FEEDING AND CIMETIDINE ON ACID SECRETION AND GASTRIC EMPTYING AFTER INTRAGASTRIC INFUSION OF 290 ML WATER INTO STOMACH

	Control	*Cimetidine*	*Sham feeding*	*Sham feeding + cimetidine*
Acid output (meq/25 min)	5.5 ± 0.9	0.3 ± 0.2**	9.0 ± 2.1	2.1 ± 0.6**
Phenol red remaining in stomach				
At 5 min (%)	72 ± 5	64 ± 7	76 ± 4	79 ± 2
At 15 min (%)	28 ± 4	26 ± 5	49 ± 6**	47 ± 7*
At 25 min (%)	19 ± 4	19 ± 6	33 ± 4*	27 ± 1

*$P < 0.05$.
**$P < 0.01$.

mixed with the gastric content and a second 5-ml sample taken. [^{125}I]PVP content of samples was determined with a gamma counter (Minigamma LKB, Bromma, Sweden). Phenol red was estimated using a spectrophotometer at 560 nm after adjustment to pH 10 with 0.25% Na_3PO_4. Acid content was determined by titration to pH 7.4 with 0.1 M NaOH using a titration assembly (Radiometer, Copenhagen, Denmark).

Gastric volumes, acid outputs, and fractional gastric emptying rates were calculated by a modification of the method of Dubois et al (6, 7). This method has been described in detail and validated elsewhere (8). In brief, for each 10-min interval, concentrations in [^{125}I]PVP were used to calculate the intragastric volumes of fluid and amounts of [^{125}I]PVP present in the stomach by the marker dilution method of George (5). A first estimate of the fractional gastric emptying rate (g) was calculated using the following equation: $M_2 = M_1 \times \exp(-gt)$ where M_1 and M_2 are the amounts of [^{125}I]PVP present in the stomach at the start and at the end, respectively, of each 10-min interval and t the duration of this interval in minutes. These estimates were then corrected for the secretion and emptying of fluid occurring during the 1-min period needed to perform the dilution procedure (6, 7). Acid output (R_H) was calculated using the equation: ($R_H = [H_2 - H_1 \times \exp(-gt)] \times g/[1 - \exp(-gt)]$ where H_1 and H_2 are the amounts of acid present in the stomach at the start and at the end of each 10-min interval. Amounts of phenol red present in the stomach at 5, 15, 25, and 35 min were calculated by multiplying phenol red concentrations by gastric volumes.

Four experiments were performed twice on each of the four dogs: (1) intragastric infusion of water without additional treatment; (2) intragastric infusion of water 30 min after intravenous injection of cimetidine (200 mg); (3) intragastric infusion of water at the end of a 10-min sham feeding period; and (4) intragastric infusion of water 30 min after intravenous injection of cimetidine (200 mg) and at the end of a 10-min period of sham feeding.

For the sham-feeding procedure, the esophagus was obstructed by pulling the esophageal mucosa with a forceps and 500 g canned food offered to the animals. The food fell from the proximal esophagus into the feeding pan and was repeatedly consumed. At the end of the sham-feeding period (10 min), the forceps was removed and the esophagostomy occluded with a tape to avoid spilling of the gastric content by gastroesophageal reflux.

The statistical significance of differences observed in emptying rates was evaluated using a two-factor (treatment, dog) analysis of variance and the factorial method 2 × 2 (9) taking into account the intragastric masses of phenol red present in the stomach 5, 15, and 25 min after infusing the meal.

RESULTS

Values for acid secretion and gastric emptying are listed in Table 1. Gastric volumes, phenol red masses remaining in the stomach, fractional emptying rates, and acidity of the gastric contents are shown in Figure 1.

During control experiments about 90% of the meal had left the stomach after 35 min, and a clear-cut acid response was observed. Cimetidine

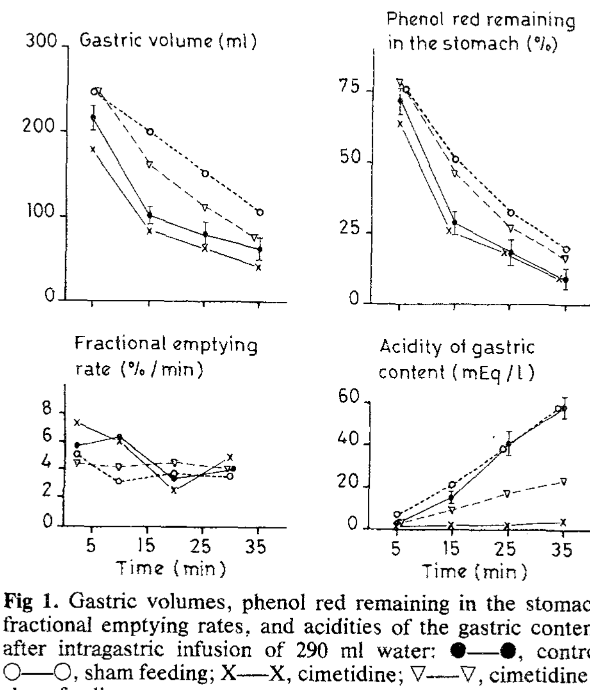

Fig 1. Gastric volumes, phenol red remaining in the stomach, fractional emptying rates, and acidities of the gastric contents after intragastric infusion of 290 ml water: ●—●, control; ○—○, sham feeding; X—X, cimetidine; ▽—▽, cimetidine + sham feeding.

almost completely suppressed the acid response but did not change the gastric emptying. Sham feeding increased the acid response and decreased the gastric emptying. Cimetidine given together with sham feeding decreased the acid response but did not alter the emptying rate as compared to sham feeding alone.

The factorial analysis of variance indicated that sham feeding with or without cimetidine decreased gastric emptying at 15 min ($P < 0.01$) and at 25 min ($P < 0.05$) but that cimetidine with or without sham feeding had no effect.

DISCUSSION

Different methods have been used to assess the gastric emptying of liquids. The tracer dilution method of George (5), as modified by Dubois et al (7), allows serial determinations of intragastric volumes with minimal disturbances of the normal emptying process. Since large variations of acid secretion and thus of volume of fluid in the stomach were expected, and in fact observed, a tracer (phenol red) was added to the meal and the emptying of this tracer used to estimate gastric emptying. Emptying of water is very rapid in dogs, and after 25 min, in some animals, the intragastric volume was too small to allow accurate determination of this volume. The estimations of the amounts of phenol red present in the stomach at 5, 15, and 25 min were thus taken into account for the estimation of gastric emptying. Another way to express gastric emptying is the fractional emptying rate (percent of tracer leaving the stomach per unit of time). It has, however, been shown in humans, monkeys, and dogs that the fractional emptying rate after a water load varies with time and is partly related to the amount of fluid present in the stomach (6–8, 10, present study). This makes the interpretation of fractional emptying rates difficult in the present case.

Our results indicate that in dogs, in contrast of what has been observed in man, sham feeding decreases gastric emptying of water. The fact that in dogs vagotomy increases the emptying rate of liquids (11) is in agreement with this hypothesis.

There are several possible explanations for the contrast between our experiments in dogs and those of Schiller et al (3) in humans. Modified sham feeding as used by Schiller et al includes only sight, smell, and taste of the food while complete sham feeding as performed in our experiments also includes swallowing of the food. Cannon and Lieb (12) have shown that swallowing induces a relaxation of the fundus in dogs. Species differences could also explain the above-mentioned contrasting results. In dogs, sham feeding induces a maximal acid response and a large release of gastrin, while in man the acid response is always submaximal and the gastrin response almost nonexistent even after prolonged sham feeding (13).

We have recently reported that, in dogs, a 5-min sham feeding period similar to that used in the present study induces a release of gastrin and somatostatin (14). Exogenous somatostatin at a dose of 0.156 μg/kg/hr inhibits gastric emptying of liquids (8). Such a dose of somatostatin increases plasma somatostatin concentrations to a level similar to that observed after sham feeding (14). This supports, but does not prove, the possibility that somatostatin is involved in the inhibition of the gastric emptying of liquids after sham feeding. Gastrin might also be involved in the motor effects of sham feeding. This is, however, unlikely since at physiological doses exogenous gastrin has no effect on gastric emptying (15, 16).

Acidification of the gastric content inhibits gastric emptying (17, 18). The effect of sham feeding could thus be produced indirectly by changes in intragastric acidity rather than directly by an effect on the gastric muscles. This is, however, unlikely because, although sham feeding induced a large acid response, there was no difference in intragastric acidity between control and sham-feeding tests (Figure 1). This lack of difference is due to the presence of a larger amount of fluid in the stomach after sham feeding and thus a larger dilution of the acid in these experiments. Moreover, inhibition of acid secretion by cimetidine did not alter the slowing effect of sham feeding on gastric emptying. It is surprising that suppression of acid secretion by cimetidine did not change gastric emptying whether the acid secretion was stimulated by sham feeding or not. According to Hunt and Knox (17), the minimal acid concentration to be present in the stomach to slow down gastric emptying is about 25 meq/liter. Such a concentration was only reached at the end of our experiments. A less likely explanation is that cimetidine has a direct inhibiting effect on gastric emptying that hides the stimulating effect resulting from suppression of acid secretion. Bertaccini and Scarpignato (19) have shown in rats that cimetidine accelerates gastric emptying. However, this effect was observed only with doses more than 10 times larger than those used in our experiments. On the other hand, Dubois et al (6) reported that metiamide, another H_2 blocker, did not change the gastric emptying rate in Zollinger-Ellison patients.

In conclusion, in dogs, sham feeding inhibits the gastric emptying of liquids probably by a mechanism independent of its stimulating effect on acid secretion.

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