

Effectiveness and safety of a new regimen of polyethylene glycol plus ascorbic acid for same-day bowel cleansing in constipated patients

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Abstract

Background and study aims : In an exploratory study we compared a new regimen of low-volume polyethylene glycol plus ascorbic acid (PEG-Asc) with the standard regimen for same-day bowel cleansing in constipated patients.

Patients and methods : Between January and June 2015 we studied consecutive patients with constipation (Rome III constipation criteria) scheduled for colonoscopy. The initial group received the standard regimen of PEG-Asc. The subsequent group received the new regimen. The new regimen involved ingestion of 10 mL of sodium picosulfate and 50g of magnesium citrate dissolved in 0.2 L of water followed by 0.2 L of PEG-Asc +0.2 L of water given 6 or 7 times over 3 hours. Bowel cleansing was prospectively evaluated using the Boston bowel preparation scale (BBPS). Bowel cleansing, adenoma detection rates and adverse events were reviewed using electronic medical records and endoscopic filing system.

Results : Sixty-two patients used the standard regimen and sixty used the new regimen. The basic characteristics of the two groups were similar. The mean volume of PEG-Asc and total liquid intake was less with the new regimen compared to the standard regimen (1.3 L vs. 2.0 L, $P<0.001$; 2.6 L vs. 3.0 L, $P<0.001$). The proportion of patients with a BBPS score ≥ 6 was significantly greater with the new than the standard regimen (93% vs. 76%, $P=0.008$). Nausea and/or vomiting was also significantly less frequent than with the standard regimen (5% vs. 16%, $P=0.046$).

Conclusions : The new regimen of PEG-Asc gave improved same-day bowel cleansing for colonoscopy in constipated patients. (*Acta gastroenterol. belg.*, 2018, 81, 485-489).

Keywords : colonoscopy ; bowel preparation ; PEG-Asc ; constipation.

Abbreviations : PEG-Asc ; polyethylene glycol plus ascorbic acid.

Introduction

Colonoscopy is a common diagnostic and therapeutic procedure. Successful colonoscopy requires adequate bowel preparation to visualize the colonic mucosa so as to detect colorectal neoplasms. Diagnostic accuracy and safety of colonoscopy depend on the quality of the colonic preparation (1,2). Polyethylene glycol plus ascorbic acid (PEG-Asc) which was released as MOVIPREP® in the United States in 2006 as a hypertonic bowel cleansing solution. The increased osmotic pressure prompts water to move into the intestinal tract from the body allowing a decrease in the oral dose required and in the bowel preparation time (3,4,5).

Generally, 2 L of PEG-Asc are taken either divided as 1 L on the evening before and 1 L on the morning

of procedure (split dosing) or as 2 L on the day of the procedure (same-day dosing). It is also recommended that patients drink an additional liter of clear liquid to prevent thirst and dehydration (4). PEG-Asc is commonly used in split regimens in the US and Europe. In Japan same-day dosing is commonly used for patients scheduled for afternoon colonoscopy. Same-day dosing with the standard regimen requires intake of two lots of 1 L of PEG-Asc + 0.5 L of water and tolerability seems to be lower than reported using split dosing of PEG-Asc from other countries.

We explored a new regimen of PEG-Asc for same-day (afternoon) colonoscopy. The new regimen involved the first intake of both 10 mL of sodium picosulfate and 50 g of magnesium citrate dissolved in 0.2 L of water, and the subsequent intake of 0.2 L of PEG-Asc +0.2 L of water repeated 6-7 times with 15 minutes between administrations. The aim of the study was to compare the new regimen of PEG-Asc with the standard regimen in terms of cleansing effectiveness, adenoma detection rate, and patient tolerability for same-day bowel cleansing for constipated patients.

Patients and Methods

Patients

Patients with constipation who underwent screening or diagnostic colonoscopy at the Showa Inan General Hospital were enrolled between January and June 2015. Constipation was defined using the Rome III constipation criteria (6). Exclusion criteria included an age less than 20 years old, pregnancy, and American Society of Anesthesiologists class III or IV.

Study design

This was a case-control study, based on historical comparisons of patients in two time periods. Data was

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collected retrospectively. The first group of patients (from January to March 2015) received the standard regimen of PEG-Asc. The subsequent group (from April to June 2015) received the new regimen of PEG-Asc. This retrospective study was approved by the ethics committee at our hospital.

Bowel preparation method

All subjects were allowed regular meals the day before; no pretreatment was required the day before colonoscopy. The standard regimen involved intake of 1 L of PEG-Asc + 0.5 L of water twice and is commonly used as a same-day regimen for afternoon colonoscopy in Japan. The new regimen involved the first intake of both 10 mL of sodium picosulfate and 50 g of magnesium citrate (Horii Pharmaceutical Co., Tokyo, Japan) dissolved in 0.2 L of water, and the subsequent intake of 0.2 L of PEG-Asc + 0.2 L of water repeated 6-7 times with 15 minutes between administrations (Fig. 1).

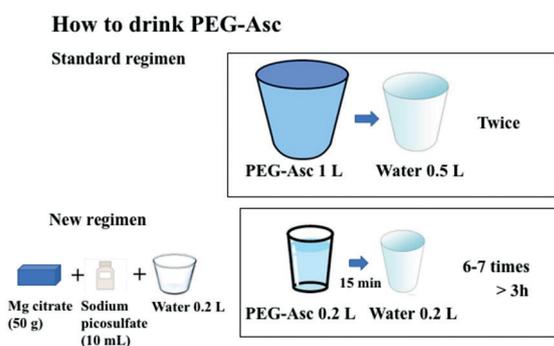


Fig. 1. — Intake schedule of the new regimen compared to the new standard of polyethylene glycol plus ascorbic acid (PEG-Asc).

Assessment of bowel cleansing

Based on the policy of our endoscopy unit the degree of bowel cleansing is assessed for each case prospectively

since January 2014 using the Boston bowel preparation scale (BBPS) (7). The range of BBPS is 0 to 9. The score of ≥ 6 in BBPS was considered to be excellent (9 or 8) or good (7 or 6) in this study. The score of 5 or less was defined as fair.

Outcome variables

The degree of bowel cleansing, the rate of polyps detected and the rate of adverse events were compared between both groups. The determination of the degree of bowel cleansing, the characteristics of polyps found, adverse events was based on a retrospective review of the patients' charts with special attention to endoscopy report.

Statistical analysis

Based on our observation that the rate of excellent/good using the new regimen was $\geq 95\%$ in non-constipated patients (unpublished data), we hypothesized that the rate of excellent/good using the new regimen would be approximately 90% in constipated patients. In our experience, the rate of excellent/good using the standard regimen was less than 70%. In order to demonstrate a superiority of our new regimen for bowel preparation, we calculated a sample size for comparing 90% in our new regimen versus 70% in standard regimen with a two-sided α of 0.05 and a power of 80% and required at least 62 participants in each arm. Statistical tests to compare the measured results for the two groups were as follows: the Chi-square test, with Yates' correction for continuity where appropriate, was used for comparison of categorical data. Fisher's exact test was used when the numbers were small. For parametric data, the Student's *t*-test was used when 2 means were compared. Differences were considered significant if the *P* value was less than 0.05. Statistical analysis was performed by using JMP® 9.0.2 version software (SAS Institute Inc., Tokyo, Japan).

Table 1. — Baseline characteristics of the subjects

Group	New regimen	Standard regimen	<i>P</i> value
No. of patients	60	62	
Mean (SD) age (y)*	72(12)	70(13)	0.56
Gender (Female)**	34	36	0.13
Indications**			
Hemo-positive stools	40	41	0.70
Screening	16	12	
Others	4	9	
Cecal intubation rate (%)*	100	100	
Mean (SD) cecal intubation time (min)*	5.8(8)	5.6(6)	0.59
Intubation rate of terminal ileum (%)*	100	100	
Mean (SD) procedure time (min)*	18(7)	17(9)	0.67

*Differences between new regimen group and standard regimen group compared by Student's *t*-test for continuous variables ; **Differences between New regimen group and Standard regimen group compared by chi-square test for categorical data.

Results

Baseline characteristics

The patients' demographic characteristics, the indications for colonoscopy, the cecal intubation rate, mean cecal intubation time, mean procedure time were similar between the two groups (Table 1).

Bowel cleansing

The mean volume of PEG-Asc intake and total liquid intake in the new regimen were less than those of the standard regimen (1.3 L vs. 2.0 L, $P<0.001$; 2.6 L vs. 3.0 L, $P<0.001$) while the mean time for preparation was similar between the two groups (3.4 h vs. 3.3 h, $P=0.56$)

(Table 2). The average interval time between the intake of the prep and the start of the colonoscopy was similar between the both groups (5.2 h vs. 4.9 h, $P=0.44$). With cleansing assessment, the number of patients with scores of Excellent or Good in the new regimen group were significantly greater than among the standard regimen [93 % (56/60) vs. 76% (47/62), $P=0.008$].

Comparison of polyps detected

The characteristics of number, size, shape, and location of polyps removed are shown in Table 3 and were similar between the two groups (the new regimen group, 189 polyps, average size 5.6 mm; the standard regimen group, 193 polyps, average size, 5.5 mm). Adenoma detection rates between two groups were similar (67% vs. 61%, $P=0.54$).

Table 2. — Comparison of bowel cleansing between the new regimen group and the standard regimen group

Group	New regimen	Standard regimen	P value
Mean (SD) PEG-Asc intake volume (L)*	1.3 (0.3)	2.0	<0.001
Mean (SD) total liquid intake volume (L)*	2.6 (0.5)	3.0	<0.001
Mean (SD) required preparation time (h)*	3.4 (0.4)	3.3 (0.5)	0.56
Mean (SD) interval time between the start of intake and the start of the colonoscopy	5.2(0.6)	4.9 (0.7)	0.44
Cleansing assessment in BBPS**			
≥6	93%(56/60)	76%(47/62)	0.008
<5	7%(4/60)	24%(15/62)	

PEG-Asc, polyethylene glycol plus ascorbic acid; BBPS, Boston bowel preparation scale ; *Differences between new regimen group and standard regimen group compared by Student's t-test for continuous variables ; **Differences between New regimen group and Standard regimen group compared by chi-square test for categorical data.

Table 3. — Comparison of polyps detected between the new regimen group and the standard regimen group

Group	New regimen	Standard regimen	P value
Total No. of polyps removed	189	193	
Mean (SD) No. of polyps/patient*	3.2(3)	3.1(3)	0.54
Mean (SD) polyp size (mm)*	5.6(2)	5.5(2)	0.39
Adenoma detection rate (%)	67	61	0.54
Characteristics of polyps**			
Size			
≤5mm	70	80	0.38
6mm<	119	113	
Shape			
Flat	18	24	0.64
Sessile	144	154	
Pedunculated	27	15	
Location			
Right colon	90	101	0.36
Left colon	99	92	
Pathology			
Adenoma	154	160	0.74
Sessile serrated adenoma/polyp	18	14	
Hyperplastic polyp	17	19	

*Differences between New regimen group and Standard regimen group compared by Student's t-test for continuous variables ; **Differences between new regimen group and standard regimen group compared by chi-square test for categorical data.

Adverse events

Nausea and/or vomiting with the new regimen was significantly less frequent compared to the standard regimen [5% (3/60) vs. 16% (10/62), $P=0.046$] (Table 4). There were no major adverse events such as syncope during bowel preparation, bleeding, and perforation during procedure in the two groups.

Table 4. — Comparison of adverse events between the new regimen group and the standard regimen group

Group	New regimen	Standard regimen	<i>P</i> value
Nausea and/or vomiting	5%(3/60)	16%(10/62)	0.046
Syncope during bowel preparation	0%	0%	
Bleeding during procedure	0%	0%	
Perforation	0%	0%	

Discussion

Generally, it is difficult for patients with chronic constipation to achieve sufficient bowel cleansing before colonoscopy and same-day bowel cleansing is often thought to be inappropriate (8,9,10). There are few studies involving methods for bowel cleansing methods for patients with chronic constipation. This study demonstrated that both cleansing efficacy and tolerability using a regimen with multiple small administrations of PEG-Asc was significantly better than 2 large doses of the same regimen for same-day bowel preparation even in constipated patients.

Although the adenoma detection rates were similar between the two groups, the new regimen enabled constipated patients to achieve a clean colon assessed as a BBPS score of ≥ 6 in 93%. The intake volume of PEG-Asc and total liquid in the new regimen was also significantly less than in the standard regimen (1.3 L vs. 2.0 L, $P < 0.001$; 2.0 L vs. 3.0 L, $P < 0.001$). In addition, the new regimen was associated with significantly less nausea and/or vomiting (5% vs. 16%, $P=0.046$). Therefore, we would like recommend the new regimen for constipated patients based on improved visualization and fewer adverse events.

It has been reported that the PEG-Asc preparation was superior to the polyethylene glycol electrolyte lavage solution (PEG-ELS) with regard to the degree of bowel cleansing (3,5). This was explained by high-osmotic PEG-Asc causing water to enter the intestinal tract from the body which improved bowel cleansing. Ascorbic acid is a water soluble vitamin and it does not accumulate in the body. Recently, it has been reported that the physiological dehydration associated with PEG-Asc was significantly greater than that with PEG-ELS at the end of dosing (11). To prevent dehydration the new regimen involved the alternative intake of 0.2 L

of PEG-Asc + 0.2 L of water. This new regimen was proceeded by intake of both sodium picosulfate (10 mL) and magnesium citrate (50 g) dissolved in 0.2 L of water before PEG-Asc intake. However, the mean volume of PEG-Asc intake and total liquid intake with the new regimen was less than with the standard regimen and was associated with less frequent nausea and/or vomiting. The reason why the new regimen of PEG-Asc was more tolerable than the standard regimen may be due to the lower volume of PEG-Asc and possibly the less feelings of thirst due to frequent water intake.

Recently, the safety and efficacy of same-day low-volume 1 L PEG-Asc bowel preparation for colonoscopy was reported in the elderly and patients with renal dysfunction (12). In that study patients were required to take a low-residue diet and 10 mL of sodium picosulfate in the evening of the day before colonoscopy. In that study the proportion with a BBPS ≥ 6 in the elderly (65-79 years old), special-elderly (80 \geq years old), and non-elderly (18-64 years old) were 94.1, 91.8, and 94.6%, respectively. Another randomized clinical study of a new regimen that involved five repeats of 0.3 L of PEG-Asc+0.15 L of water was recommended because of its shorter cleansing time without causing serious nausea (11). Our regimen also used 10 mL of sodium picosulfate and multiple small administrations of PEG-Asc which may result in lower volumes of PEG-Asc intake and fewer adverse events.

Our regimen differed from the standard regimen in two aspects; (1) both 10 mL of sodium picosulfate and 50 g of magnesium citrate dissolved in 0.2 L of water were added and (2) a small-volume PEG-Asc and additional water were taken alternatively. Although our regimen worked well for constipated patients, the study design precluded identifying whether one of the two modifications was largely responsible or whether both were required.

The present study has limitations. First, the study was a case-control study with a small number of patients. The selection of case or control was based on the entry period which is unlikely to have critical biased the patient selection. However, randomized studies will be required to confirm the beneficial effects of the new regimen for the same-day bowel cleansing in constipated patients.

In conclusion, the new regimen of frequent administration of small volumes of PEG-Asc may prove more useful than the standard regimen for same-day bowel preparation before afternoon colonoscopy even in chronic constipated patients.

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