Diuretic Action of Secretin in Dog (36111)

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Glucagon is a diuretic in dog (1–5) and man (6). Secretin is a structurally similar hormone. Glucagon has 29 amino acid residues, secretin has 27. In 14 positions the same amino acid is present in both molecules (7). The purpose of this study was to determine whether pure synthetic secretin is a diuretic in dog.

Methods. In 3 female mongrel dogs (18 to 20 kg) a midline episiotomy was done to facilitate introduction of a catheter into the urinary bladder. Studies were started 1 week after surgery. Food but not water was withheld for 18 hr before each study. Throughout each study, 150 m*M* NaCl was infused intravenously at the rate of 0.4 ml/kg-min by a peristaltic pump (Harvard Apparatus Co., Millis, MA). A balloon catheter was placed in the urinary bladder. Air was injected intermittently to insure patency of the catheter. Urine was collected continuously and divided into 30 min samples. After the volume flow rate of urine had stabilized, usually 3 to 4 hr after starting the infusion of NaCl, 2 base line 30 min samples were collected. Next, 0.5 μg/kg-min of either pure synthetic porcine secretin or glucagon was added to the saline infusion for a 30 min period. Control studies were done with 150 m*M* NaCl alone. The order of treatments was randomized and studies were separated by at least 48 hr. Each test was done twice on each of the 3 dogs. No untoward effects were observed during any test.

Pure synthetic porcine secretin was the gift of Dr. M. Ondetti, Squibb Institute, New Brunswick, NJ. Glucagon was the gift of Dr. T. M. Lin, Lilly Research Laboratories, Indianapolis, IN.

Urinary Na and K were determined by flame photometry (Model 143, Instrumentation Laboratory, Boston, MA).

Because of the large range in urine flow rates of the 3 dogs, the mean of the 2 base line 30 min periods was expressed as 100% and the subsequent collections as percentage of this level. The data for electrolyte concentration and output were similarly analyzed. Base line values are summarized in Table I.

TABLE I. Volume and Electrolytes of Urine During Infusion of 0.4 ml/kg-min 150 m*M* NaCl.

Mean and range of 2 base line 30 min collections immediately before giving test agents.

	Mean	Range
Vol (ml/30 min)	104	22 –204
Na conc (mEq/liter)	148	64 –218
Na output (mEq/30 min)	14.5	4.4– 26.9
K conc (mEq/liter)	15.5	2.9– 54.0
K output (mEq/30 min)	1.3	0.4– 3.0

The significance of changes from base line levels was tested by Students' *t* test for unpaired values. Statistically significant changes were those in which the hormone produced a greater change than the saline control at the 5% level of probability.

Results. Volume (Fig. 1). Urine volumes were significantly increased after both glucagon and secretin.

Sodium concentration (Fig. 2). Neither of the hormones significantly affected urinary Na concentration.

Sodium output (Fig. 3). Both hormones significantly increased Na output.

Potassium concentration (Fig. 4). There was a delayed but significant rise in urinary K concentration after secretin. No significant effect was observed after glucagon.

Potassium output (Fig. 5). Output of K

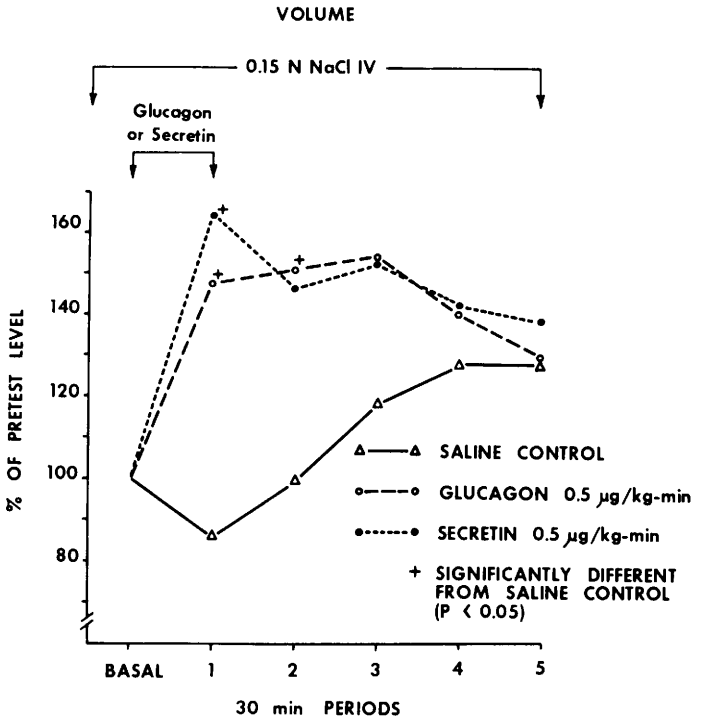

FIG. 1. Urine volumes after secretin, glucagon, or saline control, expressed as percentage of values during the hour before giving the test agent: (+) statistically significant difference from saline control ($p<.05$).

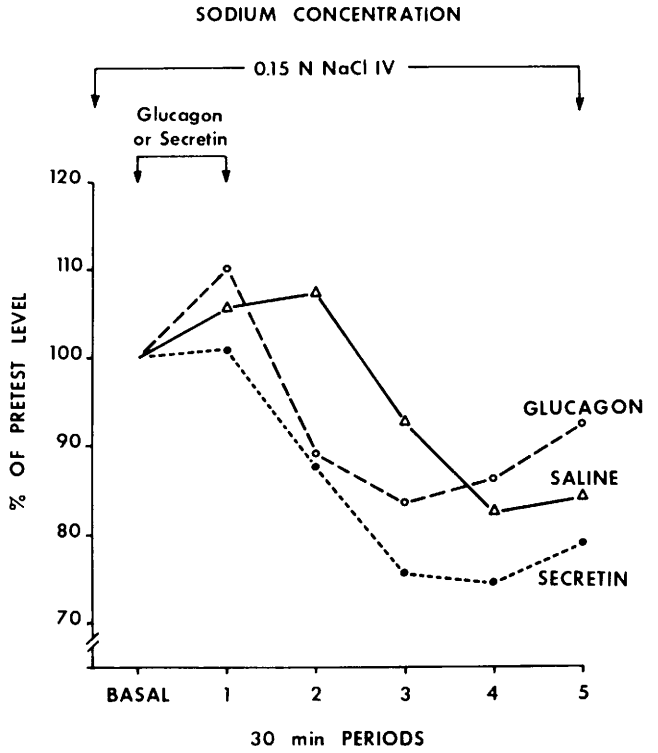

FIG. 2. Urinary NA concentration (see Fig. 1 for explanation).

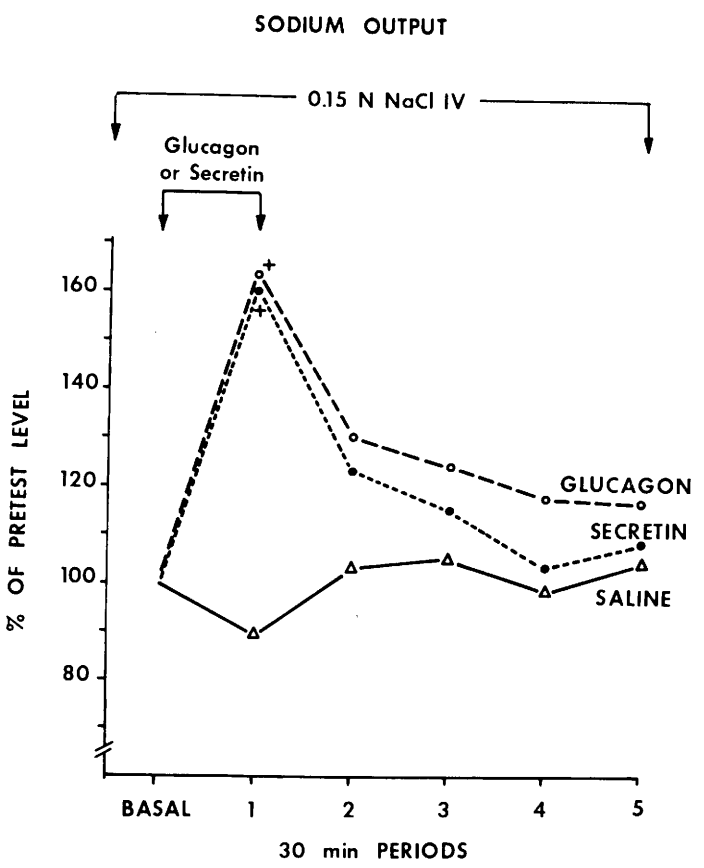

FIG. 3. Urinary Na output (see Fig. 1 for explanation).

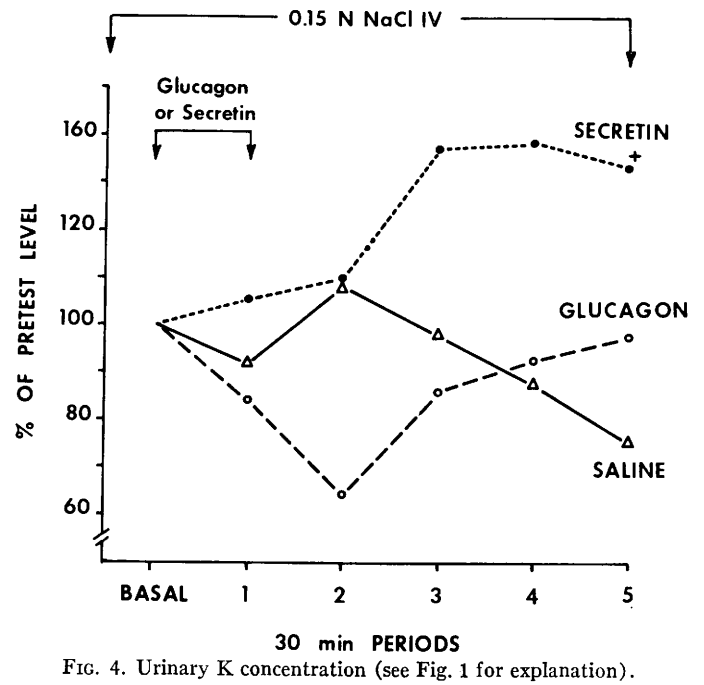

FIG. 4. Urinary K concentration (see Fig. 1 for explanation).

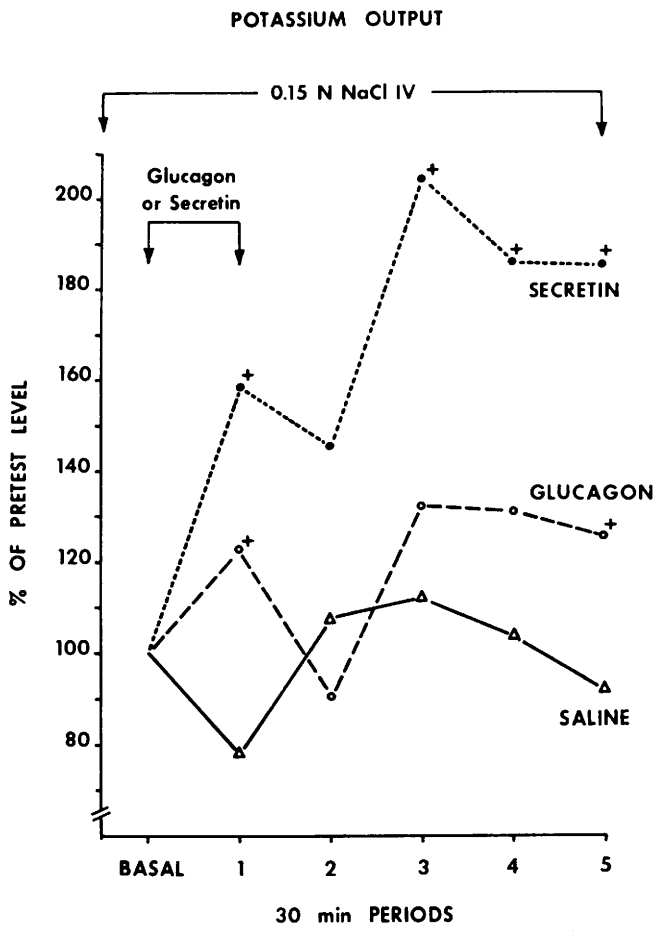

FIG. 5. Urinary K output (see Fig. 1 for explanation).

increased significantly above saline control during the administration of secretin and glucagon. After the infusion, the increase in K output was more marked with secretin than with glucagon; however, the responses were not significantly different.

Discussion. Early studies with crude secretin suggested that it might have a diuretic action (8, 9). The present study shows that glucagon and secretin given in pharmacological doses have a diuretic action in the dog. The diuresis that occurred during administration of the hormones was characterized by an increase mainly of volume with relatively little change in Na and K concentration. After secretin, K diuresis seen in the final 2 hr was contributed to by changes of both volume and concentration.

For both glucagon and secretin, the mechanism of diuretic action is not known. It seems reasonable to presume that glucagon and secretin act at the same site because of their close structural similarity, but there is no clear evidence for this. Previous investigators have described a rise in creatinine clearance with glucagon (4, 6, 10, 11), but this is not a universally accepted finding and is unlikely to be the only mechanism to explain the diuresis (1, 2, 6). The hormones are known to affect blood supply to the gut (12) and glucagon also affects renal blood flow. It is unclear whether this action is on total renal blood flow (6, 10) or possibly only on "noncortical" renal blood flow (5). An action on the renal tubule remains a distinct possibility (1, 2, 4, 6). The diuretic action of glucagon is not mediated by the concomitant increase in blood glucose (1, 6, 10). Since

secretin produces diuresis but does not cause hyperglycemia (13), the independence of these two effects is further demonstrated.

Secretin acts on many targets along the gastrointestinal tract. Glucagon shares many of these actions, including inhibition of gastric acid secretion, stimulation of hepatic bile secretion, and inhibition of motility of the stomach and intestine (12). The action of secretin is not confined to the alimentary tract. Like glucagon, it has cardiovascular actions (14) and both promote release of insulin (15). Both secretin and glucagon activate adenyl cyclase in adipose tissue (16) and possibly their actions at all targets are mediated by this mechanism.

The dose of secretin used in this study was about 60 times that required for maximal stimulation of pancreatic bicarbonate secretion and therefore can be regarded as pharmacological. The physiological significance of the action of glucagon and secretin on the kidney is uncertain.

Summary. Intravenous infusion of 0.5 μg/kg-min of glucagon or pure synthetic secretin into conscious dogs receiving 0.4 ml/kg-min of 150 m*M* NaCl caused diuresis characterized by increased volume flow with little change in electrolyte concentrations.

We thank John Washington for technical assistance. Supported by Veterans Administration research funds and by Grant GB7285X from National Science Foundation. G. O. B. is an International Postdoctoral Fellow of National Institutes of Health (FO 5 TW 1616).

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Received July 1, 1971. P.S.E.B.M., 1972, Vol. 139.