Effect of Duodenal Acidification on the Lower Esophageal Sphincter Pressure in the Dog with Special Reference to Related Gastrointestinal Hormones

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HONGO, M., ISHIMORI, A., NAGASAKI, A. and SATO, T. Effect of Duodenal Acidification on the Lower Esophageal Sphincter Pressure in the Dog with Special Reference to Related Gastrointestinal Hormones. Tohoku J. exp. Med., 1980, 131 (3), 215-219 — The role of the duodenum in the regulation of the lower esophageal sphincter pressure was studied in 3 anesthetized dogs with a duodenal fistula by relating the lower esophageal sphincter pressure with plasma gastrin and secretin level during intraduodenal acid infusion test. Instillation of hydrochloric acid into the duodenum produced an initial fall followed by a significant and sustained increase of the lower esophageal sphincter pressure. The initial fall of the lower esophageal sphincter pressure was found to correspond to a prompt but transient rise of plasma secretin concentration, while plasma gastrin did not change significantly throughout the experimental period. It is concluded that duodenum may be an important regulator of the lower esophageal sphincter pressure in the dog through secretin and other unknown factors. —— lower esophageal sphincter; gastrin; secretin; motilin

An important role of the lower esophageal sphincter (LES) is to prevent a gastro-esophageal reflux. Postprandial rise of the lower esophageal sphincter pressure (LESP) has been attributed to a release of antral gastrin, but details still remain to be controversial (Dent and Hansky 1976; Castell 1978; Eckardt et al. 1978; Koeltz et al. 1978a, b). On the other hand, it has been well recognized since the classical experiments by Bayliss and Starling in 1902 that duodenal acidification causes a release of secretin which acts as an antagonist to gastrin in various ways. The present study was carried out to see the effect of duodenal acidification on LESP and plasma gastrin and secretin concentrations in dog in order to clarify the possible role of the duodenum in the regulation of LESP.

MATERIALS AND METHODS

Three mongrel dogs weighing 18 to 21 kg were used in the study. Experiments were started two weeks after the surgery of duodenal fistula. The animals were anesthetized after an overnight fast with pentobarbital sodium given intravenously.

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and kept in light anesthesia during the experiment, i.e., they breathed spontaneously during manometric studies.

The details of our manometric equipment and method have been described elsewhere (Nagasaki et al. 1977). Namely a perfusion (1 ml per min) polyethylene catheter of 2 mm in an outer diameter with a lateral recording orifice (diameter 1.5 mm) at 5 cm proximal to the end of the catheter was used. LESP measurements were performed with a station pull-through technique.

Before the intraduodenal acid instillation through a catheter inserted into the proximal duodenum via the duodenal fistula, the catheter was closed for 20 min for observation of basal state. Then 50 ml of 0.1 N HCl or saline were instilled in one min, and the catheter was closed again for another 40 min period.

Plasma gastrin was determined by radioimmunoassay using a kit available from the CEA-IRE-SORIN Association. Plasma secretin was also determined by radioimmunoassay using a kit available from the Daiichi Isotope Laboratories, Tokyo.

Each series of experiment was performed repeatedly in each dog, i.e., in one dog (9362), 3 times of hydrochloric acid instillation and 2 times of saline instillation, and in two dogs (9361, 9363), 2 times of hydrochloric acid instillation and 1 time of saline instillation. Statistical significance was assessed by the Student’s t-test comparing with basal value.

RESULTS

The effects of intraduodenal acid or saline instillation on LESP are shown in Fig. 1. Saline did not change LESP from the basal value of 15.8±3.5 cmH$_2$O (mean±s.e.) except for an early insignificant rise to 20.4±8.4 cmH$_2$O. Acid instillation, on the contrary, decreased LESP significantly at 3 min to 9.4±1.8 cmH$_2$O ($p<0.05$) from the basal value of 14.8±3.2 cmH$_2$O, but it returned to the basal level immediately by 5 min. Thereafter the gradual increase of LESP was observed till the end of the observation period. The peak increase in LESP after acid instillation noted 40 min after to 30.3±5.6 cmH$_2$O ($p<0.05$). Plasma gastrin

![Fig. 1. Effect of intraduodenal instillation of 50 ml of 0.1 N HCl (---○) and of 50 ml of saline (-•) on lower esophageal sphincter pressure (LESP). Each point represents the mean±s.e. (8 experiments on acid, 4 experiments on saline); *$p<0.05$ compared with 0 min value.](image-url)
Duodenal Acidification and LESP

showed no significant changes after acid or saline instillation into the duodenum (Fig. 2). Duodenal acidification caused, however, a significant rise of plasma secretin from the basal concentration of $69.8 \pm 7.8$ pg/ml to a peak of $111.8 \pm 12.3$ pg/ml ($p<0.01$) 3 min after the instillation of acid. Thereafter, plasma secretin concentration decreased rapidly and returned to the basal level at 15 min (Fig. 3).

![Figure 2](image1.png)

**Fig. 2.** Effect of intraduodenal instillation of acid (•••) and saline (---) on plasma gastrin. Values are given as mean±S.E. (8 experiments on acid, 4 experiments on saline).

![Figure 3](image2.png)

**Fig. 3.** Effect of intraduodenal instillation of acid (•••) and saline (---) on plasma secretin. Values are given as mean±S.E. (8 experiments on acid, 4 experiments on saline). *$p<0.05$ compared with 0 min value.

**DISCUSSION**

In the present investigation it was demonstrated clearly that duodenal acidification caused a significant increase in plasma secretin concentration, and a significant decrease in LESP simultaneously. Since administration of secretin is known to decrease LESP (Cohen and Lipshutz 1971; Mossa et al. 1978), the fall of LESP
shown here is believed to be caused by the rise of circulating endogenous secretin. The interesting finding in this study is an increase of LESP observed thereafter without accompaniment of significant increase of gastrin or decrease of secretin. A recent study revealed that duodenal acidification causes also a release of motilin in addition to secretin in man (Mitznegg et al. 1976). However, in the dog, motilin was found to be released by duodenal alkalinization (Brown 1967), but Dryburgh (1977) and Lee et al. (1978) showed that duodenal acidification also causes plasma motilin increase. This increase of motilin by duodenal acidification was less than that by duodenal alkalinization, but it lasted longer (Dryburgh 1977). Namely the peak of plasma motilin was seen 7 min after instillation of hydrochloric acid and remained at high levels till 30 min. In our study plasma secretin returned to the basal level 15 min after acid infusion, and significant rise of LESP occurred 15 min after acid infusion. Therefore, this significant rise of LESP is thought to be caused by endogenously released motilin by duodenal acidification. Domschke et al. (1976) demonstrated duodenal acidification in man caused a rise of plasma motilin and LESP. However, they did not find an initial fall of LESP, but showed a transient rise of LESP observed immediately after instillation of acid which returned to basal level quickly. The difference between our results and theirs may be attributed to the following three factors. First, species difference, namely we investigated in dogs and they tried in men. There may be a species difference in response of motilin or LESP to various stimuli. Second, the dose of instilled acid was exactly the same in both experiments in spite of the weight difference. Our dogs weighed about 20 kg and their volunteers weighed about 70 kg. Third, difference in the way of acid instillation, namely we loaded acid into the duodenum through a duodenal fistula, but they did through an orally inserted tube.

It could be said according to the present study that in the dog duodenal acidification causes an initial transient fall of LESP probably due to release of secretin and thereafter an increase of LESP which is related to neither gastrin nor secretin. In regulation of LESP, there may be involved another factor of duodenal origin, which remains to be elucidated in the future.

References

6) Domschke, W., Lux, G., Bloom, S.R., Wünsch, E., Demling, L., Mitznegg, P. & Röesh,
Duodenal Acidification and LESP


