Inhibitory effect of high caloric load of carbohydrates or lipids on human pancreatic secretions: a jejunal brake

Nicole Vidon, Stanislas Chaussade, François Merite, Brigitte Huchet, Claire Franchisseur, and Jean-Jacques Bernier

ABSTRACT

Effects of jejunal infusion of a saline solution, a protein meal, and a mixed protein and carbohydrate meal on biliopancreatic secretions were compared in six healthy volunteers. Protein infusion stimulated biliopancreatic secretions whereas carbohydrate infusion inhibited these secretions compared with saline infusion. The roles of lipid, carbohydrate, and caloric load on the inhibition of pancreatic secretions by jejunal infusion of nutrients was investigated in six other healthy volunteers. Carbohydrate, lipid, and the mixed meal inhibited pancreatic secretions whereas the carbohydrate solution was the only one that inhibited biliary secretion. These studies indicate that the mechanism of jejunal brake seems mainly related to the jejunal caloric load. In malabsorption or in the short bowel syndrome, a high caloric load or unabsorbed nutrients in the jejunum further inhibits pancreatic secretion, contributing to the loss of nutrients from the intestinal tract. Am J Clin Nutr 1989;50:231–6.

KEY WORDS

Inhibition of pancreatic secretions, jejunal infusion, carbohydrates, lipids, caloric load

Introduction

It is well known that in humans infusion of fatty acids or essential amino acids into the duodenum (1–3) sharply increases pancreatic secretions whereas infusion of nutrients into the ileum in cats (4) and rats (5) or into the colon in man (6), dogs (7), and cats (4) inhibits these secretions. Few publications relate the effect of jejunal infusions of varying caloric physiological loads of nutrients on pancreatic secretions (8, 9). In a previous study (10) we showed that infusion of a high caloric load of Realmentyl® (Sopharga Laboratories, Puteaux, France) (3.3 kcal/min [13.8 kJ/min]; proteins 18%, lipids 27%, and carbohydrates 55%) into the jejunum of healthy men inhibited basal biliopancreatic secretions, which were previously stimulated by either an ingested meal or infusion of a saline solution. However, the infused nutrient solution contained proteins that probably stimulate these secretions; thus the inhibitory effect was probably more important than the measured effect.

The aims of this work were to prove the stimulatory effect of the infused proteins on the pancreas and the inhibitory effect of carbohydrate infusion in comparison with the effects of a saline infusion and to investigate the role of lipids, carbohydrates, and caloric load on the inhibition of biliopancreatic secretions.

Methods

Patients

The study protocol was approved by the Ethics Subcommit-tee of the Saint Lazare Hospital and written informed consent was obtained from each subject. Twelve healthy men, aged 25.3 ± 0.8 y (X ± SEM), participated in this study. The mean weight of these subjects was 66.4 ± 1.5 kg and their mean height was 176.8 ± 1.4 cm.

General procedure

The digestive response was studied with a saline or a nutrient solution. The latter contained either proteins alone or proteins together with a high concentration of lipid or carbohydrates. The solutions were infused into the jejunum. Pancreatic function was not stimulated otherwise.

Infused solutions

The composition of the test solutions is shown in Table 1. The osmolality of all five solutions was 300 mol/kg.

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TABLE 1
Composition of test solutions

<table>
<thead>
<tr>
<th>Solution</th>
<th>Proteins</th>
<th>Lipids</th>
<th>Carbohydrates</th>
<th>NaCl</th>
<th>Polyethylene glycol (PEG) 4000</th>
<th>pH</th>
<th>Caloric load</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Alburone** (proteins of milk), 21.0 g/750 mL, 18% of caloric load</td>
<td>20% (soya oil) 53.4 g/750 mL, 27% of caloric load</td>
<td>Maltrinox** (glucose 19%, oligoholosides 57%, polyholosides 24%), 59.1 g/750 mL, 55% of caloric load</td>
<td>2.34 g/750 mL</td>
<td>3.75 g/750 mL</td>
<td>6.4</td>
<td>3.5 kcal/6 mL (14.6 kJ/6 mL)</td>
</tr>
<tr>
<td>B</td>
<td>Alburone*, 21.0 g/750 mL, 18% of caloric load</td>
<td>Maltrinox, 88.0 g/750 mL, 82% of caloric load</td>
<td>PEG</td>
<td>3.75 g/750 mL</td>
<td>6.4</td>
<td>3.5 kcal/6 mL (14.6 kJ/6 mL)</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>Alburone*, 21.0 g/750 mL, 18% of caloric load</td>
<td>Intralipide* 20%, 167.3 g/750 mL, 82% of caloric load</td>
<td>PEG</td>
<td>3.75 g/750 mL</td>
<td>6.7</td>
<td>3.5 kcal/6 mL (14.6 kJ/6 mL)</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>Alburone*, 21.0 g/750 mL, 100% of caloric load</td>
<td>Intralipide* 20%, 167.3 g/750 mL, 82% of caloric load</td>
<td>PEG</td>
<td>3.75 g/750 mL</td>
<td>6.8</td>
<td>0.63 kcal/6 mL (2.6 kJ/6 mL)</td>
<td></td>
</tr>
<tr>
<td>Saline solution</td>
<td>NaCl 130 mmol/L</td>
<td>KCl 5 mmol/L</td>
<td>Mannitol 30 mmol/L</td>
<td>[14C]PEG 185 kBq/L</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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† Kabivitrum SA, Noisy-le-Grand, France.

Experimental design

The perfusion technique was described by Modigliani et al (11). Subjects fasted for 12 h before each study, which was carried out in random order each morning for 3 consecutive days. In experiment A subjects were intubated with a three-lumen tube; the infusion point, checked radiologically, was located 10 cm below the ligament of Treitz and the aspiration site was located 25 cm distal to the infusion point. When solution B was infused intraluminal content was also aspirated 50 cm distal to the infusion point to prevent unabsorbed nutrients from reaching the ileum. In experiment B subjects were intubated with a two-lumen tube; the infusion point was also located 10 cm below the ligament of Treitz and the aspiration site was located 25 cm distal to the infusion point. In both experiments saline or test solutions were infused at a constant rate of 6 mL/min.

After a 90-min basal period during which saline solution was infused, one of the three following solutions was infused each day for 75 min: solutions B and D and saline solution in experiment A and solutions A, B, and C in experiment B. Material from the aspiration site was collected over ice in 15-min aliquots.

Analytical methods

PEG 4000 concentration was measured by the turbidimetric method of Hydén (12). [14C]PEG was counted in a scintillation counter and chymotrypsin (CHT) activity was determined turbidimetrically by using a pHstat® (Radiometer, Copenhagen, Denmark) with acetyl-tyrosine-ethylester as substrate (13). Lipase activity was estimated similarly but with emulsified olive oil as substrate (14). Bile salts were measured by a fluorimetric method (15, 16) and carbohydrate concentrations, expressed as glucose values after amyloglucosidase hydrolysis, were estimated by an enzymatic method (kit from Boehringer Mannheim, Mannheim, FRG). Lipids, after hydrolysis, were expressed as total fatty acids; total fatty acids were extracted by the technique of Blakenhorn and Arhens (17) and were titrated by the Dole technique (18).

Statistical analysis

Data are expressed as mean ± SEM. Enzymatic and biliary outputs during the last four 15-min intervals of each control period and during the last five 15-min intervals of the test period were used in the statistical analysis. We tested separately the effect of each solution on CHT, lipase, and bile salt output by using a two-way analysis of variance (subjects × period) (19).

Results

In experiment A the intraluminal flow rates were not significantly different when solution B or D or saline was infused. In experiment B the intraluminal flow rates were significantly higher when solution B was infused than when either solution A or C was infused. These differences resulted from the different NaCl concentrations in the perfused solution. Therefore, enzyme or bile salt concentrations cannot be compared and, thus, in the two experiments only intraluminal outputs of these substances were compared.

[14C]PEG was used as nonabsorbable marker for the saline solution and PEG 4000 was used for the test solution. Each marker was detected only 15 min after the beginning of infusion. Thus, for the evaluation of lipase, CHT, and bile salt outputs, as well as carbohydrate and lipid absorption rates, zero time was 30 min after the beginning of infusion of the saline solution and 15 min after the beginning of infusion of the test solution. In the first sample of the test solution so defined, neither [14C]PEG nor PEG 4000 concentrations corresponded to intraluminal steady-state conditions; the intraluminal flow rate was estimated as the mean of the preceding and subsequent sampling periods.
Experiment A

Lipase outputs (Fig 1) for the 2-h infusion of saline solution were not statistically different. The solution B infusion (proteins plus carbohydrates) decreased the lipase outputs compared with baseline values but the difference was not statistically different. The solution D infusion (proteins alone) significantly increased lipase outputs ($p < 0.05$) compared with baseline values.

The CHT outputs during the 2-h infusion of saline solution were not statistically different (Fig 2). The infusion of carbohydrates and proteins decreased these CHT outputs ($p < 0.025$) whereas the infusion of proteins alone increased them ($p < 0.001$). Likewise, bile salt outputs were inhibited ($p < 0.025$) by infusion of carbohydrates and proteins whereas they were stimulated ($p < 0.001$) by infusion of proteins alone (Fig 3). Bile salt outputs were similar during the second hour of saline infusion period compared with the first hour. During infusion of solution B, $332 \pm 44$ mg carbohydrates/min, ie, $35.7 \pm 4.6$% of the solution, were absorbed.

Experiment B

The mean values of lipase outputs (Fig 4) during infusion of solution A (proteins, lipids, and carbohydrates) ($p < 0.05$), solution B (proteins and carbohydrates) ($p < 0.025$), or solution C (proteins and lipids) ($p = 0.05$) were significantly different from the saline values.

CHT outputs varied in the same manner as lipase outputs (Fig 5) when solution A or B was perfused and were significantly inhibited ($p < 0.001$) by both solutions. Perfusion of solution C also significantly inhibited ($p < 0.0001$) CHT outputs.

The change in bile salt output pattern was different (Fig 6). Infusion of solution A or C did not inhibit bile salt outputs whereas solution B significantly decreased these solutions over the whole infusion period ($p < 0.025$).
Comparison of solutions A, B, and C shows that the decrease in lipase was not significantly different. The decrease in CHT and bile salt outputs was similar when solution A, B, or C was infused.

During the last hour of infusion of solutions A and C, lipid absorption was 71.5 ± 28.2 μmol/min and 261 ± 69 μmol/min, respectively, ie, 22.3 ± 9.0% and 25.0 ± 5.8% of the infused amount.

For the last hour of infusion, carbohydrate absorption was similar with solutions A and B, 227 ± 33 and 270 ± 31 mg/min and, as a percentage of the amount infused, 46.5 ± 6.5% and 35.6 ± 4.1%, respectively. In five subjects carbohydrate absorption was higher for solution A than for solution B. There was no correlation between carbohydrate absorption and inhibition of pancreatic secretion.

Discussion

The intestinal phase of pancreatic secretion is under the control of cholecystokinin (CCK) release and cholinergic reflexes. Recently, feedback regulation of pancreatic enzyme secretion by pancreatic proteases in the duodenum was described in several species, including man (20). Few publications discuss the existence of a jejunal or ileal feedback mechanism of pancreatic exocrine secretion. In a previous study we (10) showed the inhibitory effect of nutrient jejunal perfusion on basal and stimulated pancreatic secretion and on gastric emptying after ingestion of a meal. In the present study we infused three solutions at the highest caloric load used in the previous study; all of them contained 18% proteins expressed in caloric value. Our present results confirmed the stimulation of biliopancreatic secretions by proteins (21–23). Infusion of solution A, the caloric value of which was distributed as in a normal meal (20% proteins, 30% fat, and 50% carbohydrates), showed the influence of caloric load on secretions whereas results during infusion of solution B or C showed the effect of carbohydrates and lipids, respectively.

Infusions of oleic acid into the distal part of the ileum in cats (4) or rats (5) inhibit pancreatic secretions whereas carbohydrate infusion into the ileum of human stimulates pancreatic secretions (24). We assume that in our experiment B carbohydrates did not reach the ileum; indeed, > 80% of carbohydrates must be absorbed in a 75-cm segment of jejunum. The inhibition of pancreatic secretions that we observed during infusion of solution C may not be due to lipids reaching the ileum because it began immediately after the start of infusion and disappeared soon after the end of infusion (10).

During the infusion of solution A, B, and C we observed an inhibition of enzyme secretion although all the infused solution contained proteins. This inhibition appeared more marked because it was compared with enzyme secretion induced by saline infusion and was not compared with secretions induced by protein infusion. It was similar when either solution A, B, or C was infused. Thus, caloric load seems to be the main factor involved in this inhibition. Nevertheless, solution B (carbohydrates) was the only solution to inhibit biliary secretions.

The inhibitory effect of jejunal carbohydrate infusion on total protein secretion, serving as a measure of en-
zyme secretion, was found by Dyck (25) many years ago but the methodology was very different. Dyck infused hypertonic glucose solution, without a marker such as PEG 4000, over only a 5-min period at a rate of 20 mL/min and 40 kcal/min (167.2 kcal/min). This caloric load was 10-fold higher than the caloric load we tested and was not physiological.

Our results seem to disagree with those of a previous study (26) in which we infused Realmentyl® into the jejunum at 2 kcal/min (8.4 kJ/min) and an elemental nutritional solution (Vivonex®, Eaton Laboratories, Brussels, Belgium) at 1, 2, and 3 kcal/min (4.2, 8.4, and 12.6 kJ/min). We showed that enzyme secretion was proportional to the quantity of infused nitrogen. In fact, in that study pancreatic enzyme secretion was measured after a 3-h equilibration period, i.e., the nutrient solution was infused for 3 h before determination of pancreatic secretion.

On the basis of these two experiments, we may assume that caloric load into the jejunum has a transient inhibitory effect on pancreatic secretion. These results are in agreement with results of Felder et al (27). These authors investigated the influence of continuous jejunal nutrition of different caloric loads on intestinal motility in dogs. Their results showed that after temporary inhibition caused by the beginning of continuous enteral nutrition, phase III of the myoelectric complex (MMC) reappeared with the same characteristics observed in the fasting state. The duration of the postprandial inhibition of MMCs depended on the caloric load and nature of the nutrients; the higher the caloric load, the longer the inhibition. Sava et al (28) showed that intrajejunal infusion of lipids or carbohydrates increased duration of inhibition of the MMC and that this inhibition was significantly longer with carbohydrates. These observations demonstrate the existence of a jejunal control mechanism that inhibits pancreatic secretion and intestinal motility.

Salinas et al (29) showed in dogs that jejunal distension was able to inhibit pancreatic secretion. This inhibitory effect was explained by an atropine-sensitive reflex. In our study inhibition did not seem to be the consequence of jejunal distension. Indeed, the intraluminal flow rates were ~6 mL/min in the control periods and varied from 4.5 to 7.0 mL/min at the sampling point during infusion of the nutritive solution. At these flow rates there is no intestinal distension (30).

The mechanism of this inhibition is not known. A decrease of CCK secretion does not seem to be involved. In a previous study we (unpublished observations, 1988) showed that CCK plasma concentration increased during a 3.3-kcal/min (13.8-kJ/min) jejunal infusion of nutrients whereas vasoactive intestinal peptide (VIP), somatostatin, and pancreatic polypeptide (PP) were not modified. Studies in man showed that there is a cholinergic tone (31) that conditions the pancreatic secretory response to CCK and to perfusion of intestines with amino acids (2, 32); the inhibitory effect of jejunal perfusion of solutions A, B, and C could be the consequence of the interruption of stimulatory cholinergic fibers to the pancreas (9).

In conclusion, a high caloric load of carbohydrates or lipids infused into the human jejunum decreased basal pancreatic secretions as well as secretions induced by proteins. This effect, related to a jejunal brake, might explain why pancreatic insufficiency occurs after surgical procedures such as gastrectomy or gastrojejunal anastomosis (33, 34).

These results demonstrate for clinical practice that in malabsorption, in the short bowel syndrome, or during enteral nutrition nutrient solutions must be infused into the stomach or at a low caloric rate (10).

References