学 位 論 文 の 要 旨

氏名　　越野健司

学 位 論 文 名　Effects of Mosapride on Esophageal Functions and Gastroesophageal Reflux

発 表 雑 誌 名（巻，初頁～終頁，年）　Journal of Gastroenterology and Hepatology（**25**: 1066~1071, 2010）

著 者 名　Kenji Koshino, Kyoichi Adachi, Kenji Furuta, Shunji Ohara, Terumi Morita, Shuji Nakata, Takashi Tanimura, Masaharu Miki, Yoshikazu Kinoshita

論 文 内 容 の 要 旨

INTRODUCTION

Gastro-esophageal reflux disease (GERD) is caused by pathological reflux of gastric contents into the esophagus and delayed clearance of the refluxate from the esophagus. The majority of the refluxate contents are acidic, with gastric acid the main factor related to the development of reflux symptoms and associated complications. In addition, non-acid refluxate can also cause typical and atypical reflux symptoms in some individuals with GERD. Therefore, up to 30% of patients with GERD are not successfully treated by administration of a proton pump inhibitor (PPI), a potent inhibitor of gastric acid secretion.

Mosapride, a prokinetic agent, has been reported to elevate resting lower esophageal sphincter (LES) pressure and stimulate esophageal body contractions. Because of its motor action, mosapride is expected to function as a therapeutic drug for PPI-resistant patients with GERD and a dose of 15 mg/day is widely used in Japan for treatment of upper abdominal symptoms. The present study was designed to determine whether a standard dose of mosapride

can stimulate esophageal motor function and prevent the occurrence of gastroesophageal reflux. We investigated the effects of mosapride on salivary secretion as an index of chemical esophageal clearance, esophageal body peristalsis, resting LES pressure, and diet-induced acid and non-acid gastroesophageal reflux in healthy subjects.

MATERIALS AND METHODS

Experiment 1: Effects of Mosapride on Esophageal Motor Activity and Salivary Secretion

Nine healthy volunteers (36.2±7.6 years old) were enrolled in this study. Salivary secretion, esophageal peristaltic contractions, and resting lower esophageal sphincter pressure with and without mosapride administration were recorded using a crossover protocol with high-resolution manometry.

Experiment 2: Effects of Mosapride on Diet-induced Gastroesophageal Reflux

Thirteen healthy male volunteers (36.9±7.7 years old) were enrolled, and administrated a high caloric and high volume diet. Post-prandial acidic and non-acidic gastroesophageal reflux levels were recorded using a multi-channel impedance and pH monitoring system.

RESULTS AND DISCUSSION

Effects of Mosapride on Salivary Secretion

Mosapride at a standard dose of 15 mg/day did not elevate basal or stimulated salivary secretion.

Effects of Mosapride on Esophageal Motor Function

Resting LES pressure and esophageal body peristaltic pressure in each segment of the esophagus with and without mosapride administration were determined. There was no difference between LES pressure levels during the mosapride administration and control periods. In

addition, mosapride did not augment esophageal contraction pressure in any segments of the esophagus.

Effects of Mosapride on Post-prandial Gastroesophageal Reflux

The number of total post-prandial gastroesophageal refluxes observed tended to be higher during the mosapride administration period, while the level of acid reflux was significantly higher during the mosapride administration period as compared to the control period. The bolus clearance time of gastroesophageal refluxate measured at the lower esophagus 5 cm above the LES tended to be shorter during the mosapride period than the control period, though the difference was not statistically significant. Thus, mosapride at a standard dose of 15 mg/day failed to prevent acidic and non-acidic post- prandial gastroesophageal reflux.

Contrary to our expectation, mosapride at the standard dose did not stimulate esophageal motor activity or salivary secretion, while post-prandial gastroesophageal acid reflux was increased. Therefore, mosapride at this dose is not considered to be effective for treatment of PPI-resistant GERD.

CONCLUSION

Mosapride at 15 mg per day, the standard dose in Japan, did not alter esophageal motility or salivary secretion in healthy volunteers. Additional investigations with a larger number of individuals and higher doses are necessary to establish an effective treatment protocol.