

学位論文の要旨

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学位論文名 Therapeutic Effects of Mosapride Citrate and Lansoprazole for Prevention of Aspiration Pneumonia in Patients Receiving Gastrostomy Feeding

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論文内容の要旨

INTRODUCTION

In rapidly aging societies, percutaneous gastrostomy feeding is increasingly used for patients with swallow dysfunction due to cerebrovascular and neurodegenerative diseases. The prognosis of such patients is not satisfactory, with aspiration pneumonia reported to be the most common cause of mortality and few reports of possible medical prevention. Therefore, we conducted this prospective randomized 3-armed study to clarify the therapeutic effects of mosapride and lansoprazole for prevention of pneumonia in patients receiving percutaneous endoscopic gastrostomy (PEG) feeding.

MATERIAL AND METHODS

The study subjects were 119 patients with dysphasia who required gastrostomy feeding. All had PEG tubes that were newly inserted or replaced from July 2009 to December 2011 at Kasai City Hospital. They were randomly assigned to the control (n=40; without medication), lansoprazole (n=41; 15 mg, 1/day), and mosapride (n=38; 5 mg, 3/day) groups. Fowler's body position, a left lateral decubitus position, or a supine position was employed during PEG feeding.

At enrollment, all patients underwent an endoscopic examination and the possible presence of an esophageal hiatal hernia (≥ 2 cm) was investigated. The number of days with fever

($\geq 37.8^{\circ}\text{C}$), vomiting, and antibiotics administration, as well as the occurrence of pneumonia were investigated during the 6-month observation period.

Statistical analysis was performed with SPSS 17.0 Software for Windows. Data are expressed as medians and ranges. A chi-square test was used for categorical variables, while a Kruskal-Wallis test was used to identify significant differences among the groups and a Mann-Whitney U test to detect significant differences between groups. Multiple logistic regression analysis was used to determine influential factors related to the incidence of aspiration pneumonia during the 6-month observation period. The Kaplan-Meier method and a log-rank test were used to detect differences for the initial occurrence of pneumonia during the observation period between groups. A *p*-value < 0.05 was considered to indicate statistical significance. The study protocol was approved by an institutional ethics committee (Shimane University Ethical Committee), and written informed consent was obtained from all patients or a family member.

RESULTS AND DISCUSSION

There were no significant differences among the 3 groups for male/female ratio, age, nutritional status shown by serum levels of albumin and total cholesterol, clinical background, and body position during PEG feeding. The prevalence of esophageal hiatal hernia was also not statistically different among the groups.

The median number of fever days was 5.5 (range, 0-45) in the control, 6.0 (0-41) in the lansoprazole, and 2.0 (0-25) in the mosapride groups, with the number in the latter significantly lower as compared to the others. The median number of vomiting days in the mosapride group was significantly lower than that in the lansoprazole group, while the median number of days of antibiotics administration for treatment of pneumonia in the mosapride group was significantly lower than in the other groups. The incidence of pneumonia during the 6-month observation period was also significantly lower in the mosapride group as compared to the control (7/38 vs. 16/40, $p=0.038$) and lansoprazole (vs. 20/41, $p=0.005$) groups. When the patients were divided into those with and without an esophageal hiatal hernia, mosapride showed a remarkable effect to suppress pneumonia in comparison with the control and lansoprazole groups in cases with a hiatal hernia. In patients with a hiatal hernia, the incidence of pneumonia was 4/17 (23.5%), 11/15 (73.3%), and 16/24 (66.7%) in the mosapride, control, and lansoprazole groups, respectively. Lansoprazole did not increase the incidence of pneumonia even in cases with a hiatal hernia. On the other hand, in patients without a hiatal hernia, the incidence of pneumonia

was low (<23.5%) irrespective of drug administration. Multiple logistic regression analysis revealed that mosapride treatment was a significant factor for suppression of pneumonia (adjusted odds ratio=0.288; 95% CI 0.089-0.924; P=0.036), while the presence of a hiatal hernia was a significant aggravating factor (adjusted odds ratio=6.097; 95% CI 2.469-15.15; P<0.0001). Log-rank test findings showed that the mosapride group had a lower occurrence of pneumonia as compared with the lansoprazole group (p=0.004).

Mosapride citrate, which has a prokinetic effect via stimulation of 5-HT₄ serotonin receptors on peripheral autonomic neurons and increased secretion of acetylcholine at neuro-muscular junctions, promotes upper gastrointestinal motility and prevents GER in patients with reflux diseases. In addition, mosapride may facilitate esophageal clearance of the refluxate by augmenting esophageal peristaltic contractions. These actions of mosapride are considered to suppress the occurrence of aspiration pneumonia possibly caused by PEG feeding. A previous study also found that mosapride significantly decreased the incidence of pneumonia and improved survival of gastrostomy-fed patients during a 1-year-long observation period. In our study as well, mosapride significantly decreased the incidence of pneumonia in PEG-fed patients. Interestingly, this beneficial effect of mosapride was found only in our cases with an esophageal hiatal hernia, a reported risk factor for GER, while the efficacy of mosapride was not greater in cases without a hiatal hernia. Therefore, we speculate that the prokinetic and GER-preventive effects of mosapride play an important role in PEG-fed patients for preventing aspiration pneumonia induced by reflux of gastric contents.

The observation period of 6 months in our study was relatively short for determining the effectiveness of the administrated drugs on mortality caused by aspiration pneumonia. Therefore, a prospective multicenter study with a longer observation period may be needed to clarify the efficacy of prokinetic and anti-secretory agents for long-term prevention of aspiration pneumonia in patients receiving PEG feeding.

CONCLUSION

Mosapride citrate has a preventive effect on the occurrence of pneumonia in patients receiving PEG feeding.