

Effects of Pentagastrin and Cholecystikinin on Intestinal Transport of Ions and Water in the Rat (36527)

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Pentagastrin diminishes absorption (1, 2) or causes secretion of ions and water by the small intestine of dogs, but the octapeptide of cholecystikinin, which contains the same COOH-terminal tetrapeptide as pentagastrin, does not (3). The response of intestinal transport to gastroduodenal hormones may differ in dogs and rats, however (4). We have studied the effect of pentagastrin and cholecystikinin (CCK) on net movement of ions and water in the jejunum and ileum of anesthetized rats.

Method. Male Holtzman rats were fasted overnight and anesthetized with pentobarbital (50 mg/kg) given into the peritoneal cavity. Segments of proximal jejunum and distal ileum, 25 cm long, were cannulated at each end, washed with 15 ml of warm saline and flushed with air. A tracheostomy tube was inserted and a femoral vein was cannulated.

The net movement of ions and water was studied during two successive 30 min perfusion periods in each rat. One milliliter of saline was injected intravenously before the control period (1st period), and 125 μ g/kg of pentagastrin (Ayerst), 100 U/kg of CCK (GIH), or saline was injected in a volume of 1 ml before the treatment period (2nd period). Six rats were studied in each of the three treatment groups. The differences in net movement of ions and water between the control and treatment periods (treatment — control) were calculated for each regimen and compared. Statistical significance of the mean differences was assessed with an analysis of variance.

Before the start of each period, segments were washed with warmed perfusion fluid and flushed with 5.4% CO₂-94.6% O₂. During perfusion, fluid entered the

lumens of the intestinal segments at the rate of 0.41 ml/min from a syringe infusion pump, passed through the segments, and was collected in a syringe attached to the distal cannula. At the end of each period, collection syringes were removed and capped, and residual fluid was flushed from the segment. After the treatment period, intestinal segments were removed, drained, stripped of mesentery and weighed.

Perfusion fluid was isotonic with rat plasma (305 mOsm/kg) and had the following composition (mM): NaCl, 120; KCl, 4.5; NaHCO₃, 25; Na₂HPO₄, 1.8; NaH₂PO₄, 0.2; MgSO₄, 1; CaCl₂, 1.3; mannitol, 20. The solution, equilibrated with 5.4% CO₂-94.6% O₂, had an initial pH of 7.4 and contained polyethylene glycol (PEG) labeled with ¹⁴C (1.25 μ Ci/ml) to permit calculation of net water movement (5).

"Initial" concentrations of ions and specific activity of ¹⁴C-PEG were measured in samples of fluid obtained from the input syringes and samples of fluid for "final" determinations were obtained from the collection syringes after each collection period.

Net fluxes of ions and water were calculated as follows:

$$J_{\text{net ion}} = V (\text{ion}_r \frac{\text{PEG}_i}{\text{PEG}_f} - \text{ion}_i) \text{ gWW}^{-1},$$

$$J_{\text{net H}_2\text{O}} = V \left(\frac{\text{PEG}_i}{\text{PEG}_f} - 1 \right) \text{ gWW}^{-1}.$$

A net flux that is negative indicates absorption, *i.e.*, net loss from the lumen. Ion_i and ion_r are the concentrations of the ion (μ moles/ml) measured in the initial and final samples; PEG_i and PEG_r are the specific activities of ¹⁴C-PEG (cpm/ml) measured in the initial and final samples. *V* is the volume

TABLE I. Effect of Pentagastrin and Cholecystikinin on Net Movement (Mean \pm SD) of Ions and Water in the Jejunum of the Anesthetized Rat.

	Treat- ment	Control ^a (Period 1)	Treatment ^a (Period 2)	Difference	F	p
Na	Saline	-92 \pm 28	-106 \pm 30	-14 \pm 30	0.304	> .05
	Penta	-93 \pm 29	- 96 \pm 36	- 3 \pm 35		
	CCK	-98 \pm 26	-115 \pm 15	-17 \pm 28		
K	Saline	-1.78 \pm .55	-1.68 \pm 1.01	+0.10 \pm 1.08	0.013	> .05
	Penta	-1.00 \pm 1.04	-0.14 \pm 2.80	+0.86 \pm 2.82		
	CCK	-1.33 \pm 2.04	-1.68 \pm 2.00	-0.35 \pm 3.55		
Cl	Saline	+1.4 \pm 27.9	-7.9 \pm 27.2	-9.4 \pm 31.8	0.112	> .05
	Penta	+8.1 \pm 30.2	+6.2 \pm 36.7	-1.9 \pm 28.6		
	CCK	+6.3 \pm 22.0	+3.2 \pm 25.9	-3.0 \pm 26		
HCO ₃	Saline	-108 \pm 10	-110 \pm 6	-2 \pm 11	0.228	> .05
	Penta	-111 \pm 13	-108 \pm 10	-3 \pm 21		
	CCK	-114 \pm 15	-115 \pm 12	-1 \pm 5		
H ₂ O	Saline	-0.28 \pm 0.19	-0.42 \pm 0.14	-0.14 \pm 0.19	2.008	> .05
	Penta	-0.38 \pm 0.17	-0.37 \pm 0.19	+0.01 \pm 0.17		
	CCK	-0.33 \pm 0.14	-0.52 \pm 0.09	-0.18 \pm 0.17		

^a Units of electrolyte transport are micromoles 30 min⁻¹ (g wet wt of segment)⁻¹. Units of water transport are milliliters 30 min⁻¹ (g wet wt of segment)⁻¹. Signs indicate movement into (+) or out of (-) the lumen. In each treatment group, n = 6.

(ml) of perfusion fluid pumped into the segment in 30 min; gWW is the wet weight of the intestinal segment (g). Thus, $J_{\text{net ion}}$ is expressed as $\mu\text{moles } 30 \text{ min}^{-1} \text{ gWW}^{-1}$, and $J_{\text{net H}_2\text{O}}$ is expressed as ml 30 min⁻¹ gWW⁻¹.

Concentrations of sodium and potassium were measured with a flame photometer, and chloride with an amperometric chloridometer. Bicarbonate was calculated from measurements of pH and pCO₂ using a pK' of 6.1, and specific activity of ¹⁴C-PEG was measured with a scintillation counter.

Results. The changes in the net movement of ions and water in the jejunum (Table I) and ileum (Table II) following the injection of pentagastrin or CCK did not differ significantly from the changes following injection of saline.

Discussion. Gastric acid is secreted at maximal rates in dogs when pentagastrin is infused at rates of 4 $\mu\text{g}/\text{kg}\text{-hr}$ (6) or less (7). Hence, administration of pentagastrin at rates higher than 4 $\mu\text{g}/\text{kg}\text{-hr}$ may cause responses that do not occur when endogenous gastrin is liberated by physiologic stimuli. When infused at rates of 4-8 $\mu\text{g}/\text{kg}\text{-hr}$ in

dogs, pentagastrin reduces the absorption of sodium, potassium, and water, from solutions perfusing the jejunum (2) and ileum (1, 2). At rates of about 1-16 $\mu\text{g}/\text{kg}\text{-hr}$, pentagastrin causes secretion of juice by unperfused Thiry-Vella loops of jejunum and ileum (3). Single doses of pentagastrin sufficient to cause maximal gastric acid secretion in anesthetized rats (8) did not affect the net movement of ions and water in the rat small intestine, however. Administration of the compound by single injection instead of perfusion was probably not responsible for the difference because the gastric secretory response to pentagastrin after single injection is maximal at 20 min and persists for 30 min (8). If pentobarbital contributes to the difference in response of the 2 species, the rat must be more sensitive than the dog, because the barbiturate was also used in canine studies (2). Rat and dog also differ in their responses to large doses of glucagon. Glucagon causes intestinal secretion in unperfused Thiry-Vella loops in dogs, (3) but enhances net absorption of ions and water by perfused intestine in rats (4).

TABLE II. Effect of Pentagastrin and Cholecystikinin on Net Movement (Mean \pm SD) of Ions and Water in the Ileum of the Anesthetized Rat.

	Treatment	Control ^a (Period 1)	Treatment ^a (Period 2)	Difference	F	p
Na	Saline	-46.3 \pm 31.3	-72.5 \pm 56.3	-26.2 \pm 37.6	0.189	> .05
	Penta	-36.1 \pm 33.7	-71.9 \pm 26.5	-35.8 \pm 22.5		
	CCK	-39.4 \pm 15.9	-73.0 \pm 19.6	-32.4 \pm 18.5		
K	Saline	+4.93 \pm 9.98	+3.31 \pm 6.98	-1.62 \pm 3.26	0.706	> .05
	Penta	+1.05 \pm 1.00	+0.48 \pm 0.74	-0.58 \pm 0.59		
	CCK	+2.11 \pm 2.16	+2.24 \pm 4.19	+0.13 \pm 2.98		
Cl	Saline	-95.5 \pm 42.5	-110 \pm 63.1	-14.9 \pm 39.6	0.314	> .05
	Penta	-103 \pm 36.1	-119 \pm 33.6	-15.9 \pm 27.2		
	CCK	-115 \pm 11	-141 \pm 15	-26 \pm 12		
HCO ₃	Saline	+52.3 \pm 17.9	+47.8 \pm 20.4	-4.5 \pm 10.9	0.879	> .05
	Penta	+76.5 \pm 26.6	+74.5 \pm 23.2	-2.0 \pm 11.3		
	CCK	+87.7 \pm 24.8	+78.0 \pm 23.7	-9.7 \pm 7.8		
H ₂ O	Saline	-0.05 \pm 0.20	-0.18 \pm 0.36	-0.12 \pm 0.29	1.215	> .05
	Penta	-0.04 \pm 0.19	-0.23 \pm 0.14	-0.19 \pm 0.09		
	CCK	-0.00 \pm 0.07	-0.26 \pm 0.11	-0.26 \pm 0.13		

^a Units of electrolyte transport are micromoles 30 min⁻¹ (g wet wt of segment)⁻¹. Units of water transport are milliliters 30 min⁻¹ (g wet wt of segment)⁻¹. Signs indicate movement into (+) or out of (-) the lumen. In each treatment group, n = 6.

Net movement of ions and water was not influenced by CCK in our studies or by the octapeptide of CCK in dogs (3). However, CCK enhanced absorption by short-circuited rabbit ileum (9) and reduced absorption by everted sacs of hamster small intestine *in vitro* (10). Because intestine from the same species has not been studied *in vivo* and *in vitro*, it is not possible to tell whether the response to CCK is determined by the species or by the experimental preparation.

Summary. Pentagastrin and CCK cause no significant changes in the net movement of ions and water in the jejunum and ileum of anesthetized rats.

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