

Effects of the Oral Administration of Mosapride Citrate on Capsule Endoscopy Completion Rate

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Background/Aims: In capsule endoscopy (CE), the capsule does not always reach the cecum within its battery life, which may reduce its diagnostic yield. We evaluated the effect of mosapride citrate, a 5-hydroxytryptamine-4 agonist that increases gastrointestinal motility, on CE completion. **Methods:** In a retrospective study, we performed univariate and multivariate analyses for 232 CE procedures performed at our hospital. To identify factors that affect CE completion, the following data were systematically collected: gender, age, gastric transit time (GTT), nonsteroidal anti-inflammatory drug administration, previous abdominal surgery, hospitalization, use of a polyethylene glycol solution, use of mosapride citrate (10 mg), body mass index (BMI), and total recording time. **Results:** The univariate analysis showed that oral mosapride citrate, GTT, and BMI were associated with improved CE completion. Multivariate analyses showed that oral mosapride citrate (odds ratio [OR], 1.99; 95% confidence interval [CI], 1.01 to 3.91) and GTT (OR, 2.34; 95% CI, 1.13 to 4.87) were significant factors for improving the CE completion. Oral mosapride citrate significantly shortened the GTT and small bowel transit time (SBTT). **Conclusions:** Oral mosapride citrate reduced the GTT and SBTT during CE and improved the CE completion rate. (*Gut Liver* 2012;6:339-343)

Key Words: Capsule endoscopy; Mosapride; Prokinetics

INTRODUCTION

Capsule endoscopy (CE) was developed in 2000¹ and has been useful for investigating obscure gastrointestinal bleeding (OGIB)² and other small intestinal conditions.^{3,4} To improve the diagnostic yield of CE, examination of the entire small intestine

is required. However, the examinations in about 20% of small intestinal CE procedures are incomplete, probably due to longer retention of the capsule in the stomach.⁵ To shorten the gastric transit time (GTT), various interventions have been reported, such as the administration of prokinetics.⁶⁻¹⁰ However, the results of these reports were conflicting, and the effects of these drugs on CE completion were not determined.

Mosapride citrate (Gasmotin; Dainippon Sumitomo Pharma Co., Ltd., Osaka, Japan) is a prokinetic agent that acts as a 5-hydroxytryptamine-4 (5-HT₄) agonist and increases gastrointestinal motility.¹¹ Wei *et al.*¹² conducted small pilot study and reported the effects of mosapride citrate on GTT and small intestinal transit time during CE. The primary end-point of this study was to elucidate the factors that affect CE completion. The second end-point was to evaluate the effect of mosapride citrate on CE completion rate.

MATERIALS AND METHODS

1. Enrolled patients and CE procedure

Written informed consent was obtained from all patients, and the study protocol was approved by the ethical committee of Keio University Hospital. From February 2004 to March 2010, 286 CE were consecutively performed in our hospital. We excluded 54 CE procedures (another clinical trial, 37; post-total gastrectomy, 5; retention in the stomach, 2; retention in the small bowel, 2; could not swallow the capsule, 2; recorder malfunction, 2; and missing medical records, 4). A total of 232 CE procedures were enrolled in this study. The characteristics of the study groups are shown in Table 1. The most common indication for CE was OGIB. CE was performed with the Pill-Cam SB or SB2 capsule (Given Imaging, Tokyo, Japan) or the

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Table 1. Characteristics of the Study Groups

Characteristic	Value
No. of CE procedures	232
Gender, male/female	136/96
Mean age	58.3 (8-88)
Type of capsule, PillCam SB/SB2/EndoCapsule	147/13/72
Indications for CE examination	
OGIB	138
NSAID	13
Suspected Crohn's disease	6
Anemia	3
Diarrhea	3
Others	69

CE, capsule endoscopy; OGIB, obscure gastrointestinal bleeding; NSAID, nonsteroidal anti-inflammatory drug.

EndoCapsule (Olympus Medical systems, Tokyo, Japan) after a 12-hour fasting period. Of the 232 patients, 51 (22.0%) underwent bowel cleansing with 1 to 2 L of polyethylene glycol (PEG) solution before swallowing the capsule. In addition, 126 patients (54.3%) received oral mosapride citrate (10 mg) 30 to 60 minutes before they swallowed the capsule. After 8 to 16 hours, the recorder was disconnected, sensors were removed, and recorded digital information was downloaded from the recorder and transferred to the computer. The resultant images were reviewed by using the Rapid software version 5 (Given Imaging, Tokyo, Japan) or Olympus EndoCapsule software version 1 (Olympus Medical systems). The video images of CE were analyzed by 2 well-trained endoscopists (N. H., M. N.), who had previously reviewed more than 150 CE videos. In case of discrepancy in relevant findings, the differences were resolved with consensus. In each procedure, the GTT, small-bowel transit time (SBTT), and whether the examination was completed (capsule reaching the cecum) were recorded. GTT was defined as the time interval between the first gastric image and the first duodenal

Table 2. Univariate Analysis of Factors Affecting the Capsule Endoscopy Completion Rate

Factor	No.	CE incomplete	CE complete	OR (95% CI)	p-value
No. of patients (%)	232	51 (22.9)	181 (78.0)		
Gender, n (%)					
Female	96	25 (26.0)	71 (74.0)	0.67 (0.36-1.25)	0.21
Male	136	26 (19.1)	110 (80.9)		
Use of NSAID, n (%)					
(+)	69	11 (15.9)	58 (84.1)	1.72 (0.82-3.58)	0.15
(-)	163	40 (24.5)	123 (75.5)		
Use of PEG, n (%)					
(+)	51	10 (19.6)	41 (80.4)	1.20 (0.55-2.60)	0.64
(-)	181	41 (22.7)	140 (77.3)		
Use of mosapride citrate, n (%)					
(+)	126	20 (15.9)	106 (84.1)	2.19 (1.16-4.14)	0.01
(-)	106	31 (29.2)	75 (70.8)		
GTT, n (%)					
≤45 min	182	32 (17.2)	150 (82.8)	1.33 (1.06-1.67)	0.02
>45 min	50	19 (38.0)	31 (62.0)		
Hospitalization, n (%)					
Yes	118	27 (22.9)	91 (77.1)	0.90 (0.48-1.68)	0.74
No	114	24 (21.1)	90 (78.9)		
Previous abdominal surgery, n (%)					
Yes	67	17 (25.4)	50 (74.6)	0.76 (0.39-1.49)	0.43
No	165	34 (20.6)	131 (79.4)		
Age, median (min-max), yr		61 (25-83)	62 (8-88)		0.83
Total recording time, min		477 (452-915)	477 (237-885)		0.73
BMI		20.5 (12.7-30.8)	22.0 (13.1-36.5)		0.02

CE, capsule endoscopy; OR, odds ratio; CI, confidence interval; NSAID, nonsteroidal anti-inflammatory drug; PEG, polyethylene glycol; GTT, gastric transit time; BMI, body mass index.

image. SBTT was defined as the time interval between the first duodenal image to the first cecal image. Completion rate was defined as the percentage of CE procedures in which the capsule reached the cecum. The positive findings were categorized according to standard terminology, as angiectasia, ulcer, bleeding of unknown origin, erosion, polyp/tumor, submucosal tumor, varix, and lymphangiectasia.

2. Study design

We determined whether the following potential factors were systematically collected from the patients' medical records: 1) gender, 2) age, 3) GTT, whether subdivided into more than 45-minute intervals, 4) use of nonsteroidal anti-inflammatory drugs (NSAIDs), 5) previous abdominal surgery, 6) hospitalization, 7) use of PEG solution, 8) use of mosapride citrate (10 mg), 9) body mass index (BMI), and 10) total recording time. The collected data were analyzed by univariate and multivariate analyses. To evaluate the effect of the oral administration of mosapride citrate on gastrointestinal motility, the GTT and the SBTT of the capsule were compared between the control group and mosapride administration group by univariate analysis.

3. Statistical analysis

Statistical analysis was performed by using Student's t-test for normally distributed continuous variables, Mann-Whitney U test for continuous variables that were not normally distributed, and the chi-square test for categorical variables. To identify factors that affect the completion of CE examinations, all potential factors were examined using univariate analysis. The relevant risk factors were determined by univariate analysis, and were

subsequently entered in a logistic regression model for multivariate analysis. Odds ratios (ORs) and the corresponding 95% confidence intervals (CIs) were obtained for all significant variables. A p-value of less than 0.05 was considered significant. PASW version 17 software (SPSS Japan Inc., Tokyo, Japan) was used in all statistical analyses.

RESULTS

Of the 232 CE procedures, 181 (78%) were completed. The results of the univariate analyses of all factors that might affect the completion of small intestinal examinations are shown in Table 2. The factors associated with complete examinations were oral mosapride citrate administration (OR, 2.19; p=0.01), GTT less than 45 minutes (OR, 1.33; p=0.02), and BMI (p=0.02).

All significant factors found by univariate analysis and those

Table 3. Logistic Regression Analysis of Factors Affecting Capsule Endoscopy Completion Rate

Factor	p-value	OR	95% CI
Use of NSAID	0.106	1.98	0.87-4.09
Use of mosapride citrate	0.048	1.99	1.01-3.91
Gender	0.435	0.77	0.39-1.50
BMI	0.053	1.05	1.10-1.22
Previous abdominal surgery	0.315	0.7	0.34-1.41
GTT (≤45 min)	0.022	2.34	1.13-4.87

Significance of model: $\chi^2=21.072$, p=0.002.

OR, odds ratio; CI, confidence interval; NSAID, nonsteroidal anti-inflammatory drug; BMI, body mass index; GTT, gastric transit time.

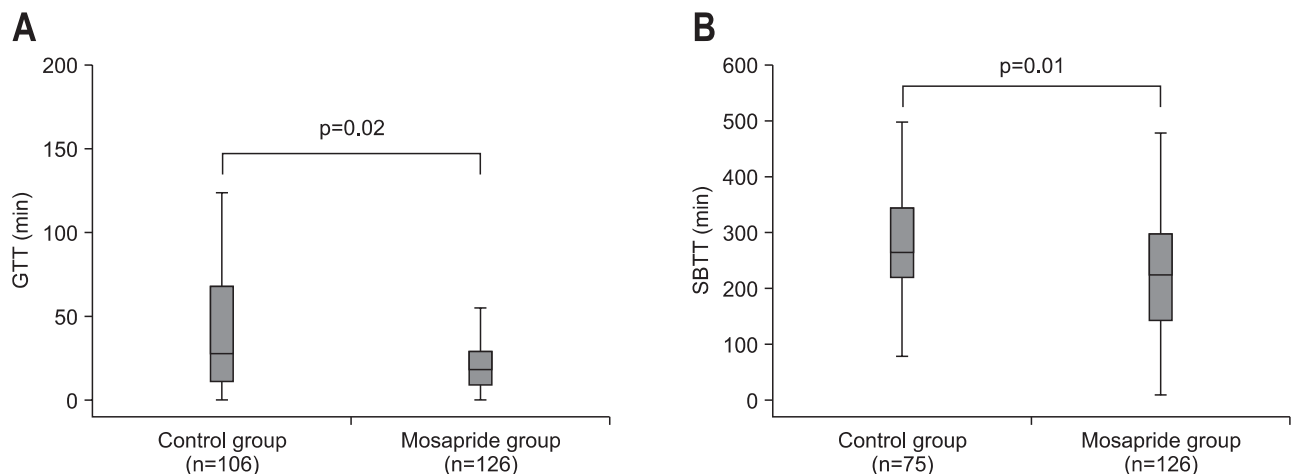


Fig. 1. (A) Effects of the administration of mosapride citrate on gastric transit time (GTT). The GTT was significantly shorter in the mosapride group than in the control (p=0.02). The median GTT was 30 minutes in the mosapride administration group and 56 minutes in the non-administration group. The data are presented in a box-and-whisker plot. The box includes those results falling between the 25th and 75th percentiles, and the median value is represented as a horizontal line inside the box (outliers and extremes are not shown). (B) Effects of the administration of mosapride citrate on small bowel transit time (SBTT). The SBTT of the capsule was significantly shorter in the mosapride group compared with the control (p=0.01). The median SBTT was 231 minutes in the mosapride administration group and 279 minutes in the non-administration group. The data are presented in a box-and-whisker plot. The box includes those results falling between 25th and 75th percentiles, and the median value is represented as a horizontal line inside the box (outliers and extremes are not shown).

factors that were thought to be related to the completion of CE examinations were analyzed by multivariate regression analysis. The results of multivariate analysis are shown in Table 3. Mosapride citrate and GTT less than 45 minutes were shown to be independent predictors of CE examination completion, whereas NSAID, gender, BMI, and previous surgery were not significant variables.

In the transit time analysis, GTT was significantly shorter in the mosapride citrate administration group than in the control group ($p=0.02$) (Fig. 1A). The median GTT was 18 minutes in the mosapride citrate administration group and 27.5 minutes in the non-administration group. The SBTT was also shorter in the mosapride citrate administration group than the non-administration group ($p=0.01$) (Fig. 1B). The median SBTT was 223 minutes in the mosapride citrate group and 266 minutes in the non-administration group. Although the SBTT was shorter in the mosapride citrate administration group than in the non-administration group, the number of positive findings was not significantly different between the two groups (Table 4). The number of patients with underlying disease was similar in both groups (the number of diabetic patients was 7 in the mosapride citrate administration group, 7 in the non-administration group, and 3 vs 4 of hemodialyzed patients). Hence, no medication which had a marked effect on the gastric or intestinal motility was administered in both the groups.

DISCUSSION

In this study, we evaluated the effect of oral mosapride citrate on CE completion and GTT. Previous reports have suggested that GTT affects CE completion.^{2,5,13,14} Moreover, other factors, such as aging,^{15,16} diabetes mellitus,¹⁴ hospitalization,¹⁶ and previous abdominal surgery¹⁷ were found to be associated with incomplete CE. We confirmed that mosapride citrate administration and GTT less than 45 minutes were independent predictors of the CE examination completion according to a logistic regression model. All of the above mentioned analyses, includ-

ing ours, were retrospective. Therefore, each study analyzed a different population and included some bias. However, our analysis revealed that mosapride citrate administration and GTT less than 45 minutes were strong predictors of CE completion. Westerhof *et al.*¹³ found that a GTT cutoff value of 45 minutes was the most significant for discriminating between incomplete and complete CE examinations. In addition, the oral administration of mosapride citrate increased CE completion rate by 15%, and the adjusted OR for CE completion in cases with oral mosapride treatment was 1.99 (95% CI, 1.01 to 3.91).

The effects of prokinetics, such as erythromycin¹⁸ and metoclopramide,^{6,9} on CE have been studied previously; however, the results of these studies were conflicting. The sample size in these studies was 50 to 150 cases. Our data suggest that prospective studies with 100 samples have a power of about 40%. Consequently, β errors will occur in 60% of these results. Although our study was retrospective, the effectiveness of mosapride citrate on CE completion should be confirmed using an adequate number of samples.

The effect of mosapride citrate on CE completion was evaluated by Wei *et al.*¹² prospectively by using 60 samples. Their pilot study showed that the completion rates of the mosapride group and control group were 93.33% (28/30) and 66.66% (20/30), respectively, and the difference between the two groups was significant. However, we found that the completion rates of the mosapride group and control group were 84.1% and 70.8%; hence, to achieve 80% power at 5% level of significance, the required sample size should be 121 in each group, i.e., total sample size of 242. Therefore, a large sample is needed to confirm the effect of mosapride citrate on CE completion.

The administration of mosapride reduced GTT and SBTT. This confirmed that serotonin 5-HT₄ receptors are located in the stomach as well as the small intestine. Reduction in GTT improved the completion rate of CE. Meanwhile, reduction in SBTT might reduce the diagnostic yield of small bowel disease. Our data showed that the oral administration of mosapride citrate improved the CE completion rate, and the diagnostic yield of small bowel disease was not significantly different between the two groups (Table 4).

Mosapride citrate is a 5-HT₄ agonist that is available in Asia. Tegaserod, another 5-HT₄ agonist, is available in the Western countries. Previous studies using tegaserod^{19,20} have shown conflicting results. However, our data suggests that tegaserod also has the potential to improve the completion rate of CE.

In conclusion, mosapride administration and GTT less than 45 minutes were independent predictors of CE completion; oral mosapride citrate, a serotonin 5-HT₄ receptor agonist, reduced the GTT and SBTT. However, a prospective randomized trial involving 250 samples is required to confirm the usefulness of this prokinetic agent.

Table 4. Number of Positive Findings between the Mosapride Administration and Control Groups

Finding	Mosapride (+) (n=126)	Mosapride (-) (n=106)	p-value
Angiectasia	7	5	0.77
Ulcer	15	13	0.93
Bleeding from unknown origin	6	6	0.76
Erosion	30	26	0.90
Polyp/Tumor	4	5	0.54
Submucosal tumor	3	1	0.40
Varix	3	3	0.37
Others	5	7	0.50
No findings	53	40	0.50

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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