Effect of octapeptide of cholecystokinin on canine pyloric pressure

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OPEN-TIPPED PERFUSED TUBES have been shown to be the most accurate sensors for measuring intraluminal spinchteric pressure (7). This report describes the manometric characteristics of the canine pylorus (i.e., gastroduodenal junction) using perfused tubes as sensors and describes the effect of the C-terminal octapeptide of cholecystokinin (OP-CCK) on pyloric pressure.

METHODS

Five mongrel dogs, 19-31 kg, were prepared with a Thomas cannula (13) in the stomach 6-8 cm proximal to the gastroduodenal junction, and a second Thomas cannula in the duodenum, 12-15 cm distal to the gastroduodenal junction. Experiments were begun at least 4 weeks after pyloric pressure.

The dogs were fasted for at least 18 hr before each study. The tube assembly was introduced through the gastric fistula. It was moved in 1-cm increments, at 15-sec intervals, back and forth across the pylorus. On separate days the C-terminal octapeptide of cholecystokinin (0.25, 0.5, and 1.0 μg/kg-hr) was infused intravenously. NaCl, 0.15 M, infused alone served as the control. Mean (+SE) resting pyloric pressure when the sensors were moved from stomach to duodenum was 14.8 ± 1.0 cm H2O. When they were moved from duodenum to stomach, it was 8.9 ± 0.9 cm H2O. The higher doses of the octapeptide of cholecystokinin (0.5 and 1.0 μg/kg-hr) produced an increase in pyloric pressure. Mean sphincter length was 1.8 cm. It is concluded that the dog pylorus was tonic and that the resting tone was increased by intravenous infusion of the C-terminal octapeptide of cholecystokinin.

RESULTS

When the sensors were moved from stomach to duodenum, the mean resting pressure of the gastroduodenal junction (i.e., pyloric sphincter) in the four separate tests which occurs at the pylorus (1), a polyethylene tube (id 1.1 mm) filled with KCl agar was placed next to one of the pressure sensors. Another KCl-agar polyethylene tube (id 0.6 mm) was placed in a leg vein. Each KCl-agar bridge was placed in a beaker containing saturated KCl and a calomel reference electrode. The reference electrodes were attached to a potentiometer (Radiometer, model PHM 22R, Copenhagen, Denmark), and the direct-writing recorder.

The Student t tests for paired and unpaired values and Chi-squared test were used in the statistical analysis of the data (12).
CHOLECYSTOKININ ON CANINE PYLORIC PRESSURE

TABLE 1. Basal pyloric pressure

<table>
<thead>
<tr>
<th></th>
<th>Stomach to Duodenum: A</th>
<th>Duodenum to Stomach: B</th>
<th>A vs. B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>116</td>
<td>114</td>
<td></td>
</tr>
<tr>
<td>Pressure, cm H2O</td>
<td>14.8 ± 1.0</td>
<td>8.9 ± 0.9</td>
<td>P &lt; 0.01</td>
</tr>
<tr>
<td>Percent 0's</td>
<td>17</td>
<td>39</td>
<td>P &lt; 0.01</td>
</tr>
<tr>
<td>Length, cm</td>
<td>1.9 ± 0.1</td>
<td>1.8 ± 0.1</td>
<td>P &gt; 0.05</td>
</tr>
</tbody>
</table>

Pressure and length values are means ± se.

FIG. 1. Change in mean pyloric pressure during saline control and graded doses of C-terminal octapeptide of cholecystokinin. Each point represents mean of 30 pullthroughs in 5 dogs.

FIG. 2. Percent of pullthroughs across pylorus when a zone of increased pressure was recorded during saline control and graded doses of C-terminal octapeptide of cholecystokinin. Each point represents results of 30 pullthroughs in 5 dogs. ZIP refers to zone of increased pressure.

were significantly more (P < 0.01) pullthroughs with zero pressure when the sensors were moved from duodenum to stomach than from stomach to duodenum (Table 1). The length of the zone of increased pressure was similar with either direction of movement of the sensors (Table 1).

In all pullthroughs the pyloric zone of increased pressure occurred at the same time the change in potential difference was recorded by the accompanying potential difference sensor. The change in potential difference across the pylorus was approximately 30 mv (stomach -25 mv, duodenum +1 to +5 mv), and occurred over 1.3 cm.

Neither NaCl alone, nor the lowest dose of OP-CCK (0.25 μg/kg-hr), significantly changed pyloric pressure. The larger doses of OP-CCK, 0.5 and 1.0 μg/kg-hr, produced a significant (P < 0.05) increase in pyloric pressure when the sensors were moved from stomach to duodenum. During OP-CCK infusion the zone of increased pressure occurred at the same location as before OP-CCK. When the sensors were moved from duodenum to stomach, mean pyloric pressure increased significantly (P < 0.05) during the 1.0 μg/kg/hr infusion (Fig. 1).

Increasing doses of OP-CCK produced a stepwise increase in percent of pullthroughs with a definite zone of increased pressure, both when the sensors were moved from stomach to duodenum and when moved from duodenum to stomach (Fig. 2).

Examples of basal and OP-CCK-stimulated pyloric pressure are shown in Fig. 3 and 4. Although this study was not designed specifically to measure gastric or duodenal motility, during OP-CCK infusions there was no apparent change in phasic activity from basal or the NaCl control.

DISCUSSION

Studies designed to measure the sphincteric activity of the pylorus have yielded conflicting results. Quigley (11), Thomas (14), and others (5) were unable to record a zone of increased pressure at the canine pylorus using anchored balloon sensors. Studies in man, using balloon or nonperfused open-tipped tubes as sensors, have also failed to record a sustained zone of increased pressure at the pylorus when the sensors were moved from duodenum to stomach (1, 2). In dog, Brink, Schlegel, and Code (4), however, recorded a pyloric sphincteric zone when either unperfused open-tipped tubes or small balloons were pulled from duodenum to stomach. The pressure they recorded by the balloon sensors was greater then that recorded by the unperfused tube sensors.

Harris, Pope, and their associates (7, 10, 15) have demonstrated that continuous perfusion of the sensing tube with water produced a more accurate measurement than either nonperfused tube or balloon sensors of both anal and gastroesophageal sphincter strength. The perfused tube technique had not been previously applied to the canine pylorus. The present study demonstrated that there was a zone of increased pressure at the dog gastroduodenal junction. Anderson and Grossman (1), using the transluminal potential difference technique, demonstrated that the gastroduodenal junction coincided with the pyloric sphincter in dogs. The zone of increased pressure was approximately 2 cm in length and increased in tone during an intravenous infusion of the C-terminal octapeptide of cholecystokinin. Intraduodenal fat, a known releaser of cholecystokinin (CCK), and intra-duodenal acid, also a releaser of CCK (3), was found by Brink et al. (4) to produce an increase in pyloric pressure in dog.

OP-CCK is several times more potent than CCK on both a weight and molar basis (9). In in vitro and in vivo guinea pig gall bladder 1 μg of OP-CCK is equivalent to approximately 30 Ivy dog units (IDU) or 10 μg of cholecystokinin (1 μg CCK equals approximately 3 IDU). In dogs with chronic pancreatic fistulas, mean peak pancreatic protein secretion was observed during OP CCK 0.5 μg/kg-hr (6). The doses of OP-CCK used in this study therefore were: near maximal, maximal, and supramaximal for pancreatic
protein secretion. In order to determine whether or not the effect of CCK on the canine pyloric sphincter was a physiologic one, it will be necessary to examine whether the release of endogenous CCK by physiologic methods produces the same effect as did exogenous OP-CCK. Because CCK (GIH Laboratory, Karolinska Institute, Stockholm, Sweden) contains approximately 90% impurities (8), it was decided to use the pure synthetic OP-CCK for this study.

We do not know why the pyloric pressure was greater when the sensors were moved from stomach to duodenum...
than when they were moved from duodenum to stomach. Possible explanations include: a duodenal neural reflex which was stimulated when the sensors were pulled from stomach to duodenum, and not stimulated when the sensors were moved from duodenum to stomach; or movement of the gastric mucosa into the pyloric sphincteric area while the sensors were pulled into the duodenum, thereby decreasing the effective size of the sphincter.

REFERENCES