Relation between inhibition of gastric secretion and absorption of fatty acids

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LONG, JAMES F., AND FRANK P. BROOKS. Relation between inhibition of gastric secretion and absorption of fatty acids. Am. J. Physiol. 209(3): 447-451. 1965.—Gastric secretion stimulated by a 100-g meat meal was inhibited by oleic acid and triolein and the inhibition correlated with absorption of the respective lipids in dogs with vagally innervated gastric pouches. Twenty-six milliliters of lipid were infused into the duodenum at 0.76 ml/min through a duodenal fistula starting 5 min before feeding. Gastric secretion was collected every 30 min and analyzed for acid and pepsin concentrations. Paraffin oil infused at the same rate gave results similar to feeding alone. Lipid absorption was determined by measuring venous plasma radioactivity at 1, 2, 3, 4, and 6 hr after feeding and infusing of C14-labeled oleic acid or triolein. Lipid in intestinal content for 3 hr after feeding was determined in acute experiments. The duration of gastric inhibition was longer and the absorption was slower with oleic acid than with triolein.

fat absorption fatty acids and gastric secretion comparative absorption of fatty acid and triglyceride pepsin secretion

THE ABSORPTION OF FAT has been suggested by Mengu (16) to be an essential link in the mechanism when fat inhibits gastric secretion. Procedures which interfere with fat absorption, such as exclusion of bile (12), exclusion of pancreatic juice, or both (11), have been shown to reduce the degree of inhibition of gastric secretion due to fat in the small intestine. These same procedures also reduced the inhibition of gastric motility accompanying the intraduodenal injection of olive oil in rats (13). Bile and pancreatic juice are necessary for optimal absorption of fat from the small intestine (19).

Long-chain fatty acids have been shown to be a more effective inhibitor of gastric motility (14) and of gastric secretion in rats (15) than the parent triglycerides. Hydrolysis of the triglycerides by pancreatic juice has been reported to be essential for the inhibition of gastric secretion in rats (15) and in dogs (16). Long-chain fatty acids must be synthesized into triglycerides in the intestinal epithelial cells prior to delivery into the intestinal lymphatics (2, 3). Bergstrom et al. reported in rats (1) and Mahn et al. reported in humans (9) that the absorption of fatty acids takes place over a longer period of time than does the absorption of an equal amount of triglyceride. Also, Carroll and Richards (4) reported that triolein and trilinolein were more completely absorbed than were the corresponding fatty acids. The present study was done to relate these differences in absorption to the inhibition of gastric secretion.

METHODS

Four dogs were prepared with vagally innervated gastric pouches (18) and duodenal fistulae (17) placed opposite the major pancreatic duct. The dogs were used for experiments 5–6 weeks after surgery. The stimulus for gastric secretion in each experiment was 100 g of raw ground beef heart given after a fast of 18–24 hr.

Nine experiments were performed after feeding only. Seven experiments were performed with 26 ml of paraffin oil infused into the duodenum at 0.76 ml/min for 35 min beginning 5 min before feeding. In 10 experiments each, triolein or oleic acid was infused into the duodenum in precisely the same manner as the paraffin oil. The experimental procedures were performed in random order.

Two microcuries of either oleic acid-1-C14 or triolein-1-C14 was added to the infusion of cold lipid in seven of the oleic acid and seven of the triolein experiments. Blood samples were taken at 0 (for background counting), and at 1, 2, 3, 4, and 6 hr after feeding. Radioactive labeled fat was not used for a second isotope experiment for at least 1 week. The lipid content of plasma was extracted with a 2:1 mixture of chloroform:methanol by the method described by Folch et al. (6). The lipid solvent was evaporated to dryness under N2 and then prepared for counting in a Packard Tri-Carb liquid-scintillation spectrometer.

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Gastric secretion was collected for 1 hr before feeding and for 6 hr after feeding. Samples of gastric juice were taken every 30 min after feeding if at least 0.5 ml of juice was secreted during the 30-min period. If less than 0.5 ml was secreted, the collection period was extended until sufficient volume for analysis was collected.

Acid concentration was determined on 0.4–1.0 ml of gastric juice by titration with 0.1 N NaOH to a phenol red end point comparable to pH 7. Pepsin concentration was determined by the hemoglobin substrate method on 0.1 ml of gastric secretion.

Two acute experiments were performed to confirm differences in rate of absorption suggested by the plasma lipid absorption curves. Dog A (wt 13.8 kg) was given radioactive triolein and dog B (wt 12.5 kg) radioactive oleic acid in exactly the same way as in the chronic experiments. Blood samples were taken as before. At 3 hr after feeding the dogs were killed with an overdose of sodium pentobarbital. The total small intestine was extended from the pyloric sphincter to the ligament of Treitz. Essentially equal segments of the remaining small bowel were isolated. Luminal content was recovered by milking the small bowel. The content was weighed, and the lipid of a 1-g mixed sample per segment was extracted and counted by the same methods used for the plasma determinations. The time of 3 hr after feeding the dogs was chosen because the inhibition of gastric secretion with triolein had ended while that with oleic acid persisted.

RESULTS

The average acid output at each 30-min collection period for the controls (feeding alone), triolein, and oleic acid experiments is illustrated in Fig. 1. (Acid output after paraffin oil was not different from control values at any period and therefore is not included.) With feeding alone the acid output increased during the first collection period and reached a maximum at 1 hr in three of the four dogs and during the 2nd hr in dog 3.

Triolein caused an almost complete inhibition of the feeding stimulus for the first 2 hr in dogs 1 and 3. In dogs 2 and 4 the inhibition was not as complete during the first 1 1/2 hr and the inhibition lasted 1 1/2 hr. Following the period of inhibition resulting from the intraduodenal infusion of triolein, the secretory rate increased and the acid output that followed was similar to the outputs for feeding alone in all the dogs except dog 1 (Table 1).

With the infusion of oleic acid, inhibition lasted 3 hr in each of the dogs and the increase that followed was more gradual than that found with triolein. The amount of acid secreted over the 6 hr collection period was less with oleic acid than with triolein for all four dogs (Table 1).

The changes in pepsin output at each 30-min collection period following the various experimental procedures were essentially the same as those shown for acid output (Fig. 2).

The total 6-hr output of acid for each experiment on each dog is shown in Table 1. It should be noted that there was considerable variation with each type of experimental procedure in individual dogs. Part of the variability between dogs was the result of different secretory capacities of the pouches. The mean for each dog is shown in Table 1 and the mean control values listed for paraffin oil, triolein, and oleic acid experiments.

Paraffin oil did not alter the 6-hr output of acid. Although total acid output was reduced in dog 1 by triolein, this was not evident in the other three animals.

**TABLE 1. Acid output for the 6-hr collection period**

<table>
<thead>
<tr>
<th>Dog No.</th>
<th>Control, mEq</th>
<th>Paraffin Oil, mEq</th>
<th>% of Control</th>
<th>Triolein, mEq</th>
<th>% of Control</th>
<th>Oleic Acid, mEq</th>
<th>% of Control</th>
</tr>
</thead>
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<tr>
<td>1</td>
<td>2.955</td>
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<td>1.229</td>
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<td>8.000</td>
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<td>5.096</td>
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<td>14.862</td>
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<td>Avg</td>
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<td>10.099</td>
<td>14.862</td>
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<td>2.275</td>
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<td>Avg</td>
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<td>Mean ± se</td>
<td>110±5</td>
<td>95±22</td>
<td>45±9</td>
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FATTY ACID INHIBITION OF GASTRIC SECRETION

FIG. 2. Pepsin output following feeding.

TABLE 2. Pepsin output for the 6-hr collection period

<table>
<thead>
<tr>
<th>Dog No.</th>
<th>Control, PU x 10^{-4}</th>
<th>Paraffin Oil, PU x 10^{-4}</th>
<th>% of Control</th>
<th>Triolein, PU x 10^{-4}</th>
<th>% of Control</th>
<th>Oleic Acid, PU x 10^{-4}</th>
<th>% of Control</th>
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<tr>
<td>1</td>
<td>5.001</td>
<td>8.382</td>
<td>1.521</td>
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<td>Avg</td>
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<td>24.118</td>
<td>10.549</td>
<td>1.376</td>
<td>18</td>
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<td>2</td>
<td>25.068</td>
<td>16.975</td>
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<tr>
<td>Avg</td>
<td>2.123</td>
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<td>2.123</td>
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<tr>
<td>Avg</td>
<td>8.308</td>
<td>8.409</td>
<td>5.191</td>
<td>4.56</td>
<td>1.448</td>
<td>2.765</td>
<td>2.765</td>
</tr>
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</table>

and the calculated mean did not differ significantly from the control.

In the case of oleic acid, however, a definite reduction was seen in all cases, yielding a mean output significantly less than the control.

Table 2 shows the total 6 hr outputs of pepsin for the four experimental groups. Paraffin oil did not inhibit pepsin secretion. The effect of triolein on total pepsin output was variable, depressing output in dogs 1 and 4 and having minimal effect in dogs 2 and 3. The mean of the four dogs was somewhat below the controls, but the depression is not statistically significant ($P = .82$).

The absorption of triolein and oleic acid into the peripheral venous plasma is illustrated in Fig. 3. The average ± se of the percent of administered radioactivity recovered at each sampling period is plotted against time. With triolein the amount of radioactivity in the plasma rises to a peak at 3 hr to 3.3% of the administered dose. With oleic acid the rate of rise of plasma radioactivity is slower than with triolein and reaches a plateau at 3 hr at 0.6% of administered dose and remains unchanged at the end of the experimental period.

The absorption curves of Fig. 3 suggested that triolein was absorbed at a more rapid rate than the oleic acid. The results of the two acute experiments confirm this hypothesis, as shown in Table 3. The length in centimeters of the segments of small intestine which contributed contents for analysis are listed in the first column. The initial segment extended from the pyloric sphincter to the ligament of Treitz. This segment had 21.5 times more material per centimeter length and approximately 10 times more radioactivity in the dog given oleic acid than for the dog given triolein. The total content of the small bowel was three times greater and the remaining radioactivity nine times greater in the dog given oleic acid.

DISCUSSION

The results of the acid and pepsin outputs in these experiments show that oleic acid is a more effective inhibitor of gastric secretion over a 6-hr period following feeding than an equal amount of triolein. The major difference in the gastric secretory response is the duration of the inhibition.

The onset of inhibition in two of the four dogs was
The triglyceride was presumably hydrolyzed to fatty acids and mono- and diglycerides by pancreatic lipase in these experiments. Thus, the delayed onset of inhibition could have been a result of the time required for the hydrolysis of the triglycerides, as experiments by other authors suggest. Sircus found olive oil to be ineffective as an inhibitor of canine gastric secretion while oleic acid was an effective inhibitor under similar experimental conditions. The addition of glycerol precursors or monoglycerides has been shown by Clark and Hubscher to cause an increase in the rate of synthesis of tripalmitin from palmitic acid. The rate-limiting step in the synthesis of triglyceride from fatty acids may be the availability of glycerol precursors. In the experiments reported here, the fatty acids were infused directly into the duodenum before feeding the animals. Glucose or other products capable of yielding glycerol were eliminated from the intestinal lumen.

With oleic acid the process of fat absorption occurred over a longer period of time than with triolein and also the inhibition of gastric secretion lasted longer. Other studies utilizing fats of various chain length provide similar results. Short-chain fatty acids are absorbed rapidly from the small intestine and cause a relatively short delay in gastric emptying time, whereas long-chain fatty acids, which are absorbed slowly, produce a more prolonged gastric emptying time.

Since fatty acids are more effective as inhibitors of gastric motility and maintain the inhibition of gastric secretion for a longer period of time than the triglyceride, it is possible that the esterification of fatty acids by the intestinal epithelial cells is an essential link in the phenomenon of gastric inhibition following lipid administration.

REFERENCES


