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ORIGINAL ARTICLE

Polyethylene glycol plus bisacodyl: A safe, cheap, and effective regimen for colonoscopy in the South Asian patients

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Abstract

Background and Aim: Data regarding the comparison of colonoscopic preparation regimens are still variable. We aimed to assess the adequacy and tolerability of two bowel preparation regimens for afternoon colonoscopy.
Methods: In a randomized, investigator-blinded trial, two preparation regimens [4-L split-dose polyethylene glycol-electrolytes (PEG-ELS) and 2-L PEG-ELS plus bisacodyl) were compared in terms of bowel cleansing efficacy and adverse effects.
Results: The mean (±SD) age (years) of the 4-L split-dose PEG-ELS group (N = 147) and the 2-L PEG-ELS plus bisacodyl (N = 155) were 44.09 (±15.62) (M:F : 2:1) and 44.12 years (±15.61) (M:F : 1.7:1), respectively. Percentage of patients with excellent and good preparation was higher in the 4-L split-dose PEG-ELS regimen compared with the 2-L PEG-ELS plus bisacodyl regimen (22.44 *vs* 17.41 and 44.21% *vs* 36.12%). Percentage of patients with fair and poor preparation was lower in 4-L split-dose PEG-ELS regimen compared with the 2-L PEG-ELS plus bisacodyl regimen (21.08% *vs* 27.74% and 12.24% *vs* 18.70%). In comparison with the 2-L PEG-ELS plus bisacodyl group, the incidences of abdominal pain (11% *vs* 15%), bloating (9% *vs* 12.24%), nausea/vomiting (8.38% *vs* 9.52%), and sleep disturbance (11% *vs* 12%) were slightly more common in the 4-L split-dose PEG-ELS group. There were no statistically significant differences between the two regimens with regard to bowel cleansing efficacy and adverse events.
Conclusions: The 2-L PEG-ELS plus bisacodyl (10 mg) preparation is as efficacious as the 4-L split-dose PEG-ELS regimen for afternoon colonoscopy. Optimal preparation for colonoscopy can be achieved with the 2-L PEG-ELS plus bisacodyl regimen with slightly fewer adverse events and lower cost compared to the 4-L split-dose PEG-ELS regimen.

Introduction

Colonoscopy is a very common procedure required for the diagnosis of various colonic diseases. Clear mucosal details can only be obtained after adequate bowel preparation. Insufficient mucosal visualization during colonoscopy can result in missed lesions, difficult progression, an increased risk of procedural complications, prolonged procedure duration, and an increased requirement of the amount of sedatives and analgesics. Poor bowel preparation is a frequent cause for incomplete procedures, resulting in the need for a repeat colonoscopy. Therefore, the quality of bowel preparation needs to be assessed and documented.[1]

In countries where the prevalence of colorectal cancer (CRC) is high, early detection of adenoma is of the utmost importance. The quality of bowel preparation is very important for screening colonoscopy performed in Western, and a few Asian, countries. Indications of colonoscopy in south Asia are different from the Western world. CRC is less prevalent in this part of the world. Usual indications for colonoscopy in south Asia are gastrointestinal bleeding (GIB), abdominal pain, and altered bowel habit caused by infective colitis, inflammatory bowel disease (IBD), ileocecal tuberculosis (ITB), hemorrhoids, and malignancies.[2]

Previous-evening single-dose or previous-evening and same-morning split-dose preparations are widely used regimens for colonoscopy. Although guidelines for adequate bowel preparation are available in the literature, data regarding the comparison of various colonoscopic preparation regimens are still variable.[1,3,4] In this study, we aimed to assess the adequacy and tolerability of 4-L split-dose polyethylene glycol-electrolytes (PEG-ELS) *versus* 2-L same-morning PEG-ELS plus previous-evening bisacodyl bowel preparation regimens for afternoon colonoscopy.

Methods

This prospective study was conducted at a tertiary care center from January 2015 to October 2017. The study was approved by the institute's ethical review committee. All patients provided informed consent before enrollment. Adult (>18 years) patients scheduled for colonoscopy for various medical reasons were recruited from the outpatient department of a teaching hospital. Exclusion criteria included the presence of severe renal impairment, pregnant or lactating women, severe congestive heart failure (NYHA III or IV), history of bowel obstruction or colonic resection, and known allergies to the medications used in the protocol. Patients were also excluded from analysis in case of failure of advancement of the colonoscope because of technical difficulties or stricture.

Colonoscopy was performed in the afternoon between 12 and 3 PM under conscious sedation (propofol-based) supervised by either a gastroenterology faculty member or trainee. All subjects were on a low-residue diet the day before the colonoscopy. Clear liquids were permitted up to 3 h before the colonoscopy. Subjects were allowed to choose any one of two bowel preparation regimens. The two colonoscopy preparation regimens were previous-evening and same-morning 4-L split-dose PEG-ELS (4-L split-dose PEG-ELS) and same-morning 2-L single-dose PEG-ELS plus previous-evening bisacodyl (2-L PEG-ELS plus bisacodyl). The 4-liter split-dose PEG-ELS regimen consisted of 2-L PEG preparation in the previous evening (5–7 PM) and 2-L PEG on the same morning (5–7 AM) of examination. In the 2-L PEG-ELS plus bisacodyl regimen, 10 mg of bisacodyl was given in the previous evening, and 2-L PEG-ELS was given on the same morning (5-7 AM) of examination. Each packet of PEG-ELS consisted of polyethylene glycol 118 g, potassium chloride 1.484 g, sodium bicarbonate 3.37 g, and sodium chloride 2.93 g, which was dissolved in two liters of water.

Two PEG-ELS protocols were randomly (computer-generated random numbers) prescribed for bowel preparation. Colon preparation was graded by an experienced endoscopist (unaware of preparation regimen) according to the Aronchick scale (AC). The endoscopy fellow was not involved in the grading of the preparations. A questionnaire describing the total volume of PEG consumed and adverse effects such as nausea, vomiting, bloating, abdominal pain, and sleep disturbance were recorded. Data such as indication of colonoscopy, associated comorbidities, successful cecal intubation, and endoscopic findings were also recorded.

Adequacy of bowel preparation is commonly assessed by AC, the Boston bowel preparation scales, and the Ottawa scale. AC is the most commonly used bowel preparation scale.[4,5] AC grades the adequacy of bowel cleansing by describing mucosal visualization of the colon on a five-parameter scale: excellent, good, fair, poor, or inadequate. AC is defined as follows: (i) excellent, a small volume of clear liquid or > 95% of mucosal surface seen; (ii) good, a large volume of clear liquid covering up to 25% of the surface, but >90% of mucosal surface is visualized; (iii) fair, presence of some semisolid stool that could not be suctioned or washed away but >90% of mucosa seen; (iv) poor, semisolid stool that could not be suctioned or washed away and < 90% of surface seen; and (v) inadequate, patients with frank solid stool.

Outcome measures. The primary outcome was adequacy of bowel cleansing. The secondary outcomes were tolerability of preparation and incidence of adverse events.

Statistical analysis. The analyses of preparation quality (AC) were performed with noninferiority of the 2-L PEG-ELS plus bisacodyl regimen compared to the 4-L split-dose PEG-ELS regimen. The sample size was based on an expected rate of successful bowel cleansing of 90% for both groups. In order to reach a 90% statistical power to detect a treatment difference of 10% at a significant level of 0.05, and taking into account a dropout rate of 10%, no less than 172 patients were needed in each arm. All results are expressed as mean ± standard deviation (SD), median (range), or frequency (%) as appropriate. Student *t*-test or the non-parametric Kruskall–Wallis test was used for continuous variables. The association between two categorical variables was tested using the Pearson Chi-square test (two-tailed χ^2 analysis) or Fisher's exact test wherever appropriate. All analyses were performed using SPSS Version 17, Chicago, IL: SPSS Inc.

Results

Screening, randomization, and compliance. During the study period, 418 patients were screened for colonoscopy on an outdoor basis. After obtaining consent, a total of 350 patients were randomized into 4-L split-dose PEG-ELS (N = 175) and 2-L PEG-ELS plus bisacodyl (N = 175) preparation regimens. Sixteen patients did not turn up for colonoscopy and, hence, were excluded from enrollment. Seven patients did not complete the proper preparation protocol and were also excluded from the study. A total of 161 and 166 patients were enrolled into the 4-L split-dose PEG-ELS and 2-L PEG-ELS plus bisacodyl groups, respectively. We could not reach the cecum in 25 patients due to stricture or obstructing lesions (21 patients) and technical difficulties such as sharp angulation and loop formation (4 patients); these patients were therefore excluded from the final data

analysis. The data of 302 patients (4-L split-dose PEG-ELS: 147; 2-L PEG-ELS plus bisacodyl: 155) were finally analyzed (Fig. 1).

The mean (SD) age of patients in the 4-L split-dose PEG-ELS group was 44.09 (±15.62) years (male:female : 2:1). The mean (SD) age of patients in the 2-L PEG-ELS plus bisacodyl group was 44.12 (±15.61) years (male:female: 1.7:1).

Abdominal pain with or without altered bowel habit was the most common indication for colonoscopy, followed by GIB, chronic diarrhea, and chronic constipation. Anemia, screening colonoscopy, malabsorption syndrome, abdominal lump, surveillance colonoscopy, ascites, and liver abscess were other uncommon indications of colonoscopy in both groups. Hemorrhoids, CRC, ITB, and IBD were the common colonoscopic findings observed. Nonspecific ileitis/colitis, amoebic colitis, diverticulosis, and polyps were less common in colonoscopic diagnosis.

Bowel cleansing. The 4-L split-dose PEG-ELS group analyzed by AC showed excellent, good, fair and poor preparations in 22.44, 44.21, 21.08, and 12.24% of subjects, respectively. The 2-L PEG-ELS plus bisacodyl group analyzed by AC showed excellent, good, fair, and poor preparations in 17.41, 36.12, 27.74, and 18.70% of subjects, respectively. Percentage of patients with excellent and good preparations was higher in the 4-L split-dose PEG-ELS regimen compared with the 2-L PEG-ELS plus bisacodyl regimen (22.44% *vs* 17.41%, $P = 0.27$, and 44.21% *vs* 36.12%, $P = 0.16$). However, the percentage of patients with fair and poor preparations was lower in the 4-L split-dose PEG-ELS regimen compared with the 2-L PEG-ELS plus bisacodyl regimen (21.08% *vs* 27.74%, $P = 0.19$, and 12.24% *vs* 18.70%, $P = 0.13$). Overall, 87.75% and 81.29% patients prepared with the 4-L split-dose PEG-ELS and 2-L PEG-ELS plus bisacodyl group, respectively, had an AC of excellent/good/fair, indicating adequate bowel preparation. A total of 12.24 and 18.70% patients prepared with the 4-L split-dose PEG-ELS and 2-L PEG-ELS plus bisacodyl regimen, respectively, had an AC of poor, indicating inadequate bowel preparation. There were no statistically significant differences seen in two regimens with regard to bowel cleansing efficacy. Colonic strictures/obstructing lesions, older age, and low extra fluid intake were risk factors identified in patients refractory to adequate bowel cleaning.

We compared the bowel cleansing rate in patients with constipation and diarrhea. There was a nonsignificant trend toward better cleansing with the 4-L split-dose PEG-ELS in patients with constipation compared with the 2-L PEG-ELS plus bisacodyl group. Overall, 91.66 and 86.66% patients with constipation prepared with 4-L split-dose PEG-ELS and 2-L PEG-ELS plus bisacodyl group, respectively, had an AC of excellent/good/fair, indicating adequate bowel preparation. However, the bowel cleansing rates in patients with diarrhea were similar in both regimens (adequate cleansing: 86.66% *vs* 86.95%).

In this study cohort, most of the colonoscopies were performed before 2 PM. A total of 55 patients underwent colonoscopy after 2 PM (24 in 4-L split-dose PEG-ELS group and 31 in 2-L PEG-ELS plus bisacodyl group). This group showed relatively inferior bowel preparation (statistically nonsignificant) compared to the colonoscopies performed before 2 PM (adequate preparation: 83.63% *vs* 87.44%).

Cecal intubation rate. Overall, in patients without significant stricture or obstructing lesions, cecal intubation/colonoscopy completion rate was possible in 98.67% (298/302). Cecal intubation/colonoscopy completion rate in the 2-L PEG-ELS plus bisacodyl and the 4-L split-dose PEG-ELS regimens were 98 and 99.35%, respectively.

Adverse effects. In comparison with the 2-L PEG-ELS plus bisacodyl group, the incidence of abdominal pain (11% *vs* 15%, $P = 0.30$), bloating (9% *vs* 12.24%, $P = 0.45$), nausea/vomiting (8.38% *vs* 9.52%, $P = 0.84$), and sleep disturbance (11% *vs* 12%, $P = 1.00$) were slightly more common in the 4-L split-dose PEG-ELS group. However, the differences in the incidence of adverse effects were statistically not significant. Severe abdominal pain was noted in three patients [4-L split-dose PEG-ELS (2) and 2-L PEG-ELS plus bisacodyl (1)]. One patient in each group had fecal incontinence. Serious complications, including ischemic colitis, were not seen in either cohort. No major anesthesia-related complications were seen. Two patients (one in each group) were aspirated during the procedure and required hospitalization and antibiotic therapy.

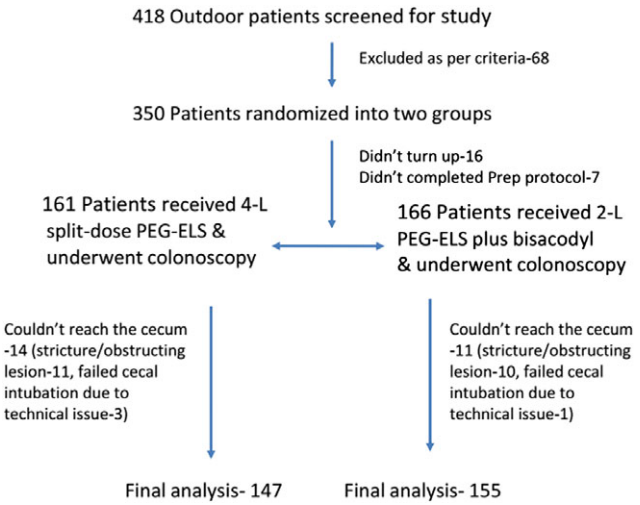

Figure 1 Study design.

Discussion

Adequate bowel cleansing is very important for successful colonoscopy. South Asian populations have lower body mass index, different diet habits, and shorter colonic transit time compared to Western countries.[6] Abdominal pain, with or without altered bowels and GI bleeding, are the common indications for colonoscopies in our institution, which is consistent with a previous study by Rehman *et al.*[2] Due to the low prevalence of CRC in south Asia, screening for adenoma is not routinely performed. Very limited data are available regarding the bowel cleansing efficacy of colonic preparation regimens in this part of the world.[7,8] Therefore, we evaluated the efficacy and safety of two bowel preparation regimens for colonoscopy. We compared the efficacy and tolerability of the 2-L PEG-ELS plus bisacodyl

regimen with the 4-L split-dose PEG-ELS preparation regimen for afternoon colonoscopy. The mean age of 2-L PEG-ELS plus bisacodyl group and 4-L split-dose PEG-ELS group was 44.12 and 44.09 years, respectively. South Asian countries have a relatively young population; therefore, the mean age of cohorts in this study was younger in both groups.

Adequacy of bowel cleansing mainly depends on the type of cleansing agents, volume of preparation, mode of administration (single dose *vs* split dose), use of adjunct agents, and timing of colonoscopy. PEG-based solutions are the most commonly used preparation agents because of an excellent safety profile.

Studies showed better bowel cleansing with 4-L split-dose preparation.[9,10] In comparison with the PEG-ELS nonsplit regimen regardless of dosage, a PEG-ELS split-dose regimen (2-L on the day before procedure +2-L on the day of the procedure) causes significantly better bowel cleansing.[11–16] A study showed improved polyp detection rate, quality of the bowel cleansing, and colonoscopy completion rates with a split-dose regimen.[17] A meta-analysis showed that 4-L split-dose PEG is better than other bowel preparation methods for colonoscopy, with comparable compliance, favorable overall experience, willingness to repeat the same preparation, and adverse events.[18]

A split-dose regimen of 4-L PEG-ELS provides high-quality bowel cleansing and is endorsed by the American College of Gastroenterology as the optimal choice for colonoscopy.[19] However, approximately 5–15% of the patients poorly tolerate PEG, mostly due to large-volume PEG ingestion. Large-volume PEG can cause abdominal fullness, bloating, cramping, nausea, vomiting, and insomnia. Aspiration pneumonia, colitis, pancreatitis, and Mallory-Weiss tears are other rare complications of large-volume PEG ingestion.[4,20]

Volume-related adverse effects can be minimized with the use of combination regimens (low-volume PEG with an adjunct) or the 2-L split preparation regimen. Low-volume preparations with an adjunct, such as stimulant laxatives, prokinetics, or sodium ascorbate, have been used in various studies. Bisacodyl is frequently used as an adjunctive agent to low-volume PEG preparation for bowel cleansing. A combination of 2-L single dose PEG and 10–20 mg bisacodyl was compared with the 4-L split-dose PEG preparation in a few studies. Studies showed similar efficacy of a regimen of bisacodyl at bedtime with 2-L PEG in the morning and a 4-L PEG split-dose regimen. In one study, a regimen of 15 mg bisacodyl at bedtime and 2-L PEG in the morning was compared to a 4-L PEG regimen. The efficacy of both regimens was similar in terms of bowel cleansing, cecal intubation time, adenoma detection rates, and adverse effects.[21] In a meta-analysis of six randomized controlled trials, low-volume PEG (2-L) with bisacodyl (10–20 mg) demonstrated similar rates of adequate bowel cleansing and less nausea, vomiting, and bloating compared to 4-L split-dose PEG.[22] Vallante *et al*. compared bisacodyl in the evening plus 2-L split-dose PEG (1 L in the evening and 1 L in the morning) with 4-L split-dose PEG bowel preparation prior to colonoscopy. The success of bowel preparation was similar in both groups (92%). Patients in the 2-L group rated the preparation as good or satisfactory in 91% compared to 77% in the 4-L PEG ($P = 0.003$). Bisacodyl plus 2-L group was better tolerated and accepted than 4-L split-dose PEG for screening colonoscopy.[23] In one study, authors compared 2-L PEG-citrate-simethicone (PEG-CS) plus 2-day bisacodyl (reinforced regimen) and 4-L PEG in patients with constipation.[24] The adequacy of bowel cleansing was comparable in both groups; however, 2-L PEG was more acceptable for ease of administration ($P < 0.001$) and willingness to repeat ($P < 0.001$) and showed better compliance. In one study, Shieh *et al*. compared a newly developed electrolyte-free PEG combined with a carbohydrate–electrolyte solution and bisacodyl with 4-L split-dose PEG. A combination of low-volume MiraLAX (electrolyte-free PEG)–Gatorade (carbohydrate-electrolyte solution) and 20 mg bisacodyl produced similar rates of excellent/good bowel cleansing (91.1% *vs* 93.6%, respectively; $P = 0.498$) compared with 4-L PEG.[25] We were unable to find the head-to-head comparison of 2-L PEG with or without bisacodyl.

Volume-related adverse effects can also be minimized using the 2-L split preparation. Authors have showed comparable efficacy and fewer adverse effects of 2-L split regimen compared to single-dose 2-L preparation. However, the data regarding the 2-L split regimen are limited, and most of these studies were specifically performed on patients attending morning outpatient colonoscopy. Hence, further studies are warranted to establish the role of 2-L split dose PEG preparation in afternoon colonoscopy.[8,26,27]

The choice of preparation also depends on the preparation-to-colonoscopy interval (PC interval). A long PC interval (>6 h) causes inferior bowel cleansing due to the deposition of thick secretion in the mucosal surface of the right colon. One study showed that an interval of 3–5 h produces better cleansing compared to longer intervals.[28] For morning procedures, the split-dose regimen causes better bowel cleansing compared to the morning regimen. For afternoon colonoscopy, the split-dose regimen and same-day morning preparation causes comparable bowel cleansing and compliance.[8] Same-day morning preparation and afternoon colonoscopy is more convenient for patients as it does not cause sleep disturbance.[7] Matro *et al*. showed equivalent cleansing efficacy and polyp detection rates in split-dose morning-only PEG and split-dose prior-evening and same-morning PEG for afternoon colonoscopy. Adverse events were less common in the morning-only preparation group.[29] However, subjects took morning-only preparation 8 h before colonoscopy. In the 2-L PEG-ELS plus bisacodyl regimen, patients received morning preparation 6 h before colonoscopy. Sleep disturbance can be further reduced with the use of a later preparation (7–9 AM) of 2-L PEG-ELS plus bisacodyl regimen compared to an earlier preparation (5–7 AM). This preparation regimen (7–9 AM) would be more acceptable to the patients and may produce better results considering the shorter PC interval.

A higher dose (≥10 mg) of bisacodyl can rarely cause abdominal cramping and ischemic colitis. However, we used 10 mg of bisacodyl in our study cohort without any serious complications. As discussed in the previous section, volume-related side effects of the 4-L PEG regimen can be avoided with the use of the 2-L PEG plus bisacodyl regimen. In addition, use of 2-L PEG-ELS plus bisacodyl can save 6 USD per procedure. The average daily per capita income in south Asia is approximately 5 USD.

Adequate bowel cleansing varies widely in different studies. Most of the studies showed adequate bowel cleansing to the tune of 85–90%. However, in a study by Repici *et al*., an adequate level of bowel cleansing was observed in 79.1% of PEG-

CS plus bisacodyl and in 70.0% of PEG-Ascorbate patients.[30] In another study by Parente *et al*., successful bowel cleansing was noted in 80.2% in the 2-L PEG-CS/bisacodyl *versus* 81.4% in the 4-L PEG group.[24] In the current study, adequate bowel preparation was noted in 87.75 and 81.29% patients prepared with 4-L split-dose PEG-ELS and 2-L PEG-ELS plus bisacodyl group, respectively, which is sufficient to diagnose a majority of the colonic lesions, except for small adenoma and small vascular lesions. Colonic adenoma is not a common lesion in south Asian patients compared to Western countries.

There are a few limitations of our study, each of which is the use of AC, which is a subjective score with relatively high interobserver variability, and the absence of inclusion of indoor patients. We did not record the exact time required for colon preparation in individual patients. We did not include a patient satisfaction questionnaire for analysis of adverse effects. The indications of colonoscopy in this region are different from Western and developed Asian countries.[2] Screening colonoscopy is not recommended in south Asian countries. We did not evaluate the polyp detection rate.

To summarize, we have compared the 4-L split-dose PEG-ELS with 2-L PEG-ELS plus bisacodyl regimens for colonoscopy performed after 4–5 h of preparation. Both groups had equivalent bowel cleansing efficacy for colonoscopy and incidence of adverse events. Our study supports an earlier observation that the 2-L PEG-ELS plus bisacodyl regimen is noninferior to the 4-L split-dose PEG-ELS preparation in terms of bowel cleansing efficacy and adverse event, especially for afternoon colonoscopy. The 2-L PEG-ELS plus bisacodyl regimen is more convenient in terms of early morning wake up and is less expensive compared to the 4-L split-dose PEG-ELS preparation. However, many authors, including the American College of Gastroenterology, consider that the 4-L split-dose PEG-ELS preparation is superior to the 2-L PEG-ELS plus bisacodyl regimen. Therefore, further investigation involving different populations is still needed in order to fully support the use of the 2-L PEG-ELS plus bisacodyl regimen for colonoscopy preparation.

Conclusion

The 2-L same-morning PEG-ELS plus previous-evening bisacodyl (10 mg) preparation is as efficacious as the 4-L split-dose (previous evening and same-morning) PEG-ELS regimen for afternoon colonoscopy. An optimal preparation for afternoon colonoscopy can be achieved with 2-L PEG-ELS plus bisacodyl regimen with slightly fewer adverse events and lower cost compared to 4-L split-dose PEG-ELS.

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