Antroduodenal motility in chronic pancreatitis:
are abnormalities related to exocrine insufficiency?

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Vu, M. K., J. Vecht, E. H. Eddes, I. Biemond, C. B. H. W. Lamers, and A. A. M. Masclee. Antroduodenal motility in chronic pancreatitis: are abnormalities related to exocrine insufficiency? Am. J. Physiol. Gastrointest. Liver Physiol. 278: G458–G466, 2000.—In patients with chronic pancreatitis (CP) the relation among exocrine pancreatic secretion, gastrointestinal hormone release, and motility is disturbed. We studied digestive and interdigestive antroduodenal motility and postprandial gut hormone release in 26 patients with CP. Fifteen of these patients had pancreatic insufficiency (PI) established by urinary para-aminobenzoic acid test and fecal fat excretion. Antroduodenal motility was recorded after ingestion of a mixed liquid meal. The effect of pancreatic enzyme supplementation was studied in 8 of the 15 CP patients with PI. The duration of the postprandial antroduodenal motor pattern was significantly (P < 0.01) prolonged in CP patients (324 ± 20 min) compared with controls (215 ± 19 min). Antral motility indexes in the first hour after meal ingestion were significantly reduced in CP patients. The interdigestive migrating motor complex cycle length was significantly (P < 0.01) shorter in CP patients (90 ± 8 min) compared with controls (129 ± 8 min). These abnormalities were more pronounced in CP patients with exocrine PI. After supplementation of pancreatic enzymes, these alterations in motility reverted toward normal. Digestive and interdigestive antroduodenal motility are abnormal in patients with CP but significantly different from controls only in those with exocrine PI. These abnormalities in antroduodenal motility in CP are related to maldigestion.

pancreatic enzyme supplementation; cholecystokinin; peptide YY

In the fasting state gastrointestinal motility is characterized by cyclic reoccurrence of a typical motor pattern, the migrating motor complex (MMC) (14, 38). Interdigestive exocrine pancreatic secretion cycles in close association with the various phases of the MMC in the duodenum (12, 27) but is dissociated from the MMC in chronic pancreatitis (CP) (29). After meal ingestion, gastrointestinal motility is converted to a feeding pattern and exocrine pancreatic secretion increases. The control of interdigestive and digestive motility and pancreatic secretion includes neural and hormonal components, several of which regulate both motility and pancreatic secretion (35, 37). Recent studies indicate that in CP patients with impaired exocrine function alterations in gastrointestinal hormonal release and motility can be observed. Postprandial release of CCK and pancreatic polypeptide (PP) is reduced in patients with exocrine pancreatic insufficiency (PI) (10, 15), gallbladder contraction is impaired (24), and gastric emptying is accelerated (20). It has been suggested that the pancreas has a role in controlling antroduodenal motility (4, 17, 21–23). In patients with CP and PI interdigestive and digestive motility may be affected, as well as gastrointestinal transit (4, 17, 22).

However, results of studies on antroduodenal motility in patients with CP have been controversial. Both normal and increased interdigestive MMC cycle frequency have been observed (17, 22, 23). Duration of postprandial motility was reduced in one study (17), whereas in another study the postprandial antroduodenal motor pattern in patients with CP was not different from controls (23). These differences in results may be related to the presence of exocrine PI in CP patients.

Therefore, we have investigated digestive and interdigestive antroduodenal motility and release of the gastrointestinal hormones CCK, PP, and peptide YY (PYY) in a large group of CP patients. The patients were divided into groups with and without exocrine PI. To further elucidate the role of exocrine PI and subsequent maldigestion, we also studied the effect of exocrine pancreatic enzyme supplementation on the aforementioned parameters. Results were compared with those obtained in healthy control subjects.

METHODS

Subjects

Two groups of subjects were studied: 26 patients with CP (21 male, 5 female; mean age 47 ± 3 yr) and 15 healthy control subjects (9 male, 6 female; mean age 39 ± 5 yr). None of the patients with CP or control subjects had previously undergone abdominal surgery. The diagnosis of CP had been established in all patients by typical clinical history and characteristic abnormalities on ultrasonography, computed tomography, and endoscopic retrograde cholangiopancreatography. Exocrine pancreatic function was assessed by the indirect para-aminobenzoic acid (PABA) test and fecal fat excretion. Fifteen of twenty-six patients with CP had evidence of impaired exocrine pancreatic function, showing urinary PABA recovery of <50% and/or fecal fat excretion of >7 g/24 h. These patients were classified as having exocrine PI. Eleven patients with CP had no evidence of exocrine PI.
Antroduodenal Motility

Antroduodenal motility was recorded using a multilumen water-perfused polyvinyl catheter (outer diameter 5 mm). The catheter incorporated eight side holes located at 3, 8, 13, 18, 23, 28, 33, and 38 cm from the distal tip. The manometry catheter was passed transnasally into the stomach and from there positioned into duodenum-jejunum under fluoroscopic control. The tip of the catheter was located just distal to the ligament of Treitz so that one or two side hole openings were in the jejunum, three to four side hole openings were in the duodenum, and at least two were in the antrum. When the correct position had been verified, the catheter was taped to the nose. At the end of each experiment, position of the catheter was checked again by fluoroscopy. Each lumen was connected to a pressure transducer and perfused with distilled water by a low-compliance pneumohydraulic perfusion system (Arndorfer Medical Systems) at a rate of 0.5 ml/min. Outputs from pressure transducers were recorded by a polygraph (Synectics Medical, Stockholm, Sweden), displayed on a monitor, and stored on a personal computer for automated and manual analysis.

Table 1. Clinical characteristics of patients with chronic pancreatitis and control subjects

<table>
<thead>
<tr>
<th>Chronic Pancreatitis</th>
<th>All</th>
<th>With PI</th>
<th>Without PI</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>26</td>
<td>15</td>
<td>11</td>
<td>15</td>
</tr>
<tr>
<td>Age</td>
<td>47 (22–67)</td>
<td>48 (22–67)</td>
<td>45 (31–66)</td>
<td>39 (21–50)</td>
</tr>
<tr>
<td>Gender, M/F</td>
<td>21/5</td>
<td>12/3</td>
<td>9/2</td>
<td>9/6</td>
</tr>
<tr>
<td>Etiology of CP</td>
<td>Unknown, no. of subjects</td>
<td>16</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>Exocrine insufficiency</td>
<td>Urinary PABA</td>
<td>15</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>Urinary PABA recovery</td>
<td>&lt;50%</td>
<td>15</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>Fecal fat, g/24 h</td>
<td>15</td>
<td>15</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Exocrine pancreatic function</td>
<td>Urinary PABA</td>
<td>15</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>Urinary PABA recovery</td>
<td>%</td>
<td>42 (3-89)</td>
<td>27 (3-44)</td>
<td>56 (54-89)</td>
</tr>
<tr>
<td>Fecal fat, g/24 h</td>
<td>22 (2-95)</td>
<td>36 (6-95)</td>
<td>5 (2-7)</td>
<td></td>
</tr>
<tr>
<td>Endocrine insufficiency</td>
<td>Impaired glucose tolerance</td>
<td>10</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Insulin dependent</td>
<td>6</td>
<td>5</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

Mean (range) parameter values are given; n, no. of subjects. CP, chronic pancreatitis; PI, pancreatic insufficiency; PABA, paraaminobenzoic acid.

Hormone Assays

Blood samples for measurement of plasma CCK, PP, and PYY were drawn at –15 min, 0 min before meal ingestion, and thereafter at 15, 30, 45, 60, 90, 120, 150, 180, 240, 300, and 360 min. Plasma CCK was measured by a sensitive and specific radioimmunoassay. This antibody binds to all CCK peptides, including sulfated CCK octapeptide, but not with gastrin. The detection limit of the assay is 0.3 pmol/l plasma. The intra-assay variation ranges from 4.6 to 11.5% and the interassay variation from 11.3 to 26.1% (9). Plasma PP concentrations were measured by a sensitive and specific radioimmunoassay as described previously (16). Plasma PYY was measured in our laboratory by a recently developed radioimmunoassay. PYY antiserum was generated in rabbits (Bachem, 1:250,000). The assay is highly specific. There is no cross-reactivity with PP or VIP. The detection limit is 10 pmol/l. Both PYY (1–36) and PYY (3–36) bind to the antibody in dilutions up to 1:250,000.

Analysis of Manometric Data

Motility patterns from antroduodenal manometry were analyzed both visually and by computer. The individual tracings were processed by special software (Polygram, Synectics Medical, Stockholm, Sweden) for adjusting baselines and extracting respiratory artifacts. However, the computer program does not recognize simultaneous pressure events as artifacts. Therefore, remaining artifacts caused by increments in intra-abdominal pressure were identified visually and excluded from analysis. Duodenal phases of the MMC were defined as follows: phase I, no more than 2 contractions/10 min for at least 5 min and preceded by phase III; phase II, irregular contractile activity at a frequency of >2/10 min and amplitude >12 mmHg; phase III, regular contractile activity at a frequency of 10–12 contractions/min for at least 2 min. Phase III activity had to be propagated over at least 2 recording sites. Antral phase III activity was defined as rhythmic contractile activity at maximum frequency (3 contractions/min) for at least 1 min in temporal relationship with duodenal phase III activity (14). Duration of the MMC cycle was taken as the interval between the beginning of phase III in the duodenum and the beginning of the next phase III cycle. Antral or duodenal origin, duration, mean amplitude,
contraction frequency, propagation velocity, and area under the curve of phase III of the MMC were measured.

The postprandial period was defined as the time interval between the end of the meal and the occurrence of the first duodenal phase III propagated over at least two channels. Only pressure waves with an amplitude ≥10 mmHg and a duration ≥1.5 s were considered true contractions. The motility indexes (MI) of the postprandial period in antrum and duodenum were calculated as area under the contraction curves (expressed in mmHg·s·h⁻¹).

Data and Statistical Analysis

Integrated incremental CCK, PP, and PYY secretion in response to the meal were determined by calculating the area under the plasma concentration time curve after subtraction of the basal value at 0 min. Possible influences of diabetes mellitus on gastrointestinal motility and secretion were analyzed in two ways: 1) by comparing the results between patients with and without diabetes within the group of CP patients with and without PI and 2) by comparing the results between CP patients with and without PI after excluding the six patients with insulin-dependent diabetes mellitus. For all parameters, differences between and within groups were analyzed by repeated ANOVA. When this indicated a probability of <0.05 for the null hypothesis, Student-Newman-Keuls analysis was performed to determine which values between or within groups differed significantly. Statistical significance was defined as a P value <0.05.

RESULTS

Antroduodenal Motility

Postprandial state. The duration of the fed motility pattern was significantly (P < 0.01) prolonged in CP patients (324 ± 20 min) compared with control subjects (215 ± 19 min). No significant difference in the duration of the fed motility patterns was found between patients with (345 ± 25 min) and without (294 ± 33 min) PI. The postprandial antral MI during the first hour after the meal was significantly (P < 0.01) reduced in the CP patient group compared with the control group (Table 2). Moreover, within the patient group, patients with PI had a significantly (P < 0.01) smaller MI compared with CP patients without PI. During the subsequent hourly intervals after the meal, the antral MI was not significantly different between CP patients and control subjects or between CP patients with and without PI (Table 2).

Table 3. Characteristics of interdigestive antroduodenal motility in CP patients and control subjects

<table>
<thead>
<tr>
<th>Chronic Pancreatitis</th>
<th>All (n = 26)</th>
<th>PI + (n = 15)</th>
<th>PI − (n = 11)</th>
<th>Controls (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMC duration, min</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase I, min</td>
<td>28.3 ± 1.0</td>
<td>28.2 ± 1.2</td>
<td>28.4 ± 1.0</td>
<td>28.5 ± 0.9</td>
</tr>
<tr>
<td>Phase II, min</td>
<td>464 ± 48</td>
<td>464 ± 48</td>
<td>464 ± 48</td>
<td>464 ± 48</td>
</tr>
<tr>
<td>Phase III, min</td>
<td>1074 ± 52</td>
<td>1074 ± 52</td>
<td>1074 ± 52</td>
<td>1074 ± 52</td>
</tr>
</tbody>
</table>

Values are means ± SE; n, no. of subjects. MMC, migrating motor complex. *P < 0.05 vs. controls.

The postprandial duodenal MI was not different between CP patients and control subjects during the first three subsequent hourly intervals after the meal or during the total fed period (Table 2). No differences were found in duodenal MI between CP patients with and without PI.

Interdigestive state. After transition from a digestive into an interdigestive motility pattern, 21 complete MMC cycles in the patient group and 22 complete MMC cycles in the control subjects were registered. The duration of complete MMC cycles was significantly (P < 0.01) reduced in CP patients compared with control subjects. The shorter duration of the MMC cycle in the patient group resulted from a significantly (P < 0.05) shorter phase II (Table 3). These differences were more pronounced in CP patients with PI compared with those without PI (Table 3). The amplitude of phase III in the CP patients (31 ± 3 mmHg) was significantly (P < 0.01) lower compared with the control group (39 ± 3 mmHg), but no significant difference was found between patients with and without exocrine PI (29 ± 4 mmHg vs. 32 ± 3 mmHg). Other phase III characteristics such as origin, duration, and propagation velocity were not significantly different between patients and controls (data not shown).

Pancreatic Enzyme Supplementation and Antroduodenal Motility

Digestive state. The duration of the fed motility pattern in the eight CP patients with PI was significantly (P < 0.05) shorter with enzyme supplementation.
(254 ± 38 min) than without enzyme supplementation (356 ± 43 min). The duration of the fed pattern after enzyme supplementation was not significantly different from that in healthy controls (215 ± 19 min). Pancreatic enzyme supplementation markedly increased antral MI during the first postprandial hour compared with that without enzyme supplementation (Table 4). During the subsequent hourly intervals after the meal no significant differences were found in antral MI between PI patients with and without enzyme substitution. Furthermore, pancreatic enzyme substitution did not affect duodenal motility index (Table 4).

Hormonal Responses

Plasma CCK. Basal plasma CCK levels in patients with CP (1.7 ± 0.2 pmol/l) were not significantly different from control subjects (1.9 ± 0.3 pmol/l; Fig. 1A). In both groups, plasma CCK levels increased significantly over basal levels starting from 15 min after meal ingestion and remained significantly increased until 120 min in the controls and 180 min in the patient group. Plasma CCK secretion during the first postprandial hour was significantly (P < 0.05) reduced in the CP patients (118 ± 14 pmol·l⁻¹·60 min⁻¹) compared with the control group (168 ± 20 pmol·l⁻¹·60 min⁻¹). No difference in CCK secretion was found between patients with and without PI (Fig. 1B).

Plasma PP. Basal plasma PP levels in the CP patients (37 ± 7 pmol/l) were not significantly different from controls (41 ± 5 pmol/l; Fig. 2A). After meal ingestion plasma PP levels increased significantly (P < 0.005–P < 0.05) in both groups and remained significantly elevated for 180 min. Postprandial PP secretion during the first hour was significantly (P < 0.01) reduced in CP patients (2,220 ± 397 pmol·l⁻¹·60 min⁻¹) compared with controls (3,198 ± 709 pmol·l⁻¹·60 min⁻¹). Compared with that in CP patients without PI, plasma PP secretion during the first postprandial hour was significantly (P < 0.01) reduced in CP patients with PI (2,993 ± 756 vs. 1,640 ± 345 pmol·l⁻¹·60 min⁻¹; Fig. 2B).

Plasma PYY. Basal plasma PYY levels were not significantly different between CP patients (20 ± 2 pmol/l) compared with controls (18 ± 1 pmol/l). After meal ingestion plasma PYY levels increased significantly.

Table 4. Postprandial antral and duodenal motility index in 60-min periods and for total fed period after ingestion of a liquid meal in PI patients with and without enzyme supplementation and control subjects

<table>
<thead>
<tr>
<th>MI</th>
<th>No Enzymes (n = 8)</th>
<th>Enzymes (n = 8)</th>
<th>Controls (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antrum 0–60 min</td>
<td>271 ± 79</td>
<td>1,429 ± 318*</td>
<td>2,473 ± 980</td>
</tr>
<tr>
<td>Antrum 60–120 min</td>
<td>1,022 ± 241</td>
<td>1,296 ± 390</td>
<td>2,501 ± 688</td>
</tr>
<tr>
<td>Antrum 120–180 min</td>
<td>2,414 ± 643</td>
<td>2,217 ± 935</td>
<td>2,760 ± 1,505</td>
</tr>
<tr>
<td>Antrum, total fed period</td>
<td>2,592 ± 389</td>
<td>3,007 ± 1,107</td>
<td>3,468 ± 762</td>
</tr>
<tr>
<td>Duodenum 0–60 min</td>
<td>3,160 ± 961</td>
<td>3,584 ± 808</td>
<td>4,325 ± 956</td>
</tr>
<tr>
<td>Duodenum 60–120 min</td>
<td>3,738 ± 564</td>
<td>3,570 ± 542</td>
<td>4,096 ± 1,000</td>
</tr>
<tr>
<td>Duodenum 120–180 min</td>
<td>4,022 ± 528</td>
<td>4,000 ± 636</td>
<td>4,013 ± 603</td>
</tr>
<tr>
<td>Duodenum, total fed period</td>
<td>4,311 ± 542</td>
<td>3,881 ± 935</td>
<td>4,634 ± 752</td>
</tr>
</tbody>
</table>

Values (in mmHg·s) are means ± SE; n, no. of subjects. *P < 0.05 vs. no enzymes.

Table 5. Characteristics of interdigestive antroduodenal motility in PI patients with and without enzyme supplementation and control subjects

<table>
<thead>
<tr>
<th></th>
<th>No Enzymes (n = 8)</th>
<th>Enzymes (n = 8)</th>
<th>Controls (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMC duration, min</td>
<td>89 ± 10</td>
<td>119 ± 13*</td>
<td>129 ± 8</td>
</tr>
<tr>
<td>Phase I, min</td>
<td>18 ± 6</td>
<td>17 ± 4</td>
<td>22 ± 2</td>
</tr>
<tr>
<td>Phase II, min</td>
<td>66 ± 6</td>
<td>96 ± 11*</td>
<td>102 ± 9</td>
</tr>
<tr>
<td>Phase III, min</td>
<td>5 ± 1.0</td>
<td>6 ± 1.0</td>
<td>5 ± 0.3</td>
</tr>
</tbody>
</table>

Values are means ± SE; n, no. of subjects. *P < 0.01 vs. no enzymes.
cantly (P < 0.01) over basal levels starting from 15 min until 240 min in controls and until 300 min in the CP patients (Fig. 3A). Plasma PYY levels in CP patients were significantly (P < 0.05) increased over controls from 30 to 180 min after meal ingestion. Integrated postprandial PYY secretion in CP patients was also significantly (P < 0.05) higher compared with controls (2,840 ± 470 vs. 1,380 ± 340 pmol·l\(^{-1}\)·360 min\(^{-1}\)). When analyzed separately according to exocrine function, only in the patients with PI were plasma PYY levels significantly increased over those in controls. This was true for basal plasma PYY levels and those from 15 to 240 min after meal ingestion (Fig. 3B). Plasma PYY levels were higher in CP patients with exocrine PI compared with patients without PI, although this difference was not statistically significant.

**Pancreatic Enzyme Supplementation and Hormone Responses**

**Plasma CCK.** Pancreatic enzyme supplementation significantly (P < 0.05) increased postprandial plasma CCK levels in CP patients over those without enzyme supplementation (Fig. 4). After enzyme supplementation integrated plasma CCK secretion during the first postprandial hour (148 ± 16 pmol·l\(^{-1}\)·60 min\(^{-1}\)) was not significantly different from controls (168 ± 20 pmol·l\(^{-1}\)·60 min\(^{-1}\)) but was significantly (P < 0.05) higher compared with those without enzyme supplementation (77 ± 17 pmol·l\(^{-1}\)·60 min\(^{-1}\)).
Plasma PP. Supplementation of pancreatic enzymes did not alter postprandial PP release. The integrated plasma PP secretions during the first postprandial hour were 1,205 ± 515 and 1,242 ± 335 pmol·l⁻¹·60 min⁻¹, respectively, with and without addition of pancreatic enzymes.

Plasma PYY. Postprandial plasma PYY decreased significantly (P < 0.05) to levels comparable with controls after supplementation of pancreatic enzymes (Fig. 5). Integrated postprandial PYY release after enzyme supplementation (839 ± 127 pmol·l⁻¹·360 min⁻¹) was significantly (P < 0.05) lower compared with that without enzyme supplementation (2,683 ± 315 pmol·l⁻¹·360 min⁻¹) and was not significantly different from healthy controls (1,380 ± 340 pmol·l⁻¹·360 min⁻¹).

Role of Endocrine Insufficiency

Of the 15 CP patients with exocrine PI, 5 patients had insulin-dependent diabetes mellitus. Within this group, the mean duration of the fed pattern was not significantly different between CP patients with exocrine PI either with (361 ± 37 min) or without (345 ± 32 min) diabetes compared with controls (215 ± 19 min). Antral hypomotility during the first hour of the fed period was present (P ≤ 0.05) in both groups compared with controls (2,473 ± 980 mmHg·s·h⁻¹), but no significant difference was found between CP patients with (368 ± 165 mmHg·s·h⁻¹) and without (257 ± 92 mmHg·s·h⁻¹) diabetes mellitus. In addition, no significant differences in the duration of MMC cycle phases I, II, and III were found between patients with exocrine PI with and without diabetes (data not shown). When the results were analyzed between CP patients with and without exocrine PI after excluding six CP patients with diabetes mellitus from the study, differences in gastrointestinal motility and secretion still existed and remained significant between CP patients with and without exocrine PI (Table 6).

**DISCUSSION**

Our results demonstrate that antroduodenal motility is altered in patients with CP. The duration of the postprandial motor pattern was significantly prolonged and the interdigestive motility pattern was characterized by shorter duration of the MMC cycle because of a reduction in duration of phase II. These abnormalities were more pronounced in CP patients with PI. After addition of pancreatic enzymes, these alterations in antroduodenal motility reverted toward normal.

Recently, several studies were published about antroduodenal motility in patients with chronic pancreatitis. Malfertheiner et al. (22, 23) and Pieramico et al. (29) did not observe any changes in interdigestive motility in patients with CP vs. controls, whereas Layer et al. (17) found that the duration of the interdigestive motor cycle was significantly reduced. We were able to confirm the results of Layer et al. by finding a shorter duration of the MMC cycle with shorter phase II in CP patients. Differences in results between the studies of Layer et al. (17) and ours compared with those of Malfertheiner (22, 23) and Pieramico (29) may be related to several factors. First, the degree of exocrine PI in CP patients may have an important role. Whereas Malfertheiner et al. and Pieramico et al. studied 15 CP patients without steatorrhea, Layer et al. investigated patients with severely impaired exocrine function. In the present study, the duration of the MMC cycle was shorter compared with controls only in patients with and not in those without exocrine PI. Several explanations could be considered. This finding could be caused by autonomic neuropathy secondary to diabetes mellitus. However, none of the six patients with insulin-dependent diabetes mellitus had evidence of autonomic neuropathy and similar motility results were obtained between patients with and without diabetes. Therefore, the possibility that autonomic neuropathy affects antroduodenal motility seems unlikely. Furthermore, Samson and Smout (33) showed that MMC cycle length is actually prolonged, not shortened, in diabetic patients with autonomic neuropathy. Second, the presence of endocrine PI and subsequent hyperglycemia may be a confounding factor because it has been demonstrated that hyperglycemia shortens MMC cycle length by

<table>
<thead>
<tr>
<th>Duration fed pattern, min</th>
<th>PI+ (n = 10)</th>
<th>PI− (n = 10)</th>
<th>Controls (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI antrum 0–60 min, mmHg·s</td>
<td>331 ± 35*</td>
<td>326 ± 34*</td>
<td>215 ± 19</td>
</tr>
<tr>
<td>MMC duration, min</td>
<td>77 ± 16*</td>
<td>106 ± 12</td>
<td>129 ± 8</td>
</tr>
<tr>
<td>Plasma PP, pmol·l⁻¹·60 min⁻¹</td>
<td>1,788 ± 222†</td>
<td>2,476 ± 422*</td>
<td>3,918 ± 709</td>
</tr>
<tr>
<td>Plasma CCK, pmol·l⁻¹·60 min⁻¹</td>
<td>120 ± 17*</td>
<td>133 ± 19</td>
<td>168 ± 20</td>
</tr>
<tr>
<td>Plasma PYY, pmol·l⁻¹·360 min⁻¹</td>
<td>2,915 ± 154*</td>
<td>2,218 ± 479</td>
<td>1,380 ± 340</td>
</tr>
</tbody>
</table>

Values are means ± SE; n, no. of subjects. PP, pancreatic polypeptide; PYY, peptide YY. *P < 0.05 vs. controls; †P < 0.05 vs. PI−.
shortening the duration of phase II (7). During the experiments plasma glucose levels were kept in the euglycemic range of 4–8 mmol/l. It is more likely that exocrine PI and subsequent malabsorption activated “ileal brake” mechanisms that facilitate the occurrence of phase III and thereby shorten MMC cycle length. Normalization of the MMC cycle length after pancreatic enzyme supplementation further supports this idea.

The occurrence of antral hypomotility gastric emptying of nutrient concentration after ingestion of a semiliquid meal. Apart from the duration, differences in postprandial antral motility index in the first postprandial hour was significantly reduced. As a consequence of antral hypomotility gastric emptying of nutrients may be delayed. Recently, Layer et al. (17) suggested that the observed abnormalities are related to exocrine PI and subsequent malabsorption but not to CP per se. The observed changes in the duration of the fed pattern, MMC cycle, and phase II toward normal with the addition of pancreatic enzymes support this concept. Recently, Bassotti et al. (5) reported abnormalities in interdigestive antral hypomotility in adult patients with untreated celiac sprue similar to those we have observed in CP patients with PI. Combining the results of these studies, it is tempting to relate the abnormalities in antral hypomotility to intraluminal conditions rather than to the disease per se.

Ingestion of the liquid meal induced a rapid increase in plasma CCK levels both in patients and controls. CCK may be involved in the conversion of a fasted into a fed antral motility pattern (25, 35, 37). Postprandial CCK release is impaired in CP patients with PI (10, 24). In the present study, integrated plasma CCK secretion was significantly reduced in CP patients in the first postprandial hour. Malabsorption of triglycerides and proteins as a result of exocrine PI could be responsible for this finding. Hildebrand et al. (8) showed that an adequate digestion of triglycerides by pancreatic lipase is necessary for release of CCK in response to food, particularly during the immediate postprandial phase. In support of this concept and in line with earlier studies (10, 24) we have found that pancreatic enzyme supplementation increased postprandial plasma CCK levels toward control values. Postprandial CCK levels remained elevated over basal for a longer period in CP patients than in controls, possibly contributing to prolonged duration of the fed motor pattern. Our findings contrast with those of others who found a significantly shorter duration of the fed motility pattern in CP (17). These differences are not easily explained and may have been influenced by patient characteristics, degree of exocrine PI, meal composition (higher fat and caloric content in our study), CCK secretion, or activation of the ileal brake.

In contrast to the proximal gut hormone CCK, basal and postprandial plasma levels of the distal gut hormone PYY were significantly increased in CP patients with exocrine PI. PYY is found in highest concentrations in the mucosa of the distal gut (2) and is considered one of the mediators of the so-called ileal brake (18, 31). In the present study, PYY was chosen as a marker of the ileal brake because there is substantial evidence suggesting that plasma PYY levels correlate with ileal fat-induced delayed gastric emptying (31), prolonged small intestinal transit, and inhibition of small intestinal motility (32, 36). In humans, infusion of PYY delays gastric emptying and small intestinal transit in a dose-dependent manner (34). Elevated
plasma PYY levels have been found in diseases associated with malabsorption such as celiac sprue, cystic fibrosis, and dumping syndrome (1, 3, 26). These findings support the idea that alterations in plasma PYY secretion in PI patients result from malabsorption. The presence of undigested and unabsorbed nutrients in the distal gut activates the ileal brake with concomitant PYY release. This results in feedback regulation of proximal gut motor function such as prolongation of the fed pattern to optimize nutrient uptake and absorption. Normalization of postprandial plasma PYY secretion and duration of the fed pattern after pancreatic enzyme supplementation should be considered as evidence supporting this concept.

It is concluded that in patients with CP and exocrine PI, but not in those with normal exocrine function, 1) duration of postprandial antral motility is significantly prolonged and early postprandial antral motility is significantly reduced; 2) interdigestive MMC cycle length is significantly reduced because of shortening of phase III; 3) endogenous secretion of CCK and PP is decreased, whereas PYY secretion is increased; and 4) alterations in antral motility and hormone responses in CP patients are related to intraluminal malabsorption and malabsorption and revert toward normal with enzyme supplementation.

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REFERENCES


