Bile Acid Output and the Interdigestive Migrating Motor Complex in Normals and in Cholecystectomy Patients

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Bile acid output in the duodenum was studied in relation to the interdigestive migrating motor complex in normal subjects and in cholecystectomy patients. In normal volunteers the bile acid output preceding a duodenal activity front (217 ± 89 μmol/30 min) was 374% of the output following a front (58 ± 24 μmol/30 min) (P < 0.05). In cholecystectomy patients the prefront output (354 ± 64 μmol/30 min) was 195% of the value obtained in the postfront period (234 ± 59 μmol/30 min) (P < 0.05). These results indicate that the bile acid output into the duodenum during the interdigestive phase is fluctuating in accordance with the interdigestive motility complex.

The most characteristic part of the interdigestive migrating motor complex is the activity front.1 It is phase III of the complex as described by Code and Marlett.2 Recently we have shown that the development of an activity front in the gastroduodenal area in humans is associated with an increased secretion of pepsin and HCl by the stomach and amylase and bicarbonate by the pancreas. We have called this phenomenon the secretory component of the migrating motor complex.3 This paper presents evidence that bile acid output into the duodenum is also coupled to the migrating motor complex.

Methods

In all experiments a similar catheter assembly comprising 4 polyethylene tubes (Clay Adams PE 205, Becton, Dickinson & Co., Parsippany, N.Y.) was used. Three catheters had a single side opening located 25 cm apart. The fourth catheter had multiple side openings over a distance of about 6 cm distally to the orifice of the most proximal catheter. The catheter assembly was positioned under fluoroscopic control so that the proximal opening lay in the middle portion of the descending duodenum approximately at the level of the papilla of Vater. Polyethylene glycol (PEG) in a concentration of 10 g/liter was perfused through this catheter at a constant rate of 1 ml/min. The duodenal contents were continuously aspirated by means of the multiple side opening catheter and divided in 5-min fractions.

Upper intestinal motor activity was measured by means of the two remaining catheters which were continuously perfused with tap water at a rate of 0.7 ml/min. Details of the manometric recording technique have been presented in a previous report.4 The recording orifices lay approximately 5 cm below the angle of Treitz and 25 cm more distally. Finally a separate gastric suction tube (Salem tube, 14 CH, 102 cm, Sherwood Medical Industries, Petit Rechain, Belgium) was positioned in the most dependent portion of the stomach for continuous aspiration of the gastric secretions.

All experiments were started after an overnight fast. The study was continued until at least two cycles of the migrating motor complex had passed. The collected fractions were numbered, and the numbers rated on the motility records for synchronization. Bile acids were determined enzymatically according to the method of Koss et al.5 Polyethylene glycol was measured turbidimetrically with the use of arabic gum as an emulsifier.6 The recovery of polyethylene glycol in the samples was used to correct the bile acids measured during the 5-min sampling periods for incomplete aspiration. The recovery computed over all samples used in this study was 65 ± 10% (mean ± SD) and essentially independent of the sampling period. The analysis of the manometric tracings and the criteria used for identification of activity fronts have been described previously.4 The most important step in the analysis was the

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identification of the activity front (phase III of the migrating motor complex). The following criteria were used for the identification of the front: (a) appearance of a noninterrupted burst of pressure waves, produced at a rhythm of about 12/min at the level of the angle of Treitz; (b) aboral progression of the activity front over the two recording orifices; (c) a period of complete quiescence after the activity front. The activity fronts were identified independently by 2 of the authors without interobserver variation. The characteristics of the activity fronts were not different from those given in an earlier report. The mean interval was 102 ± 18 min, and the progression velocity was 8.6 ± 1.2 cm/min (mean ± SEM).

The time of onset of an activity front at the level of the proximal recording orifice was taken as a reference point, and biochemical determinations were grouped for the 30-min periods preceding and following the front. The sample at the time of the activity front was taken as the first sample of the postactivity front period. Only those results covering a complete 60-min period (30 min pre-AF plus 30 min post-AF), and related to activity fronts spaced at least 60 min apart, were taken into account. Results were analyzed by Student's paired t-test.

Two experimental groups were investigated. The first group consisted of 7 normal volunteers without any known gastrointestinal or biliary disease. The second group consisted of 7 cholecystectomy patients, who were examined 14 days postoperatively, when they were free of symptoms. In each patient the common bile duct was not enlarged on intravenous cholangiography, and no signs of residual gall stones were found with liver function tests, intravenous cholangiography, and gray scale sonography. Informed consent was obtained from both volunteers and patients, and the experimental protocol was approved by the human experimentation committee of the University Hospital.

Results

In the first experimental group of 7 normal volunteers, the total collection period of the duodenal aspirates amounted to 28 hr and 40 min. During this period 19 activity fronts were observed. In one volunteer five migrating motor complexes occurred during an observation period of 255 min (mean interval 56 min) and pooling the data into pre- and postactivity front periods of 30 min resulted in considerable overlap. The results of this volunteer are excluded from the statistical analysis but are reproduced in Figure 1. It will be seen that each activity front was preceded by a large peak in bile acid output into the duodenum. From the 14 fronts observed in the remaining six volunteers, two occurred immediately at the start of the experiment. They are also excluded, because data for the preactivity front period were lacking. During the 30-min periods preceding the 12 activity fronts taken into account, the mean bile acid output was 217 ± 89 µmol against 58 ± 24 µmol during the 30-min periods after a front. The mean difference, 159 µmol/30 min, was significant at the 5% level (P < 0.05).

In the second experimental group of 7 cholecystectomy patients the total collection period of duodenal aspirates was 25 hr and 15 min, and 13 activity fronts were observed. Pooling of data into pre- and postactivity front periods of 30 min was possible for 11 fronts. The mean bile acid output during the 30-min period preceding a front amounted to 354 ± 64 µmol/30 min and 234 ± 59 µmol during the 30-min period after a front. The mean difference, 120 µmol/30 min, was significant at the 5% level (P < 0.05). The data for the bile acid outputs are summarized in Figure 2.

In the group of normal volunteers the mean bile acid concentration before the front was 6.4 ± 1.3 mM; after the front it was 4.3 ± 1.2 mM. In the group of cholecystectomy patients the figures were 9.0 ± 1.6 and 9.4 ± 1.8 mM, respectively. The differences between either patients and normals, or between pre- and postactivity front periods are statistically not significant. However, the bile acid outputs during the postactivity front period, differed significantly between patients and volunteers (P < 0.05).

Figure 1. Bile acid output in consecutive 5-min fractions in volunteer PD. The start of activity fronts in the upper duodenum is indicated by arrows. It should be noted that the two smaller peaks of bile acid output (fractions 19 and 32) were associated with a burst of pressure waves recorded in the distal catheter only.
Discussion

During the interdigestive state the motility of the small intestine of humans as well as that of several animal species is characterized by a cyclically recurring pattern of motor activity which has been called the interdigestive migrating motor complex. Code and Marlett divided the complex into four phases, the most characteristic of which is phase III or the activity front. In a recent study in humans, we demonstrated that this motor activity front in the duodenum is accompanied by an increased secretory activity of the stomach and the pancreas; it is preceded by an increase in gastric acid and pepsin output and followed by a peak of bicarbonate and amylase secretion in the duodenum. We have called this phenomenon the secretory component of the migrating motor complex.

Our present study indicates that biliary secretion is also involved in this secretory component of the migrating motor complex of humans; in 7 normal volunteers the bile acid output in the duodenum during the 30-min period before the occurrence of the activity front was 374% higher than the output during the 30-min period after the front. Our studies further indicate that the contraction of the gallbladder is probably not the major factor in this cyclic output of biliary secretion, because in cholecystectomy patients this pattern is preserved. The differential output of bile acids cannot be caused by a differential recovery of bile after the activity front, because recovery during both pre- and postactivity front periods was essentially constant (60 ± 9% vs. 61 ± 12% in the volunteers and 59 ± 12% vs. 71 ± 8% in the patients, mean ± SD). The question arises whether the cyclic output of bile salts in the duodenum is a cyclic secretion of bile acids by the liver or a cyclic motor function of the sphincter of Oddi, as it has been shown recently that the delivery of bile into the duodenum in response to meals is wave-like and predominantly controlled by the sphincter of Oddi. The fact, however, that the peak of bile acid output in the duodenum precedes the activity front, whereas, as we have shown previously, the output of amylase and bicarbonate in the duodenum is maximal in the postactivity front period, suggests that the sphincter of Oddi does not have a major role in this cyclic phenomenon.

The factors that regulate the cyclic bile acid secretion in relation to the migrating motor complex are unknown. Motilin seems to be involved in the cyclic occurrence of the motor phenomenon. A hitherto unknown neural or hormonal mechanism may account for the cyclic secretion. It is also possible that the absorption of bile acids is enhanced on their arrival with the activity front in the distal ileum, which coincides with the preactivity front period of the meal cycle in the duodenum; an enhanced absorption of bile acids in the ileum would indeed accelerate the secretion of bile acids by the liver. It is interesting to note that the bile acid output in the duodenum differs significantly in cholecystectomy patients and normal volunteers. The higher rate in the patients probably reflects the absence of the reservoir function of the gallbladder. Whatever the mechanism may be, our studies clearly indicate that in the interdigestive period the bile acid output into the duodenum varies cyclically according to the different phases of the migrating motor complex.

The total output of bile acids after a meal is in the order of 10 mM. This is of course much larger than the outputs reported in this paper. From the data given by La Russo et al. the output rate after a meal is approximately 2.5 mM/hr. Previous values for the fasting state which did not take the cyclical secretion reported in this paper into consideration, were around 0.5 mM/hr. This is comparable to the overall mean of our data. Pomare and Heaton found a bile acid pool of 6.3 mM in normal subjects compared with 3.2 mM in cholecystectomy patients. Although the outputs associated with the activity front are much smaller than the total bile acid pool, our results may have important implications for the interpretation of observations on the enterohepatic circulation of bile acids especially in cholecystectomy patients.
References


