Changes in the Volume of Evacuated Bile Associated with Emesis in Dogs

Naohiro FURUKAWA

Department of Physiology, Kawasaki Medical School, Kurashiki, 701-01 Japan

Summary: Changes in the volume of evacuated bile as well as the extrahepatic biliary motilities associated with emesis were studied in decerebrated dogs. The motilities of both the gallbladder and sphincter of Oddi were enhanced with retching. The mean volume of evacuated

bile significantly decreased during retching. These results suggested that the extrahepatic biliary motilities with emesis are not related to bile evacuation. [Japanese Journal of Physiology, 46, 177–181, 1996]

Key words: bile evacuation, retching, extrahepatic biliary motilities.

It is well known that vomited matter is frequently stained by bilirubin. Although it is unknown when the bile is evacuated into the duodenum, this phenomenon is referred to as evidence of a retrograde peristalsis related to emesis [1]. Ohasi [2] demonstrated that the canine gallbladder contracts with emesis induced by apomorphine. However, recently, we reported that the motility of the sphincter of Oddi is also enhanced with emesis [3]. Therefore, it is unclear whether bile evacuation is facilitated or decreased by emesis. If bile flow into the duodenum is not increased, gallbladder contraction with emesis is probably related to functions other than bile evacuation. This study was undertaken to investigate the changes in the volume of evacuated bile through the sphincter of Oddi associated with emesis.

Six mongrel dogs unfed for 16 h were anesthetized with ketamine (25 mg/kg) and decerebrated precollicularly. Then they were paralyzed with gallamine triethiodide (2 mg/kg, i.v.) and artificially ventilated. Body temperature was maintained at near 37.5°C and mean systemic arterial pressure was monitored. The details of these methods were reported previously [3]. Since repeated stimulations usually induced similar motility patterns in the gallbladder and sphincter of Oddi with emesis in the same dog, flow resistance through the sphincter of Oddi was recorded as the first step, and subsequently, the volume of evacuated bile through the sphincter of Oddi was measured as the

second step (Fig. 1) in the same dog. Two polyethylene catheters were inserted into the common bile duct toward the gallbladder (catheter 1) and duodenum (catheter 2), respectively. Two additional polyethylene catheters were inserted into the gallbladder fundus (catheters 3 and 4). When the flow resistance through the sphincter of Oddi was measured, catheter 1 was clamped and Tyrode's solution was infused through catheter 2 at a constant rate with an infusion pump. Catheter 3 was led to a pressure transducer to measure gallbladder pressure. Catheter 4 was used to control gallbladder volume (Fig. 1A). When the volume of the evacuated bile through the sphincter of Oddi was measured, catheters 1 and 2 were connected to a closed glass chamber, and drops of bile passing through the chamber were counted using a photoelectric drop counter. Catheter 3 was led to a pressure transducer and catheter 4 was connected to an infusion pump to control basal bile evacuation (Fig. 1B). In both cases, a force transducer was sewn onto the duodenum to measure duodenal motility.

In all of the dogs, the centrifugal discharge from the phrenic nerve and the nerve to the rectus abdominis were led out with bipolar platinum wire electrodes. Neural discharge was converted into frequency histograms of 200-ms bins using spike counters, which were recorded with a pen recorder. The details of these methods were reported previously [3].

The dorsal or ventral vagal trunk was cut just above

Received on January 24, 1996; accepted on February 26, 1996

Correspondence should be addressed to: Naohiro Furukawa, Department of Physiology, Kawasaki Medical School, Kurashiki, 701-01 Japan. Tel: +81-864-62-1111 ext. 3511, Fax: +81-864-62-1199

Fig. 1. Schematic representation of the experimental model. A: Method for measurement of gallbladder pressure and flow resistance through the sphincter of Oddi. **B:** Method for measurements of gallbladder pressure and volume of bile flow through the sphincter of Oddi. In the same dogs, the volume of bile flow was measured subsequently to measurement of flow resistance through the sphincter of Oddi by changing the connection of catheters.

the diaphragm. Retching was induced by electrical stimulation (0.5 ms, 15–25 V, 5–20 Hz) of the central part of the severed vagal trunk. Coactivating rhythmic volleys of the phrenic nerve and the nerve to the rectus abdominis were used as an index of retching [4]. Vagal stimulation was discontinued after the cessation of retching.

The dorsal vagal trunk was stimulated in three dogs and the ventral vagal trunk was stimulated in the other three dogs. Before measurement of the volume of evacuated bile, the changes in the motilities of the gallbladder and the sphincter of Oddi with emesis

were observed three or four times. In every dog, similar motility patterns were elicited by repeated stimulations. Gallbladder pressure was slightly elevated with retching in all of the dogs. The motility of the sphincter of Oddi was enhanced with retching in four dogs. It was enhanced with retching but transiently depressed just after the initiation of retching in two dogs, in one of which the dorsal vagal trunk was stimulated and in the other the ventral vagal trunk was stimulated. After these observations, the connections of the catheters were changed, and the volume of evacuated bile before and after vagal stimulation was measured.

Fig. 2. Two types of responses in the gallbladder and sphincter of Oddi, and bile evacuation. A and B were obtained from two different dogs. A: In this dog, the motilities of the sphincter of Oddi and the duodenum were only enhanced with retching (a), and bile evacuation was continuously inhibited until the duodenal motility became small (b). **B:** In this dog, the motilities of the sphincter of Oddi and duodenum were enhanced with retching, but transiently inhibited just after the initiation of retching (a). A transient facilitation of bile evacuation was observed in association with the inhibition (b). The broken lines indicate periods of retching induced by afferent stimulation of the ventral vagal trunk in A and the dorsal vagal trunk in B. Phr. N., centrifugal activity of the phrenic nerve represented as frequency histograms with 200-ms bins; Abd. M. N., centrifugal activity of the nerve to the rectus abdominis represented as frequency histograms with 200-ms bins; Gallbladder, gallbladder pressure; Oddi's S., flow resistance through the sphincter of Oddi; Duodenum, duodenal contractility; Bile, drops of bile. Time marks (large) at top indicate 1-min intervals.

After a rest period of more than 15 min, the changes in the motilities were again recorded, and changes in the volume of evacuated bile were measured subsequently. These procedures were repeated four times in each dog.

The latencies of occurrence of retching after vagal stimulation were always 15 to 20 s in four dogs, but

were more than 30 s and varied among four stimulations in two dogs. Furthermore, the duration of retching varied widely in the latter two dogs. Therefore, only the bile flow data from the former four dogs, in two of which the dorsal vagal trunk was stimulated and in the other two the ventral vagal trunk was stimulated, were statistically analyzed. The data obtained

from four stimulations were analyzed in each of the four dogs as the mean volumes of evacuated bile every 0.2 min before and after the initiation of retching. Furthermore, the mean values in the four dogs were again averaged, and the statistical significance of the differences between the mean basal value and the mean response were analyzed by Student's *t*-test for paired data.

In two dogs, the motilities of the sphincter of Oddi and the duodenum were enhanced after vagal stimulation, and bile evacuation was depressed about 10 s after stimulation (just before retching) by every four stimulations (Fig. 2A). In the other two dogs, the motilities of the sphincter of Oddi and the duodenum were enhanced after vagal stimulation, but were transiently inhibited just after the initiation of retching by every four stimulations. In the latter two dogs, bile evacuation was depressed or changed very little before retching, slightly facilitated just after the initiation of retching, and again depressed during retching by two stimulations (Fig. 2A). However, by the other two stimulations, bile evacuation was only depressed during stimulation. The mean volume of bile flow in four dogs was significantly decreased during the periods of 0.4–0.6 and 0.6–0.8 min after the initiation of retching. After the cessation of retching, mean bile flow increased slightly but not significantly (Fig. 3). The mean value in the basal condition was $11.7 \pm 2.2 \mu\text{l}/0.2 \text{ min}$ (mean $\pm$ SE), which was estimated from the data during 1 to 3 min before stimulation. That decreased to $8.2 \pm 2.5 \mu\text{l}/0.2 \text{ min}$ during the period of 0.4–0.6 min after the initiation of retching.

These results clarified that bile evacuation is inhibited in association with emesis regardless of gallbladder contraction, because the motility of the sphincter of Oddi is also enhanced. We have already suggested that the excitatory effects in the gallbladder and the sphincter of Oddi are related to emesis but they are not caused by a direct vago-vagal reflex [3]. Therefore, the inhibition in bile evacuation observed in this study also seems to be related to emesis rather than to a vago-vagal reflex. We previously reported that canine salivary secretion from the submaxillary glands is facilitated with emesis by the activity of some afferent relay stations related to emesis [5]. Hypersalivation with emesis is thought to be desirable to prevent damage to the mucosa of the pharynx or esophagus by expelled gastric acid or other gastric contents. However, since bile is thought to damage the mucosa of the stomach when the intestinal contents is brought to the stomach by retrograde flow with emesis, the inhibition of bile evacuation with emesis seems to be reasonable. Bilirubin, which is frequently observed in

Fig. 3. Changes in the volume of evacuated bile before and after retching. Dotted column (cont): mean basal flow obtained from data during the 2-min period before the first open column; checked columns: during these periods, retching was continued in all of the dogs; hatched columns: during these periods, retching was continued in some cases, but was not continued in the other cases. The bars above Vagus stim. indicate the duration of stimulation of the ventral or dorsal vagal trunk. Filled bar: during these periods, vagal stimulation was continued in all of the dogs; hatched bar: during these periods, stimulation was continued in some cases, but discontinued in the other cases. The bars above Retching indicate the duration of retching. Times for the above-mentioned filled and hatched bars were the same as those for the checked and hatched columns, respectively. The vertical bars above the columns indicate standard errors.

vomited matter, is thought to be evacuated before emetic stimulation. In conscious dogs, using force transducers, retrograde giant contraction in the gastrointestinal tract has been observed preceding vomiting [6, 7]. It has been reported that this contraction begins in the middle part of the small intestine and propagates to the gastric antrum. Although no relationship has yet been directly investigated between retrograde transport of intestinal contents and intestinal motilities, it is possible that bilirubin evacuated over a relatively long time before emesis is expelled by vomiting.

Why does the gallbladder contract with emesis even though the contraction can not evacuate bile? The gallbladder contraction seems to be related to retrograde transport of intestinal contents preceding vomiting. Recently, in decerebrated dogs, I observed that isotonic mannitol solution which was injected into the small intestine was reversely transported to the proximal duodenum during retching several times (unpub-

lished data). In the present study, a similar motility pattern in the small intestine was thought to have been elicited. Since the intestinal contents are repeatedly transported to the duodenum during retching, the gallbladder may contract to prevent the reflux of the intestinal contents to the common bile duct.

In conclusion, the results of this study clarified that bile evacuation is inhibited with emesis and suggested that gallbladder contraction during retching is related to other functions than bile evacuation.

REFERENCES

1. Alvarez WC: Reverse peristalsis in the bowel, a precursor of vomiting. *J Am Med Assoc* 85: 1051–1054, 1925
2. Ohasi K: On the movements of the colon and the gallbladder during nausea and vomiting. *J Physiol Soc Jpn* 30: 771–778, 1968
3. Qu R-y, Furukawa N, and Fukuda H: Changes in extra-hepatic biliary motilities with emesis in dogs. *J Auton Nerv Syst* 56: 87–96, 1995
4. Koga T and Fukuda H: Characteristic behavior of the respiratory muscles, esophagus, and external anal and urethral sphincters during straining, retching, and vomiting in the decerebrate dogs. *Jpn J Physiol* 40: 789–807, 1990
5. Furukawa N and Okada H: Canine salivary secretion from the submaxillary glands before and during retching. *Am J Physiol* 267: G810–G817, 1994
6. Lang IM, Sarna SK, and Condon RE: Gastrointestinal motor correlates of vomiting in the dog: Quantification and characterization as an independent phenomenon. *Gastroenterology* 90: 40–47, 1986
7. Lang IM, Marvig J, and Sarna SK: The role of the enteric nervous system in the initiation and propagation of the gastrointestinal motor correlates of vomiting. *Dig Dis Sci* 32: 918, 1987