

学位論文の要旨

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学位論文名 Usefulness of Catheterless Radiotelemetry pH Monitoring System to Examine the Relationship between Duodenal Acidity and Upper Gastrointestinal Symptoms

発表雑誌名 Journal of Gastroenterology and Hepatology
(巻, 初頁～終頁, 年) (26, 98～103, 2011)

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論文内容の要旨

INTRODUCTION

Functional dyspepsia (FD) is a clinical syndrome defined by recurrent or persistent pain or discomfort centered in the upper abdomen without evidence of any organic disease likely to explain the symptoms. Multiple pathophysiologic mechanisms are considered to be related to the occurrence of FD symptoms, such as delayed gastric emptying, impaired gastric accommodation, abnormal duodenojejunal motility, gastric hypersensitivity to distension, and central nervous system dysregulation. Recently, several studies have demonstrated that duodenal acidity is one of the important factors responsible for generation of FD symptoms. However, the relationship between increased intraduodenal acidity and occurrence of dyspeptic symptoms has not been investigated. The Bravo[®] pH monitoring system (Medtronic; Minneapolis, MN) is a catheterless radiotelemetry pH monitoring system. A previous study reported that intragastric and intraduodenal acidities could be investigated with this system by endoscopic fixation of a Bravo[®] pH capsule to the mucosa of the stomach and duodenum. In the present study, we investigated the usefulness of our novel method for measuring intraduodenal pH with this system to examine the relationship between duodenal acidity and upper-GI symptoms during intragastric acid infusion tests.

MATERIALS AND METHODS

The study subjects were 6 healthy volunteers without *Helicobacter pylori* infection or upper gastrointestinal disease (females: 3, mean age 22.1 years). A Bravo® pH capsule equipped with a 7-cm-long nylon loop was endoscopically inserted into the stomach using endoscopic forceps, then the nylon loop was firmly attached to the lesser curvature of the antrum (about 1 cm orad from the pyloric ring) using an endoscopic hemoclip. The capsule was then introduced into the second portion of the duodenum using endoscopic forceps. Following an overnight fast, intragastric infusions of 300 mL of acid or pure water (30 mL/minute for 10 minutes) via a 5-French ED tube were randomly performed at 24 and 48 hours after attachment of the capsule, employing a crossover design. The severity of several upper gastro-intestinal symptoms was assessed using a 10-cm visual analogue scale every 2 minutes for up to 30 minutes, after which the area under the severity scale-time curve (cm x minutes) was calculated. The symptoms investigated in this study were those related to discomfort (heaviness in the stomach, bloating, nausea, belching), pain (dull pain, cramping pain, pricking pain in the stomach), reflux (tickling or tingling in the chest, sour or bitter taste, feeling that something is stuck in the chest, burning sensation in the chest), and satiety. After completion of the two infusion tests, the capsule was endoscopically removed. The percentage time during which intraduodenal pH was below 4.0 and time-course change of intraduodenal pH during 30 minutes were examined, and the relationships between intra-duodenal acidity and occurrence of several upper gastro-intestinal symptoms analyzed.

RESULTS AND DISCUSSION

Intraduodenal pH and the severity of upper gastrointestinal symptoms during acid and water infusion were successfully investigated in all 6 study subjects. Intraduodenal pH gradually decreased after the start of acid infusion and was significantly reduced at the end of infusion in comparison with that after the end of water infusion. The percentage time during which intraduodenal pH was below 4.0 during the 30-minute period of acid infusion were significantly higher than that during water infusion ($61.4 \pm 6.1\%$ vs. $24.8 \pm 6.5\%$, $p=0.03$).

The number of subjects who experienced upper gastrointestinal symptoms was greater during acid infusion than water infusion. Several kinds of symptoms were rated as more severe by the study subjects during acid infusion and the total score of the area under the severity scale-time curve for all 12 symptoms during acid infusion was significantly higher (87.1 ± 26.9 vs. 22.5 ± 8.4 cm x minutes, $p=0.03$). The severity of discomfort symptoms was also higher and pain symptoms were observed mainly during acid infusion. Reflux symptoms and satiety were rarely observed during either type of infusion. When the relationship between degree of upper

gastrointestinal symptoms and an intraduodenal pH lower than 4.0 was investigated, a statistically significant correlation was observed between dull pain in the stomach and percentage time during which intraduodenal pH was below 4.0 ($R^2=0.342$, $p=0.044$).

Recently, several investigators have demonstrated that duodenal acidification causes various dyspeptic symptoms, not only in FD patients, but also healthy subjects. In addition, duodenal acidification has been reported to inhibit gastric emptying, antral contraction, *inter-digestive motility*, and *gastric relaxation*. The *inhibitory effect of duodenal acidification on upper gastrointestinal motor functions* is considered to provoke several symptoms of dyspepsia. We previously demonstrated that infusion of acid into the stomach induces several dyspeptic symptoms. In the present study, we also noted that infusion of acid into the stomach provokes both discomfort and pain symptoms. In addition, the present results clearly showed that the occurrence of several dyspeptic symptoms during acid infusion is related to increased intraduodenal acidity.

It has been shown that intraduodenal pH can be successfully recorded in healthy controls and FD patients after placement of the Bravo[®] capsule pH monitoring system on the wall of the duodenal bulb by using a short thread and hemoclip. In this study, we fixed the Bravo[®] capsule to the lesser curvature of the antrum using a 7-cm long nylon loop thread and an endoscopic hemoclip. Intraduodenal pH was successfully examined in all subjects and all capsules were safely removed endoscopically after completion of the study. Our method seems to be safer than previous reported, since the gastric wall is thicker than the duodenal wall and is not easily perforated during endoscopic procedures. Thus, our novel intraduodenal pH monitoring method that utilizes a catheterless radiotelemetry system is considered useful for further examinations of the relationships between duodenal acidity and upper-GI symptoms.

CONCLUSION

We showed that intraduodenal pH can be measured using our novel method with a newly designed catheterless radiotelemetry pH monitoring system. Our findings indicate that occurrence of several dyspeptic symptoms during acid infusion is related to increased intraduodenal acidity.