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Abstract

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KEYWORDS: bile duct, bile excretion, choledocus, motilin, sphincter of Oddi.

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— BRIEF NOTE —

EFFECT OF MOTILIN ON THE SPHINCTER OF ODDI IN THE DOG

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Abstract. To investigate the action of motilin on the sphincter of Oddi, the flow rate of the perfusate (FRP) discharged into the duodenal lumem through the orifice of the common bile duct was measured by means of an electric drop counter in decerebrated dogs. Motilin in doses above 0.5 μg/kg i.v. reduced or stopped the FRP. The fifty percent recovery time of FRP was 20 min and full recovery time was 30 min. The reduction of FRP induced by motilin was unaffected by denervation and atropinization. These results suggest that motilin caused an increase in tone of the sphincter of Oddi by acting on the sphincter muscle.

Key words : bile duct, bile excretion, choledocus, motilin, sphincter of Oddi.

Motilin has a potent excitatory action on gastrointestinal motility. It has been suggested that this peptide drives interdigestive motor activity (1) and myoelectric activity (2). Motilin causes gallbladder contractions in the dog (3, 4). However, the effect of motilin on the motility of the sphincter of Oddi or the rate of bile excretion through the sphincter of Oddi into the duodenal lumen has not been studied. The present experiment was, therefore, designed to study the effect of motilin on the sphincter of Oddi.

Ten dogs starved for 24 h were decerebrated under chloralose anesthesia (80 mg/kg, i.v.) and immobilized by intravenous injection of gallamine (1 mg/kg) at appropriate intervals. Respiration was artificially maintained throughout the experiment. To study changes in the tone of the sphincter of Oddi, the common bile duct was perfused through a cannula inserted from the hepatic side, the cannula being connected to a pressure bottle filled with Tyrode's solution. The perfusion pressure was maintained at given pressures ranging from 10 to 25 cmH_2O. The flow rate of the perfusate discharged into the duodenal lumen through the orifice of the common bile duct (FRP) was measured by means of an electric drop counter placed between the pressure bottle and the inflow cannula (5), and the number of drops was counted by a rate meter over a suitable time. Motility of the duodenum anal to the orifice of the bile duct was recorded by a balloon-pressure transducer. Synthetic motilin was stored at a temperature of

−10℃ as a solution (100 μg/ml distilled water) and injected doses were freshly diluted for each experiment. Motilin was infused into the lateral saphenous vein over a 2 min period. To study the influence of autonomic nerves on motilin action, vagotomy was performed at the neck and splanchnicotomy was done extraperitoneally. In some experiments, blockade of the conduction of vagal impulses was reversibly performed by cooling the cervical vagi as described in the previous paper (3).

Relation between FRP and duodenal motility. FRP during the observation period of 1 h was 87 ± 18.1 drops/5 min at a perfusion pressure of 14 cmH_2O in four dogs. There was no correlation between temporal changes in FRP and fluctuations in duodenal tone ranging from 5 to 15 cmH_2O of intraduodenal pressure increase or decrease. It was, therefore, confirmed that the change in FRP was due to active increase and decrease in the tone of the sphincter of Oddi.

Effect of motilin on FRP and duodenal motility. FRP was markedly reduced or stopped by infusion of motilin at a dose above 0.5 μg/kg but unaffected at a dose below 0.1 μg/kg. As shown in Fig. 1 A, FRP at a perfusion pressure of 14 cmH_2O was markedly reduced with a latency of about 2 min after beginning the motilin infusion (0.5 μg/kg), almost completely stopped for about 8 min,

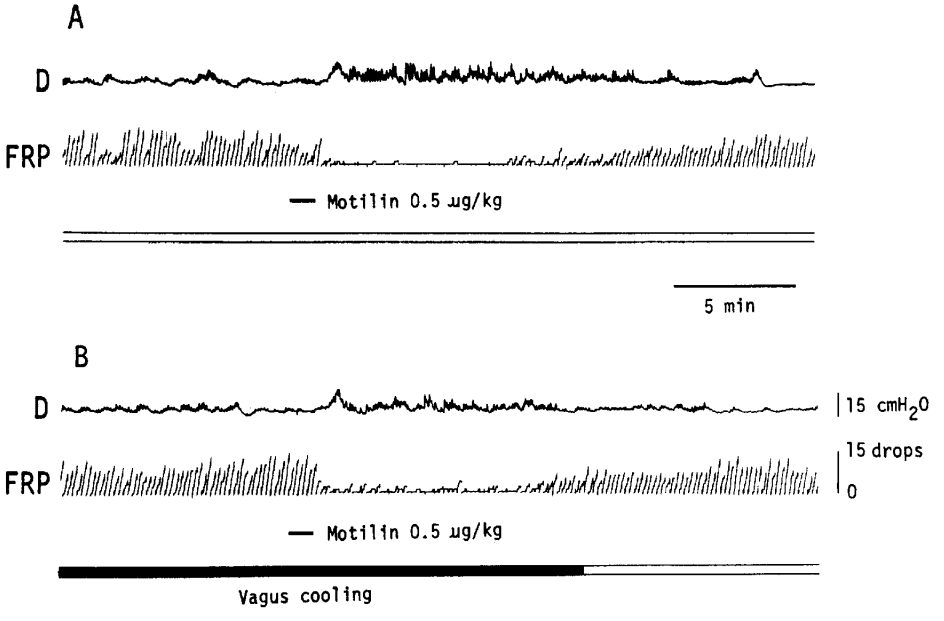

Fig. 1. Effect of vagus cooling on the response of the duodenum (D) and the flow rate of the perfusate discharged into the duodenal lumen through the orifice of the bile duct (FRP) to motilin (0.5 μg/kg). Perfusion pressure through the sphincter was maintained at 14 cmH_2O. Motilin caused marked reduction of FRP and increase in duodenal motility (A). These effects of motilin were unchanged during cold blockade of the vagus nerve (B).

then gradually recovered. The fifty percent recovery time of FRP was 20 min and full recovery time was 30 min. Motilin (0.5 μg/kg) also induced an increase in basal tone (5-20 cmH_2O in pressure increase) and amplitude of rhythmic contractions of the duodenum (Fig. 1 A) as has been reported previously (3). The latency and duration of the excitatory response in the duodenum were similar to those of the inhibitory response in FRP. Thus, the reduction of FRP might be influenced by an increase in tone of the duodenum because the bile duct is surrounded by duodenal muscles at the orifice of the bile duct. It is, however, suggested that an important factor influencing FRP is the change in tone of the sphincter of Oddi but not in duodenal tone since, as described above, there was no correlation between changes in FRP and the duodenal tone even when the increase in duodenal tone which occurred spontaneously was similar in extent to that induced by motilin infusion. It is, therefore, reasonable to consider that reduction of FRP by motilin mainly reflected increase in tone of the sphincter of Oddi but not increase in duodenal tone. It is concluded that motilin causes contraction of the sphincter of Oddi. It was confirmed that motilin caused excitation of myoelectric activity of the bile duct and duodenum in pigeons in which the muscle layer of the bile duct fully developed and separated by connective tissue from the duodenal muscle layer (6).

Reduction of FRP produced by motilin (0.5 μg/kg) was not influenced by cold blockade of cervical vagi (Fig. 1B) or bilateral vagotomy (Fig. 2C). Splanchnicotomy also failed to change the response of FRP to motilin (Fig. 2 B). Atropine (0.2 mg/kg, i.v.) failed to antagonize the motilin effect on FRP (Fig. 2 D).

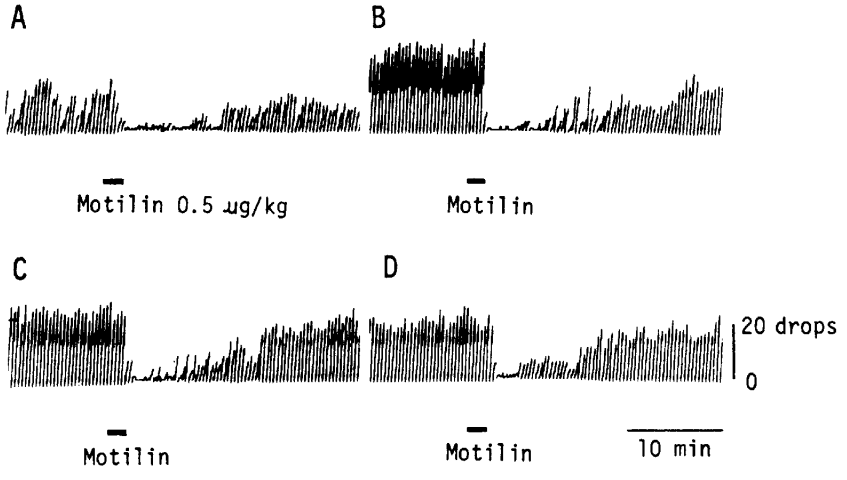

Fig. 2. Effects of splanchnicotomy, vagotomy and pretreatment of atropine on the reduction of FRP induced by motilin (0.5 μg/kg). Perfusion pressure was maintained at 23 cmH_2O. A: Control, B, C and D: After successive treatment of splanchnicotomy, vagotomy and atropinization (0.2 mg/kg).

From these results it appeared that motilin caused an increase in tone of the sphincter of Oddi by acting on the sphincter muscle. Therefore, the action of motilin on the sphincter of Oddi may be different from the action on the gallbladder in which motilin caused contraction by mainly acting on the nervous tissue (3).

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