Prospective controlled study on the effects of polyethylene glycol in capsule endoscopy

Takafumi Ito, Ken Ohata, Akiko Ono, Hideyuki Chiba, Yosuke Tsuji, Hajime Sato, Nobuyuki Matsuhashi

Abstract

AIM: To prospectively confirm whether a small amount of polyethylene glycol (PEG) ingested after swallowing endoscopy capsule improves image quality and completion rate.

METHODS: Forty-four consecutive patients referred to us for capsule endoscopy (CE) were randomized to two groups. All patients were restricted to clear fluids for 12 h before the examination. Patients in group A (22 cases) received no additional preparation, while those in group B (20 cases) ingested 500 mL of PEG within a 2 h period starting 30 min after swallowing the capsule. Clear fluids and meals were allowed 2 h and 4 h after capsule ingestion, respectively. Image quality was assessed as the percentage of visualized bowel surface area as follows: 1: < 25%; 2: 25%-49%; 3: 50%-74%; 4: 75%-89%; 5: > 90%. The small bowel record was divided into five segments by time, and the score for each segment was evaluated. All CE examinations were performed with the Pillcam SB capsule endoscopy system (Given Imaging Co. Ltd., Yoqnem).

RESULTS: This study ended in December 2009, because sample size was considered large enough. A total of 44 patients were enrolled. Two patients in group B were excluded from the analysis because small bowel images could not be obtained from these patients; one had a full stomach, while the other presented with a massive gastric bleed. Thus, 22 patients from group A and 20 patients from group B completed the study. There was no significant difference in age (P = 0.22), sex (P = 0.31), and indication for CE. No significant adverse events occurred in any of the study patients. In group A, image quality deteriorated as the capsule progressed distally. However, in group B, image quality was maintained to the distal small bowel. In each of the five segments, the visibility score was significantly higher in group B than in group A (segment 1: 4.3 ± 0.7 vs 4.7 ± 0.5, P = 0.03; segment 2: 4.2 ± 0.9 vs 4.8 ± 0.4, P = 0.01; segment 3: 4.0 ± 1.0 vs 4.6 ± 0.7, P = 0.04; segment 4: 3.6 ± 1.1 vs 4.5 ± 0.6, P = 0.003; segment 5: 2.7 ± 1.0 vs 4.4 ± 0.8, P = 0.00004). Thus, the use of PEG during CE examination significantly improved image quality in all time segments, and this effect was more pronounced in the distal ileum. However, in group B, image quality was maintained to the distal small bowel. In each of the five segments, the visibility score was significantly higher in group B than in group A (segment 1: 4.3 ± 0.7 vs 4.7 ± 0.5, P = 0.03; segment 2: 4.2 ± 0.9 vs 4.8 ± 0.4, P = 0.01; segment 3: 4.0 ± 1.0 vs 4.6 ± 0.7, P = 0.04; segment 4: 3.6 ± 1.1 vs 4.5 ± 0.6, P = 0.003; segment 5: 2.7 ± 1.0 vs 4.4 ± 0.8, P = 0.00004). Thus, the use of PEG during CE examination significantly improved image quality in all time segments, and this effect was more pronounced in the distal ileum. The completion rate to the cecum was not significantly different between groups A and B (81.8% vs 85.0%, P = 0.89). There was no difference in the gastric transit time between groups (36.2 ± 35.0 min vs 54.0 ± 56.6 min, P = 0.23), but the small bowel transit time was significantly longer in group A than in group B (246.0 ± 107.0 min vs 171.0 ± 104.0 min, P = 0.04).

CONCLUSION: The ingestion of a small amount of PEG after the swallowing of an endoscopy capsule significantly improved CE image quality, but did not enhance the completion rate to the cecum.

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Key words: Capsule endoscopy; Completion rate; Image quality; Polyethylene glycol; Preparation
INTRODUCTION

Capsule endoscopy (CE) is the first-line procedure to explore small bowel pathology\[1-4\]. The preparation for CE suggested by the manufacturers of CE systems consists only of a clear liquid diet and an 8 h fast. Preparing the bowel with simethicone has been reported to bring about significantly better visibility by reducing intraluminal bubbles\[5,6\]. The diagnostic yield of CE, however, can be limited due to reduced visibility of the mucosal surface caused by residual material or dark colored bile, especially in the distal small bowel. In addition, CE sometimes fails to reach the cecum within the battery life of the capsule, resulting in a failure to visualize the distal small intestine\[7\]. It has been suggested that ingesting a small amount of polyethylene glycol (PEG) after the ingestion of the capsule may improve both the quality of the CE images and the likelihood that the cecum will be visualized before the capsule’s battery life ends (completion rate to the cecum)\[8\]. This study aimed to prospectively confirm whether a small amount of PEG solution ingested after the swallowing of the endoscopy capsule improves CE image quality and the completion rate to the cecum.

MATERIALS AND METHODS

This study was a single-center, prospective, single-blind, parallel, randomized controlled trial that was approved by the ethical committee at Kanto Medical Center NTT EC. This study was registered on February 9, 2009 in the UMIN-Clinical Trials Registry with a test ID of UMIN 000001696 (https://upload.umin.ac.jp/cgi-bin/ctrctr.cgi?function=brows and action=brows and type=detail and recptno=R000002039 and admin=0 and language=J) and was carried out in our hospital during a period from March 2009 to December 2009. Written informed consent was obtained from all patients, and the study was carried out in accordance with the Declaration of Helsinki (1989). There was no funding or other support for this study.

Patients referred to our institution for CE during the aforementioned period were prospectively randomized by the envelope method to group A or B. Randomization was done by means of sealed opaque envelopes.

Envelopes were provided by the study coordinator at our institute. Gastroenterologists enrolled the participants, and an assistant at the Endoscopy Center of our institute assigned patients to group A or B by the envelope method. All patients were restricted to clear fluids for 12 h before the examination, ingested 80 mg of simethicone at the time of capsule ingestion, and were then placed in the right lateral position for an hour. Patients in group A received no further preparation, but 30 min after swallowing the endoscopy capsule, the patients in group B ingested 500 mL of a PEG solution within a 2 h period. Clear fluids and meals were allowed 2 h and 4 h after capsule ingestion, respectively. After that, patients were free to leave the hospital, with instructions to return at the end of the 8 h study period to have the data recorder removed. All CE examinations were performed with the Pillcam SB capsule endoscopy system (Given Imaging Co. Ltd., Yoqneam). A single experienced reviewer blinded to the preparation analyzed each capsule study using Rapid Reader 5 software (Given Imaging Co. Ltd.). The primary outcome measures of the study were CE image quality and completion rate to the cecum, while the secondary outcome measures were gastric transit time (GTT) and small bowel transit time (SBTT). The image quality was evaluated only in cases in which the capsule reached the cecum within the examination period. The visibility of the mucosal surface was assessed as the percentage of visualized bowel surface area as follows: 1: < 25%; 2: 25%-49%; 3: 50%-74%; 4: 75%-89%; 5: > 90\%\[8\]. The small bowel record was divided into five segments by time, and the score for each segment was evaluated. The completion rate to the cecum was assessed based on the CE images.

Based on the preliminary examination, the sample size was determined based on the number of subjects needed to detect a 15\% change in the mean visualization score and a 30\% change in the mean transit time between the two groups at \( \alpha = 0.05 \) and power = 0.70. Interpretation of significance was adjusted for multiple comparisons by the Bonferroni’s method. Parametric data were expressed as mean ± SD. The Students’ two-sided \( t \)-test was used to compare parametric data between the groups. Nonparametric data were expressed as frequencies and were compared between the groups with the \( \chi^2 \) test. A P value of less than 0.05 was regarded as statistically significant in all tests.

RESULTS

This study ended in December 2009, because sample size was considered enough already. A total of 44 patients were enrolled. Two patients in group B were excluded from the analysis because small bowel images could not be obtained from these patients; one had a full stomach, while the other presented with a massive gastric bleed. Thus, 22 patients from Group A and 20 patients from group B completed the study. The demographic data of the 2 groups, as well as the indication for each CE, are shown in Table 1. There was no significant difference in...
In each of the 5 segments, the visibility score was significantly higher in group B than in group A (segment 1: 4.3 ± 0.7 vs 4.7 ± 0.5, P = 0.03; segment 2: 4.2 ± 0.9 vs 4.8 ± 0.4, P = 0.01; segment 3: 4.0 ± 1.0 vs 4.6 ± 0.7, P = 0.04; segment 4: 3.6 ± 1.1 vs 4.5 ± 0.6, P = 0.003; segment 5: 2.7 ± 1.0 vs 4.4 ± 0.8, P = 0.00004). The completion rate to the cecum was not significantly different between groups A and B (81.8% vs 85.0%, P = 0.89) (data not shown). There was no difference in the GTT between groups (36.2 ± 35.0 min vs 54.0 ± 56.6 min, P = 0.23), but the SBTT was significantly longer in group A than in group B (246 ± 107 min vs 171 ± 104 min, P = 0.04).

**DISCUSSION**

Some studies have suggested that bowel preparation that utilizes large amounts of purgatives can lead to higher quality CE images and/or accelerate the gastrointestinal transit of the CE. On the other hand, others have failed to demonstrate image quality improvement in studies utilizing a large amount of purgatives in the bowel preparation. All of these studies examined the effects of bowel preparation given prior to CE. In the present study, we examined the effects of PEG on CE image quality and completion rate to the cecum when PEG is given during, not before, the CE procedure. One great advantage of CE is its extreme non-invasiveness. However, it is a considerable burden for patients to have to take the large amount of purgatives needed as preparation for CE. Thus, we previously tried to see whether a small amount of PEG given during the CE procedure could improve the CE image quality and completion rate. In that retrospective study, we suggested that such an enhancement may improve both CE image quality and cecal completion rate. The present study was undertaken to confirm those effects in a prospective randomized controlled study. PEG passes smoothly through the intestine, as such, it is assumed to move much faster through the intestine than an endoscopy capsule. Therefore, if PEG is given before capsule ingestion, it may well be completely cleared from an area of the intestine by the time the endoscopy capsule reaches that area. Thus, we administered the solution after capsule ingestion. In addition, PEG is completely transparent. As such, the clarity of a view through PEG was thought to be superior to that of a view through natural intestinal fluid. The PEG solution was given starting 30 min after the swallowing of the capsule because the median pylorus passing time of an endoscopic capsule is approximately 20 min in our department (data not shown).

The present study confirmed that a small amount of PEG given after endoscopy capsule ingestion significantly improves image quality, especially in the lower segments of the small intestine. As CE imaging is disturbed by residual material or dark colored bile, especially in the distal small bowel, we feel that the image enhancing effect of this intervention is of significant worth. Furthermore, this procedure causes almost no discomfort to patients.

In regards to the completion rate to the cecum, conflicting results have been reported. Some have suggested that purgatives have completion enhancing effects, while others have failed to show such an effect. Our previous retrospective study described above suggested that a small amount of PEG given after capsule ingestion may improve the cecal completion rate, but the present prospective single blinded randomized study failed to confirm that effect. However, the present study did show that the SBTT is shortened by this enhancement. Therefore, the administration of an additional intervention that can shorten the GTT in conjunction with a small amount of PEG given after capsule ingestion may be useful in improving completion rate. One intriguing possibility for such an intervention would be prokinetics, as they have been suggested to shorten the GTT and improve completion rate to the cecum.

In conclusion, we show that as little as 500 mL of a PEG solution given after the swallowing of an endoscopy capsule can significantly improve the quality of the CE images in a prospective randomized study. Therefore, we recommend the ingestion of a small amount of PEG after the swallowing of the capsule as a standard enhancement of CE.

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**Table 1** Demographic data of patients and their indications for capsule endoscopy

| Group A (simethicone only) | Group B (simethicone + PEG) | P value |
|---------------------------|----------------------------|---------|
| n                         |                            |         |
| Age, yr, mean ± SD        | 50.4 ± 14.6                | 0.22    |
| Sex                       | 0.31                       |         |
| Men                       | 11                         |         |
| Women                     | 11                         |         |
| Indication for CE, n      |                            |         |
| OGB                       | 20                         |         |
| Suspected polyposis       | 2                          |         |
| Suspected CD              | 0                          |         |

CE: Capsule endoscopy; OGB: Obscure gastrointestinal bleeding; PEG: Polyethylene glycol; CD: Crohn’s disease.
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COMMENTS

Background
Capsule endoscopy (CE) is the first-line procedure to explore small bowel pathology. The preparation for CE suggested by the manufacturers of CE systems consists only of a clear liquid diet and an 8 h fast. Preparing the bowel with simethicone has been reported to bring about significantly better visibility by reducing intraluminal bubbles. The diagnostic yield of CE, however, can be limited due to reduced visibility of the mucosal surface caused by residual material or dark colored bile, especially in the distal small bowel. In addition, CE sometimes fails to reach the cecum within the battery life of the capsule, resulting in a failure to visualize the distal small intestine.

Research frontiers
It has been suggested that ingesting a small amount of polyethylene glycol (PEG) after the ingestion of the capsule may improve both the quality of the CE images and the likelihood that the cecum will be visualized before the capsule’s battery life ends (completion rate to the cecum). This study aimed to prospectively confirm whether a small amount of PEG solution ingested after the swallowing of the endoscopy capsule improves CE image quality and the completion rate to the cecum.

Innovations and breakthroughs
In the present study, the beneficial effects of a small amount of PEG solution on CE image quality were demonstrated in a prospective single-blinded randomized controlled study. In the study group without preparation, the image quality deteriorated as the capsule progressed distally. However, in the group that took 500 ml of PEG solution after capsule ingestion, image quality was maintained to the distal small bowel.

Applications
Ingestion of at least 500 ml of PEG solution brings about an excellent clarity in CE images without any discomfort. This study prospectively confirmed the suggested beneficial effect of PEG solution on CE images, and can provide evidence for an effective, safe, cost-effective and minimally invasive preparation of capsule endoscopy in clinical practice.

Peer review
Here is an interesting single-blinded prospective randomized controlled study regarding the effects of PEG on capsule endoscopy image quality and completion rate to the cecum when PEG is given during, and not before, the capsule endoscopy procedure. Data on this topic is limited and therefore the study is welcome. What is more, the study has an excellent methodology and the results are really interesting.

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