

Endoscopic Evaluation of Gastric Emptying and Effect of Mosapride Citrate on Gastric Emptying

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Purpose: Gastric emptying has been evaluated by scintigraphy in spite of its limitations of time consumption, cost, and danger of radioisotope. Endoscopy is a simple technique, however, its validation for gastric emptying and quantification of food has not yet been investigated. The aim of our study was to assess endoscopic gastric emptying compared with scintigraphy and radiopaque markers (ROMs) studies. We also investigated the effect of a single dose of mosapride on gastric emptying. **Materials and Methods:** Fifteen healthy volunteers underwent scintigraphy. Next day, subjects received a standard solid meal with ROMs and underwent endoscopy and simple abdomen X-ray after 3 hrs. After one week, the same procedure was repeated after ingestion of mosapride (5 mg for group 1, n = 8; 10 mg for group 2, n = 7) 15 min before the meal. Quantification of gastric residue by endoscopy was scored from 0 to 3, and the scores were added up. **Results:** All subjects completed the study without any complication. The gastric emptying rate [$T_{1/2}$ (min)] was in normal range (65.6 ± 12.6 min). Endoscopic gastric emptying was correlated significantly with gastric clearance of ROMs ($r = 0.627$, $p = 0.012$). Endoscopic gastric emptying and gastric clearance of ROMs after administration of mosapride showed significant differences in the 10 mg group ($p < 0.05$). **Conclusion:** Endoscopy can evaluate gastric emptying safely and simply on an outpatient basis. A 10 mg dose of mosapride enhanced gastric emptying, assessed by both endoscopy and ROMs.

Key Words: Gastric emptying, endoscopy, scintigraphy, radiopaque markers, mosapride

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INTRODUCTION

Disturbed gastric motility often plays an important role in gastric motility disorders and is associated with various symptoms. Gastric motility disorders occur whenever the processes of interdigestive motility, gastric reservoir function, or gastric emptying are not properly controlled.¹ Gastric emptying is a complex process influenced by a variety of factors, including meal content, hormones, nerves, muscles, and functional resistance of the duodenum.²

The methods used for evaluation of gastric emptying are variable and complementary. They include methods such as scintigraphic gastric emptying,² ultrasonography,³ breath $^{13}\text{CO}_2$,⁴ single positron emission computer tomography (SPECT),⁵ and MRI.⁶⁻⁸ Gastric emptying can also be evaluated with the use of radiography 6 hr after the ingestion of nondigestible ROMs.⁹ This simple test is readily available, noninvasive, and inexpensive, but it assesses the emptying of nondigestible solids rather than digestible solids.⁹⁻¹¹ Other methods include manometry and electrogastrography, which may be helpful for evaluation of gastric motor function.¹²

Radionuclide gastric emptying, scintigraphy involving ingestion of an egg meal cooked with a technetium radiolabel, is typically the first standard method in the evaluation of gastric motor function and assessment of gastric emptying rate.^{1,12}

Although scintigraphy is quantitative, this method is complicated, time-consuming, and costly (expensive gamma camera).^{9,13} Some disadvantages include the use of radioactive substances and the poor level of standardization of meal composition and measuring times depending on different laboratories.¹

Attila, et al.¹³ evaluated gastric emptying by endoscopic technique, and showed the feasibility, tolerability, and safety of unsedated transnasal esophagogastrosopy (T-EG) in qualitative evaluation of gastric emptying. However, the T-EG is not universal, and there has been no study on the usage of conventional endoscopy for the evaluation of gastric emptying. Its validation for measuring gastric emptying and quantification of food has not yet been investigated.

Mosapride, a substituted benzamide, is a 5-HT₄ receptor agonist.¹⁴⁻¹⁶ This drug does not antagonize dopamine D2 receptors, but selectively acts on 5-HT₄ receptors, thus enhancing gastrointestinal motility after accelerating acetylcholine release from nerves in the gastrointestinal tract.¹⁶

The aim of our study, therefore, was to assess endoscopic gastric emptying and compare with scintigraphy and ROMs studies using conventional endoscopy. We also investigated the effect of a single dose of mosapride on gastric emptying.

MATERIALS AND METHODS

Subjects

Fifteen healthy volunteers (5 men, 10 women; range, 20-59 yr) were enrolled. Volunteers did not have any history of gastrointestinal disorders or symptoms suggestive of gastric emptying abnormalities. Their scintigraphic gastric emptying rates [$T_{1/2}$ (min)] were in normal range (65.6 ± 12.6 min; range, 49.9-86 min). We obtained a written informed consent from all subjects, and this study protocol was approved by the Yonsei University College of Medicine

Ethics Committee.

Standard meal

This solid meal consisted of 50 g of scrambled eggs (75 kcal) and 210 g of boiled rice (315 kcal, Korean standard diet) that was labeled *in vitro* with 500 microcuries of 99mTc-pertechnetate. The meal used for scintigraphic evaluation of solid gastric emptying was prepared at our institution. We studied 3 methods with the same standard solid meal over a period of 2 weeks (Fig. 1).

Scintigraphic gastric emptying

After a 12-hr fast, subjects underwent scintigraphy after ingestion of the standard solid meal. Examination was done in the sitting position. Scintigraphic scanning was performed using a gamma camera with a low-energy, all-purpose, parallel-hole collimator. One-min images in the anterior and posterior projections were obtained, and the geometric mean from the 2 values was calculated to correct for anterior/posterior movements of the gastric contents. Correction was also done for physical decay of the isotope. Gastric activity to decrease to half of the original value ($T_{1/2}$) was calculated.

Gastric clearance of ROMs and endoscopic gastric emptying

On the second day, subjects received the standard solid meal with 20 ROMs. Then, they underwent a simple abdomen X-ray, and residual ROMs were counted. Subsequently, conventional EGD without conscious sedation was performed by a single endoscopist. The stomach was comprehensively examined for the presence or absence of food residue and the entire procedure was videotaped for future analysis. The status of residual foods was classified as no residue (-, score 0), small amount of food residue (+, score 1), moderate amount of food residue (++, score 2), and large amount of food residue (+++, score 3) at 3 parts (antrum, body, and fundus), and the scores were added up

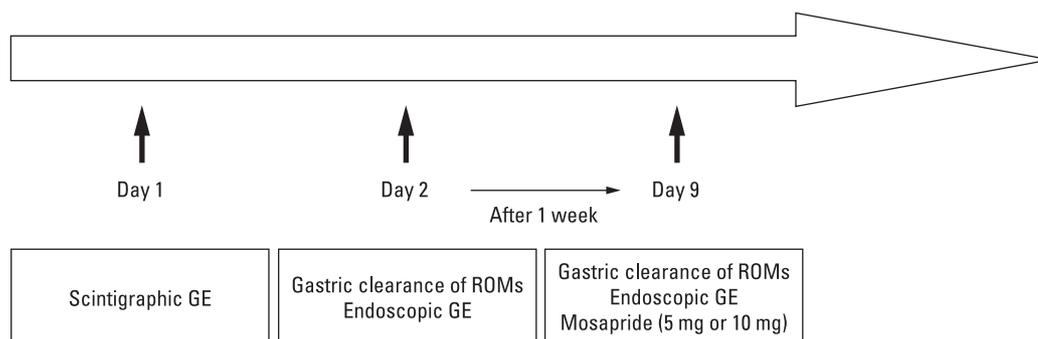


Fig. 1. Illustrated figure of study protocol. ROMs, radiopaque markers; GE, gastric emptying.

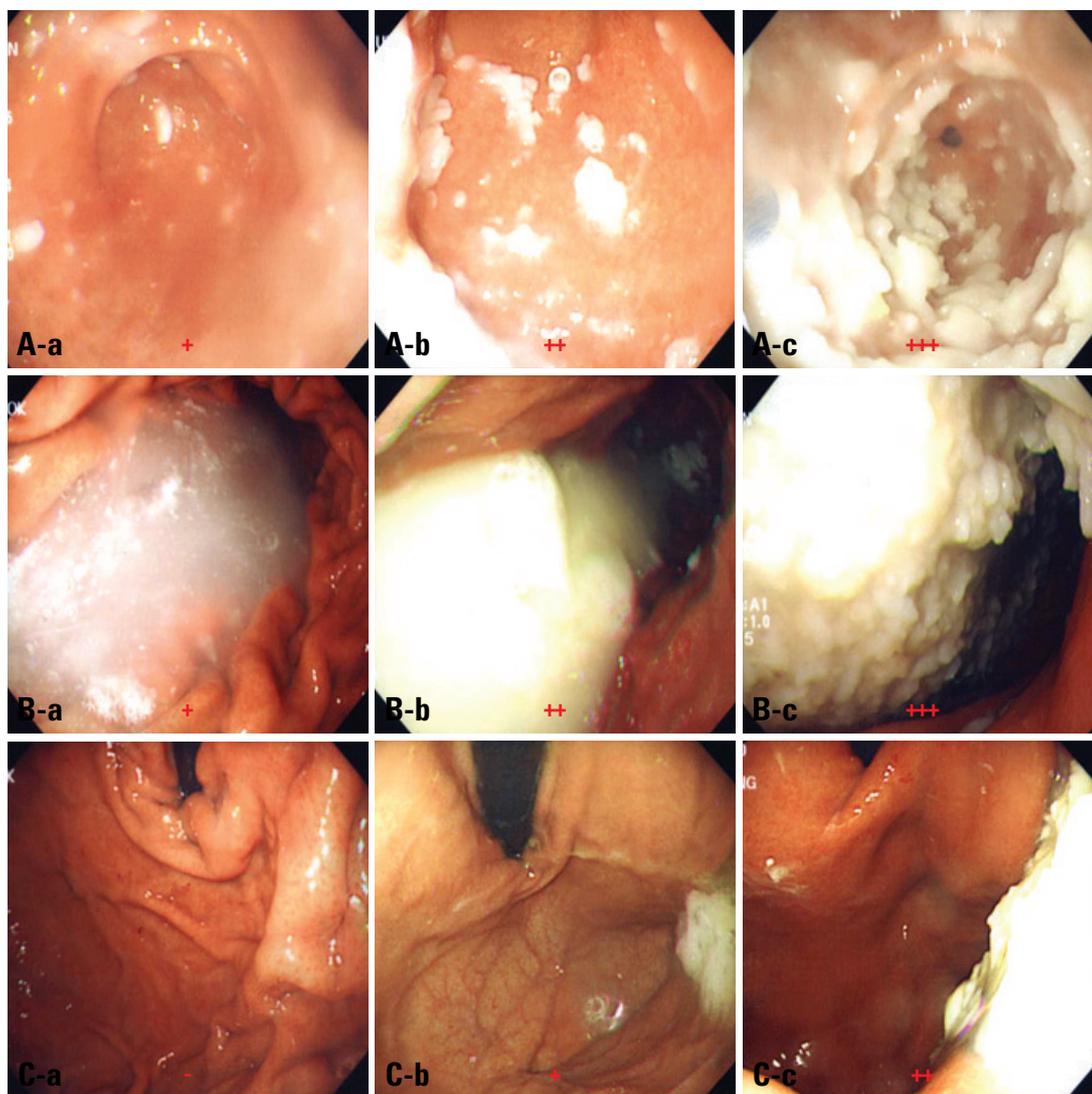


Fig. 2. Scoring of endoscopic gastric emptying. (A) Antrum. (B) Body. (C) Fundus. Score; -, 0; +, 1; ++, 2; +++, 3.

(total score 8) (Fig. 2).

Effect of mosapride citrate on gastric emptying

After one week, volunteers took 5 mg (n = 8) or 10 mg (n = 7) of mosapride 15 min before the meal with ROMs. Then, they underwent a simple abdomen X-ray and conventional EGD after 3 hrs.

Statistics

Statistical analysis was carried out using Statistical Package for Social Science (SPSS) for Windows V11.5 (SPSS Inc, Chicago, IL, USA). We analyzed the correlation among gastric emptying time, endoscopic gastric emptying, and gastric clearance by ROMs (Spearman correlation). Analyses of endoscopic gastric emptying and gastric clearance of ROMs were performed according to dose increment of mosapride using Mann-Whitney U test and Wilcoxon signed rank test. A $p < 0.05$ was considered statistically significant.

RESULTS

All subjects completed the study without any complications.

Comparison between endoscopic gastric emptying, scintigraphy, and gastric clearance of ROMs

The endoscopic gastric emptying score in females was significantly higher than in males (mean, 5.8 vs. 3; $p = 0.015$), however, scintigraphic gastric emptying rate was not significantly different. Endoscopic gastric emptying score and scintigraphic gastric emptying rate did not show a significant correlation.

The gastric clearance of ROMs did not show significant difference by gender. Endoscopic gastric emptying was correlated significantly with gastric clearance of ROMs ($r = 0.627$, $p = 0.012$) (Fig. 3). However, the scintigraphic emptying time and gastric clearance of ROMs did not show

significant correlation.

Effect of mosapride on gastric emptying

The endoscopic gastric emptying and gastric clearance of ROMs after administration of mosapride did not show significant differences in the 5 mg group, but showed significant differences in the 10 mg group ($p = 0.017$, $p = 0.027$, respectively) (Fig. 4). Furthermore, they did not show significant difference by gender.

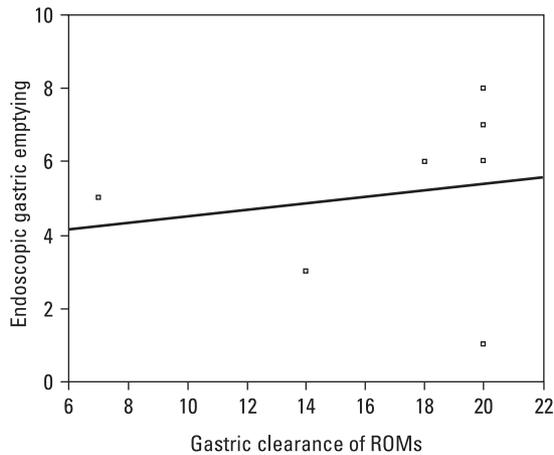


Fig. 3. Correlation between endoscopic gastric emptying and gastric clearance of radiopaque markers (ROMs) ($r = 0.627$, $p = 0.012$).

DISCUSSION

As mentioned earlier, the most frequently used test to evaluate gastric emptying is scintigraphic gastric emptying, however, it has several disadvantages, particularly the lack of general availability. Therefore, we used conventional endoscopic technique for qualitative assessment of gastric emptying. Although this method is not quantitative, it could be done simply in less a time and without utilization of radioactive substances.

Attila, et al.¹³ showed the feasibility, tolerability, and safety of unsedated transnasal esophagogastroscopy in qualitative evaluation of gastric emptying, and suggested that it could potentially satisfy the need for clinical information in a large number of situations where quantitative assessment is not needed for decision-making or for the initiation of therapy. Unlike our study, however, they used T-EG, which is not universal and its validation for measuring gastric emptying and quantification of food has not yet been investigated. We used conventional endoscopic technique and compared it with scintigraphy and gastric clearance of ROMs. Furthermore, we also tried to quantify by scoring food residue in stomach via endoscopic findings.

Gastric clearance of ROMs has been proposed as an

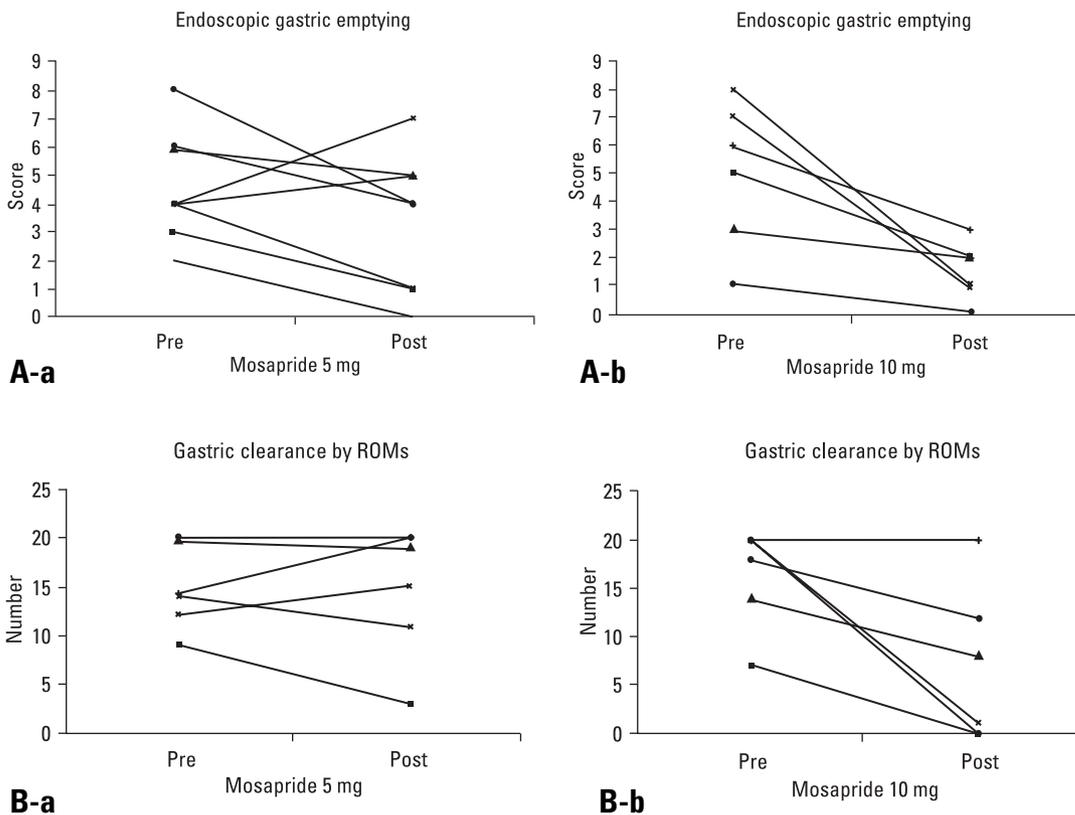


Fig. 4. Change of endoscopic gastric emptying and gastric clearance of radiopaque markers (ROMs) after ingestion of 5 mg or 10 mg mosapride citrate. (A) Endoscopic gastric emptying. (a) $p = 0.158$, (b) $p = 0.017$, (B) Gastric clearance of ROMs. (a) $p = 0.892$, (b) $p = 0.027$.

easy and noninvasive technique for assessment of gastric emptying.⁹ Feldman, et al.¹¹ concluded that gastric emptying of ROMs may be a more sensitive indicator of gastric motor dysfunction than scintigraphic gastric emptying study, and Stotzer, et al.¹⁷ concluded that scintigraphic emptying of solids and emptying of ROMs are closely correlated. This method is available in every hospital, but its reliability has been disputed: Some authors found no correlations between scintigraphic gastric emptying of solids and emptying of ROMs, whereas while others found good correlations.¹⁷ Stotzer, et al.¹⁷ suggested that an absence of correlations between solid emptying and emptying of ROMs was due to delayed onset of the migrating motor complex as an another cause of delayed ROM-emptying.

Although scintigraphic emptying time and endoscopic gastric emptying time or gastric clearance of ROMs did not show significant correlation in our study, we found that endoscopic gastric emptying was significantly correlated with gastric clearance of ROMs ($r = 0.627, p = 0.012$). Scintigraphic gastric emptying study and endoscopic gastric emptying study are studies for the measurement of digestible solid meal emptying whereas gastric clearance of ROMs represents emptying of an indigestible solid meal. Our present study consisted of healthy volunteers and we thought that there may be a correlation between scintigraphic gastric emptying study and endoscopic gastric emptying study. However, in our study, endoscopic gastric emptying study and gastric clearance of ROMs were carried out on the same day with digestible and indigestible solid meal, while scintigraphic gastric emptying study was conducted on an another day with digestible solid meal. Therefore, this discrepancy might have occurred by different meal and different date of performing. It might also be due to intraindividual variations.

Stotzer, et al.¹⁷ showed that gastric clearance of ROMs was slower in healthy women than in men. We have shown that endoscopic gastric emptying was slower in females than in males, but gastric clearance of ROMs was the same. It is highly likely that the discrepancy might have been developed by invasiveness of endoscopy and also difference of time interval at which two different studies were performed on the same day. In fact, our study was not corrected for gender (female predominance), and a larger scale study is needed to clarify the gender-specific changes.

An important limitation of endoscopic evaluation of gastric emptying is its invasiveness, but endoscopy is a general examination for patients with upper gastrointestinal symptoms, such as anorexia, nausea, and abdominal pain. Since endoscopy is relatively simple and inexpensive in Korea, it can be performed easily in most clinical settings. Also, exact quantification of gastric emptying can not done

by endoscopic gastric emptying: it can identify only the presence or absence of food residue, and its amount can be estimated roughly although we tried to quantify via scoring of the status of residual foods. Our endoscopic grading system may have inter- and intra-observer variations for judgement. However, the quantitative data of gastric emptying in most clinical settings are not expected to change the management of patients. In fact, the usefulness of gastric emptying data in directing therapy and predicting response to therapy remains controversial, partly because of the vast differences in technical factors and interpretations between studies. Impaired gastric emptying may or may not predict therapeutic outcomes.¹² Therefore, if quantification of an emptying abnormality is not needed, this endoscopic method may be helpful when physicians assess gastric emptying simply, rapidly and inexpensively in clinical practice.

The optimal time for endoscopic evaluation to determine emptying for patients is an another point to be considered. In order to determine the optimal time of endoscopic examination beforehand, 2 subjects in the present study preliminarily underwent endoscopy at 2, 3, and 4 hrs, and we did not find any gastric residue at 4 hrs. In addition, the migrating motor complex cycle, a cyclical motor pattern of the stomach and the small intestine, lasts between 90 and 120 min.¹ Therefore, we conducted endoscopic examination in healthy volunteers at 3 hrs after the ingestion of standard solid meal, however, this time interval does not appear to apply in patients with delayed gastric emptying.

We also studied the effect of different dosages of mosapride on gastric emptying. Delayed gastric emptying may be involved in the etiology of various gastrointestinal complaints and drugs that enhance gastrointestinal motility by various actions are used to treat such gastrointestinal complaints. Of these, mosapride is a 5-HT₄ receptor agonist that accelerates gastrointestinal motility via acetylcholine.¹⁴⁻¹⁶ Namely, mosapride selectively stimulates 5-HT₄ receptors on cholinergic nerves in the gastrointestinal tract, thus increasing acetylcholine release and enhancing gastrointestinal motility. These effects in turn accelerate gastric emptying.¹⁶ Wei, et al.¹⁸ determined the effect of oral mosapride on gastrointestinal transit time and diagnostic yield of capsule endoscopy (CE), and found that 10 mg of mosapride taken 1 hr before capsule ingestion could improve gastric emptying time, and increase the possibility of capsules reaching the cecum, and had the potential to improve the diagnostic rate of CE. Our present study demonstrated that 10 mg of mosapride enhanced gastric emptying, assessed by endoscopic gastric emptying and gastric clearance of ROMs. However, a larger scale study is needed to compare with control measures such as scintigraphy. They did not show significant difference by gender.

We think that our study could not adequately evaluate gender factor because of small number of subjects and the predominance of females.

Although scintigraphy is conventional measurements for evaluation of gastric emptying, it is highly expensive and bothersome. Therefore, gastric clearance of ROMs has been proposed as an another technique, and our present study showed a significant correlation with endoscopic evaluation of gastric emptying. In conclusion, we suggest that the gastric emptying test using conventional endoscopy can be used as a simple and safe alternative method in outpatients. We also think that a single 10 mg dose of mosapride is applicable to treatment of acute gastroparesis patients, but larger controlled studies should be performed in the future.

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REFERENCES

1. Tack J. Gastric motor disorders. *Best Pract Res Clin Gastroenterol* 2007;21:633-44.
2. Bouras EP, Scolapio JS. Gastric motility disorders: management that optimizes nutritional status. *J Clin Gastroenterol* 2004;38:549-57.
3. Bolondi L, Bortolotti M, Santi V, Calletti T, Gaiani S, Labó G. Measurement of gastric emptying time by real-time ultrasonography. *Gastroenterology* 1985;89:752-9.
4. Choi MG, Camilleri M, Burton DD, Zinsmeister AR, Forstrom LA, Nair KS. 13C-Octanoic acid breath test for gastric emptying of solids: accuracy, reproducibility and comparison with scintigraphy. *Gastroenterology* 1997;112:1155-62.
5. Simonian HP, Maurer AH, Knight LC, Kantor S, Kontos D, Megalooikonomou V, et al. Simultaneous assessment of gastric accommodation and emptying: studies with liquid and solid meals. *J Nucl Med* 2004;45:1155-60.
6. Schwizer W, Fraser R, Borovicka J, Asal K, Crelier G, Kunz P, et al. Measurement of proximal and distal gastric motility with magnetic resonance imaging. *Am J Physiol* 1996;271:G217-22.
7. Feinle C, Kunz P, Boesiger P, Fried M, Schwizer W. Scintigraphic validation of a magnetic resonance imaging method to study gastric emptying of a solid meal in humans. *Gut* 1999;44:106-11.
8. Sanjeevi A. Gastric motility. *Curr Opin Gastroenterol* 2007;23:625-30.
9. Park HJ, Jung JK, Song KS, Lee SI, Itoh Z, Park IS. Effect of erythromycin on gastric emptying in healthy individuals assessed by radio-opaque markers and plasma acetaminophen levels. *J Gastroenterol* 1997;32:734-9.
10. Jung JK, Park HJ, Moon YJ, Lee SI, Kim KW, Park IS. Gastric emptying assessed by radio-opaque markers in healthy young men and the effect of erythromycin. *Korean J Gastroenterol* 1997;30:148-55.
11. Feldman M, Smith HJ, Simon TR. Gastric emptying of solid radiopaque markers: studies in healthy subjects and diabetic patients. *Gastroenterology* 1984;87:895-902.
12. Camilleri M, Hasler WL, Parkman HP, Quigley EM, Soffer E. Measurement of gastrointestinal motility in the GI laboratory. *Gastroenterology* 1998;115:747-62.
13. Attila T, Hellman RS, Krasnow AZ, Hofmann CL, Saeian K, Dua KS, et al. Feasibility and safety of endoscopic evaluation of gastric emptying. *Endoscopy* 2005;37:240-3.
14. Ji SW, Park HJ, Cho JS, Lim JH, Lee SI. Investigation into the effects of mosapride on motility of Guinea pig stomach, ileum, and colon. *Yonsei Med J* 2003;44:653-64.
15. Kim HS, Choi EJ, Park H. The effect of mosapride citrate on proximal and distal colonic motor function in the guinea-pig in vitro. *Neurogastroenterol Motil* 2008;20:169-76.
16. Endo J, Nomura M, Morishita S, Uemura N, Inoue S, Kishi S, et al. Influence of mosapride citrate on gastric motility and autonomic nervous function: evaluation by spectral analyses of heart rate and blood pressure variabilities, and by electrogastrography. *J Gastroenterol* 2002;37:888-95.
17. Stotzer PO, Fjälling M, Grétarsdóttir J, Abrahamsson H. Assessment of gastric emptying: comparison of solid scintigraphic emptying and emptying of radiopaque markers in patients and healthy subjects. *Dig Dis Sci* 1999;44:729-34.
18. Wei W, Ge ZZ, Lu H, Gao YJ, Hu YB, Xiao SD. Effect of mosapride on gastrointestinal transit time and diagnostic yield of capsule endoscopy. *J Gastroenterol Hepatol* 2007;22:1605-8.