Canine intestinal secretion during and after rapid distention of the small bowel

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INTESTINAL OBSTRUCTION frequently leads to intestinal distention from pooling of fluids and gases proximal to the obstruction (13). In 1933, Herrin and Meek (10) observed that distention of an intestinal loop by a water-filled balloon led to secretion of fluid into the lumen. Others have shown that obstruction of the intestine is followed by a decline in the net rate of water and electrolyte absorption from the lumen (12). Still today it remains unclear whether the fluid flow observed with distention results from enhanced secretion (10), decline in absorption, or transudation resulting from mucosal damage. Extrinsic denervation of the small intestine has been reported to have no effect (3, 10) on intestinal secretion during and after distention. In 1933, Herrin and Meek (10) observed that distention of an intestinal loop by a water-filled balloon led to secretion of fluid into the lumen. Others have shown that obstruction of the intestine is followed by a decline in the net rate of water and electrolyte absorption from the lumen (12). Still today it remains unclear whether the fluid flow observed with distention results from enhanced secretion (10), decline in absorption, or transudation resulting from mucosal damage. Extrinsic denervation of the small intestine has been reported to have no effect (3, 10) on intestinal secretion during and after distention.

In the present study, the problem was reinvestigated using extrinsically denervated Thiry-Vella loops of intestine in dogs. The relationship between distention volume and rate of fluid transfer was studied. The effect of cholinergic blocking drugs on the response was also studied, and clearance of plasma protein into the loops before, during, and following distention was determined.

METHODS

Animal preparations. Four mongrel dogs (13–20 kg) were prepared with modified Thiry-Vella loops 15 cm in length. The segments were denervated by cutting all visible fibers and by stripping all adventitia from the branch of the mesenteric artery supplying the segment of small intestine. The proximal end was brought to the surface as a mucocutaneous fistula; the distal end was fitted with a Gregory (7) cannula. The continuity of the bowel was reestablished by end-to-end anastomosis. Each dog had both a jejunal and an ileal loop. The jejunal loops began about 15 cm caudal to the ligament of Treitz. The ileal loops ended about 15 cm orally to the ileocecal junction. Experiments were begun no sooner than 2 wk after surgery. Food, but not water, was withheld 18–24 h before each test. The animals were used no more often than 3 days/wk with at least 48 h between tests.

One animal developed a fistula between the skin and the ileal loop after 10 days of use and therefore was excluded from subsequent experiments. Two animals died after 4.5 and 5 mo of experiments.

Collection of secretions. During experiments, loop secretions were collected continuously from the Gregory cannula at the distal ends of the loops. Every 15 min, 20 ml of air from a syringe with a rubber tube attached were gently blown through the proximal stoma of the loop to flush out any fluid which had pooled within. Volumes collected were read every 30 min before and following the distention period. During distentions, volumes were read and the loops were flushed with air only once at the conclusion of the 45-min distention period.

Method of distention. The loops were distended by inserting an inflatable condom through the proximal stoma. The condom was supported by a semirigid, polyethylene tube (2 mm diameter) attached to a rigid hypodermic needle. Water was introduced into the condom via the needle and tubing (Fig. 1). The distention apparatus was inserted so that the loops were distended from a point 2 cm beyond the external opening of the stoma.

Loops were distended for 45 min. Basal collections were taken for a minimum of 0.5 h before distention, and collection continued for 2.5 h after distention or until the flow rate returned to basal control levels, whichever came first. On different experimental days, the loops were distended with 0 (apparatus inserted but not inflated), 4, 10, 15, 20, and 30 ml of water, while the pressure within the condom was
simultaneously monitored by a strain-gauge transducer (Statham Instruments, model P23BD) and recorded on a polygraph (Sanborn, model 350-2700). With the distention apparatus outside the body, the balloon could be filled with as much as 200 ml water without an increase in pressure. All distentions and collections were performed on ileal loops unless otherwise stated.

**Drugs.** Atropine or hexamethonium was injected after one or more basal collections had been obtained, and the distention was begun 30 min after injection of the drug. Atropine sulfate (Burrough Wellcome & Co.) was injected subcutaneously in a dose of 0.1 mg/kg. Hexamethonium hydrochloride (K & K Chemicals, Los Angeles) was injected intravenously in a dose of 4 mg/kg.

**Plasma clearance.** Leakage of plasma protein into loops during distention was determined by measuring the clearance of plasma-protein bound \(^{32}\text{Cr}\) before, during, and after distention. In these experiments \(^{32}\text{CrCl}_3\) (New England Nuclear) was injected intravenously not less than 36 h prior to the distention. Plasma and loop samples were counted in a well counter (Nuclear-Chicago, model 132). Plasma radioactivity was determined on the day of distention before and after the experiment; activity ranged from 75 to 330 counts/min above background. Leakage of plasma (ml) into loops was calculated as follows:

\[
V_p = \frac{V_s}{V_t} \times \frac{(\text{counts/min})_s}{(\text{counts/min})_p}
\]

where \(V_p\) = milliliters plasma cleared into the sample, \(V_s\) = volume (ml) of sample; \((\text{counts/min})_s\) = counts per minute (over background) per milliliter of sample; and \((\text{counts/min})_p\) = counts per minute (over background) per milliliter of plasma.

In a few experiments the concentrations of sodium, potassium, chloride, and bicarbonate in the ileal effluent were determined: \(\text{Na}^+\) and \(\text{K}^+\) by flame photometer; \(\text{Cl}^-\) by chloridometer. Bicarbonate was determined by adding an excess of HCl to a sample, boiling, and backtitrating with dilute NaOH to pH 7.

Interspersed throughout the course of these studies were control experiments in which basal outputs from unstimulated loops were measured for 5 h during which no significant fluctuation from initial levels was observed. Basal output during these 5-h control studies and during the initial period of other studies did not differ significantly and so were pooled. Neither the basal control outputs nor the outputs in response to a standard amount of distention (20 ml) varied significantly over the 6-mo course of these studies. Studies of distention alone and distention plus drugs were done in random order. Using the Student t test for unpaired values, we compared the outputs during and after distention (alone or with drugs) with basal control outputs and also compared outputs during and after distention alone with outputs during and after distention plus drugs.

**Results**

**Basal flow.** The mean basal flow rate of juice from unstimulated loops was 49 \pm 3 \mu l/min. Atropine and hexamethonium each lowered the basal rate of secretion (Fig. 2). Beginning 30 min after injection, atropine lowered basal secretory rates significantly \((P < 0.05)\) for two 30-min periods, and hexamethonium lowered basal secretory rates significantly \((P < 0.05)\) for four consecutive periods.

**Flow rate responses to distention.** Contact between the intestinal mucosa and the deflated condom (0-ml distention) for 45 min significantly increased the flow rate during the period of contact and maintained it significantly above basal levels for the first 30 min following contact \((P < 0.05)\). This response to mechanical contact was abolished by both atropine and hexamethonium (Fig. 3).

Distention with 4-, 10-, and 15-ml volumes, like the 0-ml distention, produced a significant increase in output rate during the period of distention and the first postdistention period (Table 1). Increased output during the second postdistention period was noted after 10 ml but not 4- or 15-ml distention (Table 2).

Distention with 20- and 30-ml volumes produced a different pattern of response (Table 1). With these volumes, the rates of flow were not significantly increased over basal rates during distention, but were significantly elevated for five postdistention periods after the 20-ml distention and four postdistention periods after the 30-ml distention. Hexamethonium, but not atropine, significantly reduced this response to 20-ml distention (Fig. 4), though fluid output rose in response to 20-ml distention even after hexamethonium.

**Fig. 1.** Distention apparatus consisting of latex condom fastened to a semirigid, polyethylene tube into which has been inserted a rigid hypodermic needle. Condom was inflated by injecting water through the needle.

**Fig. 2.** Effect of atropine and hexamethonium on basal intestinal secretory rates from Thiry-Vella ileal loops. Drugs injected at Time 30. Control: 9 observations on 3 dogs (9/3); hexamethonium: 6/3; atropine 3/3; means and standard errors.
Intraluminal pressure changes during distention. Intraluminal pressure was increased initially and fell during the course of sustained distention, regardless of the distending volume. With volumes of 15 ml or less, intraluminal pressure showed only a small rise unrelated to the magnitude of the distending volume. When the distending volumes were greater than 15 ml, there were larger rises in intraluminal pressure, proportional to the distending volume (Fig. 5). When the loops were distended with a 20-ml volume, intraluminal pressure fell from 255 ± 25 cmH2O to 80 ± 15 cmH2O over the 45-min test period. Eighty-five percent of the pressure fall occurred in the first 10 min of distention. Neither atropine nor hexamethonium changed these pressure-time relationships (data not shown).

Plasma protein leakage. Plasma protein leakage (milliliters cleared) into the loops increased slightly (Fig. 6) during and following the distention with 20 ml. This was attributable to an increased volume of juice with no significant change in concentration of radioactivity. Volumes of plasma cleared before, during, and after distention accounted for less than 15% of the loop outputs.

Jejunal secretion during ileal distention. Fluid output of denervated jejunum did not increase when the denervated ileum was distended with 20 ml volumes (Table 2).

Electrolyte concentrations in ileal secretions. Electrolyte concentrations in ileal secretions (Table 3) remained constant before, during, and after 20 ml distentions.

Discussion

Some design features of this study could have influenced the results. In traditional fashion (4, 11), Thiry-Vella loops were used to study intestinal secretory responses. In Thiry-Vella loops of rat jejunum, the mucosa atrophies, loses its ability to absorb glucose, and shows a decrease in specific activities of mucosal enzymes (5) over a period of 6-10 wk following construction of the loops. Whether such changes also develop in Thiry-Vella loops of dog intestine is not known; however, older work has indicated that electrolyte fluxes do not change significantly with time in Thiry loops of dog intestine studied over periods of years (1). Since we did not measure the water and electrolyte absorptive capacity of these loops, we do not know whether this capacity changed as the result of chronic loop infection or mucosal atrophy with time. Nevertheless, in all cases the effects of distention were compared to control responses observed throughout the course of the study. Neither basal secretion rates nor secretory responses to 20-ml distentions significantly changed over a period of 2-24 wk following surgery. We attempted to denervate the loops by transecting all visible nerve fibers in the mesentery. It is possible that this technique did not produce complete extrinsic denervation. The procedure was undertaken as a matter of convenience because in studies preliminary to the present experiments...
TABLE 2. Simultaneous jejunal and ileal volume responses to 20-ml ileal distention

<table>
<thead>
<tr>
<th>Period</th>
<th>Jejunal Loop</th>
<th>Ileal Loop</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal</td>
<td>61 ± 50</td>
<td>69 ± 2</td>
</tr>
<tr>
<td>Distention</td>
<td>19 ± 8</td>
<td>61 ± 10</td>
</tr>
<tr>
<td>Postdistention 1</td>
<td>12 ± 6</td>
<td>173 ± 38</td>
</tr>
<tr>
<td>Postdistention 2</td>
<td>7 ± 2</td>
<td>144 ± 28</td>
</tr>
<tr>
<td>Postdistention 3</td>
<td>16 ± 3</td>
<td>131 ± 25</td>
</tr>
<tr>
<td>Postdistention 4</td>
<td>12 ± 5</td>
<td>126 ± 24</td>
</tr>
<tr>
<td>Postdistention 5</td>
<td>15 ± 6</td>
<td>196 ± 18</td>
</tr>
</tbody>
</table>

Mean (µl/min) ± SE (three tests in three dogs).

FIG. 5. Intraluminal pressure at beginning and end of 45-min distention with various volumes, 4 ml: 6/4; 15 ml: 6/4; 20 ml: 7/4; 30 ml: 7/4; means and standard errors.

FIG. 6. Total intestinal secretion from Thiry-Vella ileal loops and plasma clearance into the bowel. Distention (20 ml) was applied at 30–75 min. Total volume: 8/3; plasma clearance 8/3; means and standard errors.

TABLE 3. Mean electrolyte concentrations in ileal effluent before, during, and after 20-ml ileal loop distention

<table>
<thead>
<tr>
<th>Period</th>
<th>Na⁺</th>
<th>K⁺</th>
<th>Cl⁻</th>
<th>HCO₃⁻</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal</td>
<td>133 ± 3</td>
<td>8.4 ± 0.4</td>
<td>88 ± 5</td>
<td>45 ± 3</td>
</tr>
<tr>
<td>Distention</td>
<td>149 ± 3</td>
<td>8.0 ± 0.4</td>
<td>83 ± 1</td>
<td>53 ± 4</td>
</tr>
<tr>
<td>Postdistention</td>
<td>158 ± 3</td>
<td>9.1 ± 0.6</td>
<td>91 ± 3</td>
<td>50 ± 5</td>
</tr>
</tbody>
</table>

Mean (meq/liter) ± SE (five tests in three dogs).

we observed that distention of innervated loops invariably made the dogs salivate, retch, and exhibit apparent discomfort. In those dogs secretory responses to distention before denervation were unchanged when the dogs were restudied 2 wk or more after the loops were denervated at a second operation; yet the dogs no longer retched or became excited during distentions, an observation previously made by Herrin and Meek (10). All studies were commenced at least 2 wk after surgery, an ample period of time to allow “paralytic (denervation) secretion” to cease (4, 6). Basal secretory rates from our extrinsically denervated loops were of the same magnitude as basal secretory rates reported by others from innervated canine Thiry-Vella loops (4, 11). Although atropine (and hexamethonium) diminished basal secretory rates from these denervated loops and atropine likewise reduces “paralytic secretion” (4), a similar effect of atropine on basal secretion has been previously demonstrated in innervated canine Thiry-Vella loops (11).
In these experiments two types of flow rate responses were seen as the result of small-bowel distention: 1) increased flow during the distention and/or mechanical contact and for the 0.5 h following the distention (contemporary response); and 2) no increase in flow rate during distention but sustained increased output for 2 h or more following distention (sustained response). The former response was seen as the result of physical contact of the mucosa with the uninflated distention apparatus or as the result of distention with small volumes (4–15 ml) associated with very small increases in intraluminal pressure. This response could be abolished with either atropine or hexamethonium, an observation which suggests, but does not prove, that the response was mediated by intrinsic neural reflexes. We believe the first type of response resulted from contact stimulation of the mucosal surface which has long been known to stimulate secretion from the small-bowel mucosa (4) and colonic mucosa (2). In the latter organ, such secretion resulting from contact stimulation apparently is not abolished by extrinsic denervation of the bowel but is abolished by atropine (2).

The second type of response (that is, sustained increase in flow following distention) was seen when distending volumes were large and the intraluminal pressure was high. We believe this second type of response resulted from actual distention of the bowel (as evidenced by significant rises in intraluminal pressure) rather than mechanical contact alone. The large differences between initial and final pressure indicate bowel wall accommodation during distention. Hexamethonium reduced the fluid transfer response without changing the intraluminal time-pressure course. Plasma protein clearance studies indicated that only a fraction of this response resulted from plasma leakage into the loops. Even during the periods of increased output, the percentage of plasma in the intestinal juice remained constant (approximately 12%).

The exact mechanism(s) that produced secretion after distention with larger volumes cannot be deduced from our experiments. We measured only net secretion into the loops, and therefore, could not differentiate between increased secretion and decreased absorption (9). While plasma protein clearance values indicated that secretion did not arise from fluid or electrolyte transfer from the loops to the intestinal lumen we also observed continued secretion from the loops for 4–6 h after distention was discontinued.

REFERENCES

1. Berger, E. Y., G. Kanzaki, M. A. Homer, and J. M. Steele. Simultaneous collection of secretion from jejunal loops did not show an increase in jejunal output as the ileal output rose either in response to low-volume distention (mechanical contact) or high-volume distention. Thus, these experiments did not provide evidence of hormonal mediation of the secretory responses observed.

