Effect of Secretin and Cholecystokinin on Canine Gastric Electrical Activity* (33720)

KEITH A. KELLY, EDWARD R. WOODWARD[1], AND CHARLES F. CODE

Mayo Clinic and Mayo Foundation: Section of Physiology, and of Surgery, Rochester, Minnesota 55901

Some workers have stated that secretin and cholecystokinin inhibit gastric motility and slow gastric emptying (1–4). Others have not confirmed these functions (5, 6). The objective of the present experiments was to determine the effect of secretin and cholecystokinin on gastric myoelectrical activity during a steady state of gastric contractions.

Methods. Four mongrel female dogs (8–11 kg) were operated on with general anesthesia and aseptic techniques. Eight monopolar Ag–AgCl electrodes, each projecting 2 mm from a Teflon disk as described in a previous report (7), were implanted serially on the anterior serosal surface of the stomach midway between the greater and lesser curvatures. The first electrode was placed at the oral extremity of the fundus and the eighth, 1 cm orad to the pylorus. The remaining electrodes were spaced at approximately 3-cm intervals between these two. A ninth electrode was sewn onto the midportion of the descending duodenum. Leads from the electrodes were joined to a 9-pin tube socket mounted in a metal cannula placed in the right midabdominal wall. A gastric cannula was inserted in the midportion of the greater curvature of the stomach and brought out through the midline.

Recording sessions were begun 2 weeks postoperatively. The dogs were fasted 18–24 hr and then suspended comfortably in a sling. Leads connected the pins in the metal cannula via a junction box to a Brush, Mark 200, rectilinear pen recorder. Alternating current amplifiers with a time constant of 1 sec were used. Monopolar recordings were made using a subcutaneous indifferent electrode in the right hind limb of the animal.

Each experiment was divided into five sequential 15-min periods (periods A, 1, 2, 3, and 4). Gastric electrical activity was recorded continuously. Water (10 ml/min) was instilled via the gastric cannula by using a constant-infusion pump throughout all periods in every experiment. In control experiments, performed twice in each dog, NaCl solution (154 meq/liter) was infused into a left hind limb vein (1 ml/min) during all five periods.

During the secretin experiments, repeated three times in each dog, the NaCl solution was infused intravenously for the first 30 min (periods A and 1), and then secretin[2] was added to the NaCl infusion, so that 0.1 unit/kg/min was given during the next 15 min (period 2). Secretin was then discontinued and only NaCl was given for the next 15 min (period 3). A final 15-min infusion of NaCl with secretin, at the same dose as before, was then given (period 4), and the experiment was concluded.

Cholecystokinin (cholecystokinin-pancreozymin)[2] was given (0.1 unit/kg/min) instead of secretin in periods 2 and 4 in a similar, third set of experiments performed twice in each animal.

The electrical recordings from period A, the transitional period during which electrical activity was changing from a fasting pattern to that found during the intragastric instillation of water, were discarded. The electrical recordings of periods 1 through 4 were analyzed by determining the incidence of action potentials associated with the pacesetter potential (PP) detected by electrode 8, the mean frequency (cycles/min) of the PP at electrode 8, and the mean time (sec) required for conduction of the PP between

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[1] Visiting Scientist in Physiology.

[2] Supplied by Professor Erik Jorpes, GIH Research Unit, Chemistry Dept., Karolinska Institutet, Stockholm, Sweden.

TABLE I. Incidence of Antral Action Potentials during Constant Intragastric Infusion of Water.

Dog	Period:	Percentage of antral PP with action potentials[a] 1	2	3	4
1		53	83	66	62
		67	71	81	100
2		46	52	63	65
		58	82	85	88
3		79	80	87	89
		73	76	74	73
4		81	87	84	90
		68	93	90	90

[a] During 6-min interval begun 7 min after start of each period; results of two tests on each dog on different days are given.

electrodes 7 and 8 during a 60-min interval beginning 7 min after the start of each of these periods. The recordings from electrodes placed in the distal antrum (electrodes 7 and 8) were selected for analysis because the PP and superimposed action potentials were most clearly defined in them.

Results. Action potentials were associated with 46–81% of the cycles of the antral PP during period 1 in control tests when only NaCl was infused intravenously (Table I). A small increase in the incidence of action potentials occurred during the ensuing 45 min in seven of the eight control experiments; there was no change in the eighth.

The incidence of antral action potentials began to decrease within 2 min after the start of the secretin infusion (period 2) in 11 of 12 tests (Fig. 1). By 10 min the incidence of antral action potentials was reduced by 69–100% from that noted in period 1 in 11 of 12 tests and by 42% in the twelfth (Table II). The incidence of antral action potentials increased within 3 min after secretin infusion was stopped (period 3) in three of the four dogs and within 5 min in the fourth (Fig. 1); after 10 min it had returned to control levels (Table II). When secretin was infused a second time (period 4), a second decrease in the incidence of antral action potentials was noted within 2 min in all 12 tests. By 10 min after the start of secretion infusion in this period, the incidence of antral action potentials was reduced from that of period 3 by 68–100% in 10 of 12 tests and by 44 and 55% in 2 (Table II).

In contrast, cholecystokinin infusions produced small and inconsistent changes in the incidence of antral action potentials, decreasing the incidence by 2–11%, compared to the preceding control period, in 5 of 16 tests and increasing the incidence by 12–39% in 11 (Table III). In one animal (dog 1), a transient (1–2 min) inhibition of action potentials occurred after the start of the cholecystokinin infusion. However, even in this animal, when the records at 10 min after the start of the cholecystokinin infusion were analyzed, there was little change in the incidence of antral action potentials (Table III).

The mean frequency of PP of the four dogs in the periods when saline was infused during the control, secretin, and cholecystokinin experiments was 4.9 cycles/min, and the mean time required for conduction of the antral PP between electrodes 7 and 8 in the

TABLE II. Effect of Secretin on Incidence of Antral Action Potentials during Constant Intragastric Infusion of Water.

Dog	Period:	Percentage of antral PP with action potentials[a] 1 Control	2 Secretin	3 Control	4 Secretin
1		90	21	79	16
		48	7	76	8
		47	0	88	0
2		45	0	45	20
		78	10	90	20
		32	6	36	20
3		47	27	53	13
		33	10	60	19
		87	10	80	16
4		50	13	53	17
		80	24	73	10
		42	13	90	16

[a] During 6-min interval begun 7 min after start of each period; results of three tests on each dog on different days are given.

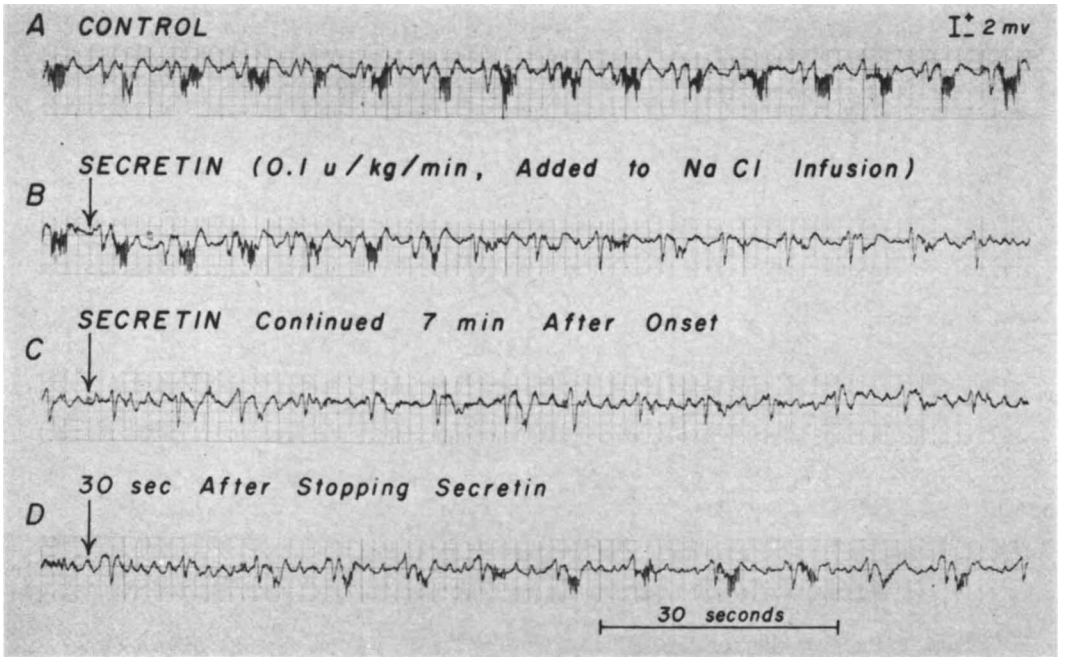

FIG. 1. Effect of secretin on canine antral electrical activity during continuous intragastric infusion of water (10 ml/min) and continuous intravenous infusion of NaCl, 154 meq/liter (1 ml/min).

four dogs was 2.1 sec. The frequency and velocity of conduction did not change significantly during infusions of secretin or cholecystokinin.

TABLE III. Effect of Cholecystokinin on Incidence of Antral Action Potentials during Constant Intragastric Infusion of Water.

	Percentage of antral PP with action potentials[a]			
Period:	1	2	3	4
Dog	Control	Cholecystokinin	Control	Cholecystokinin
1	52	91	82	100
	77	86	92	90
2	32	37	33	41
	37	33	35	44
3	70	90	73	90
	43	60	60	56
4	75	90	65	90
	74	72	81	73

[a] During 6-min interval begun 7 min after start of each period; results of two tests on each dog on different days are given.

Discussion. These experiments show that continuous intravenous infusion of secretin decisively inhibits the occurrence of gastric antral action potentials, while cholecystokinin has no such effect. The effect of secretin is rapid in onset and prompt in disappearance.

Gastric action potentials have been correlated with gastric contractions (8). Our experiments support the concept that the slowed gastric emptying accompanying duodenal acidification is the consequence of release of secretin from the duodenum. The tests do not explain how secretin produces this effect. It may act directly on the contractile elements of the gastric smooth muscle cells or possibly indirectly through controlling mechanisms.

Summary. In four mongrel female dogs, gastric antral action potentials excited by a constant infusion of water into the lumen of the stomach were markedly inhibited by intravenous infusions of secretin but were not inhibited by similar infusions of cholecystokinin. The data suggest that secretin slows gastric emptying by decreasing gastric con-

tractions whereas cholecystokinin does not. The reduced gastric emptying associated with duodenal acidification may thus be the consequence of release of secretin.

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Localization of Calcium in the Thyroids of Rats* (33721)

E. KAELLIS (Introduced by A. S. Gordon)

Department of Oral Biology, College of Dentistry, University of Saskatchewan, Saskatoon, Canada

The thyroid gland contains relatively high concentrations of calcium. This has been reported as a mean value of 35 mg/100 g of wet weight in rats (1), and in humans as a mean of about 34 (2), 39 (3), and 52[1] (4) mg/100 g of wet weight. With the exception of the aorta, one value cited (3) was the highest of the 27 nonsupportive tissues reported (cartilaginous tissues such as larynx and trachea were higher, as are, of course, bones and teeth). In 1965 Kaellis and Goldsmith (1) found that thyroidal calcium concentrations in rats declined with thiourea treatment and rose with either inanition or the use of a high calcium–low iodine diet. This was part of a study of thyroidal citrate concentrations; and they proposed that the thyroid captures calcium along with citrate (which is also present in high concentration), and that this calcium was subsequently bound to thyroglobulin in such a manner as to inhibit the production of thyroxine. The present study was undertaken to determine the sites of localization of calcium in the thyroid by histochemical methods and to observe changes occurring in animals rendered hypercalcemic.

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[1] Calculated, assuming 75% water.

TABLE I. Treatment of Rats.

Group	No. of rats	Treatment
I	11	Regular rat chow and water *ad libitum*
II	6	As in Gr. I with 2% $CaCO_3$ (w/w) added to the chow
III	6	Low calcium diet and water *ad libitum*, i.p. injections of dihydrotachysterol o.d., 5 days, 2.5 mg/kg of body wt.

Procedure. A total of 23 male CFN rats was used. This strain and sex were chosen to permit application of previously-reported results (1). The body weight of the rats averaged about 250 g at the time of death. During the 5 days of observation while the rats were under either control or experimental conditions, they all gained weight with the exception of a single animal (in Group II), the weight of which stayed very nearly the same. The animals were divided into groups as shown in Table I.

For all the experimental and for six of the controls the glyoxal bis(2-hydroxyanil) (GBHA) method of Kashiwa and Sigman (5), slightly modified, was used because of its sensitivity and discreteness in localization.