Bowel preparation with split-dose polyethylene glycol before colonoscopy: a meta-analysis of randomized controlled trials CME

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Background: Polyethylene glycol (PEG) is a commonly used bowel preparation for colonoscopy. Unfortunately, the standard large-volume solution may reduce patient compliance. Split-dosing of PEG has been studied in various randomized, controlled trials (RCTs). However, results have been conflicting.

Objective: We conducted a meta-analysis to assess the role of split-dose PEG versus full-dose PEG for bowel preparation before colonoscopy.

Design: Multiple databases were searched (January 2011). RCTs on adults comparing full-dose and split-dose of PEG for bowel preparation before colonoscopy were included and analyzed by calculating pooled estimates of quality of bowel preparation, preparation compliance, willingness to repeat the same preparation, and side effects by using odds ratio (OR) by fixed and random-effects models.

Setting: Literature search.

Patients: Per RCTs.

Main Outcome Measurements: Satisfactory bowel preparation, willingness to repeat same bowel preparation, patient compliance, and side effects.

Results: Five trials met inclusion criteria (N = 1232). Split-dose PEG significantly increased the number of satisfactory bowel preparations (OR 3.70; 95% CI, 2.79-4.91; $P < .01$) and willingness to repeat the same preparation (OR 1.76; 95% CI, 1.06-2.91; $P = .03$) compared with full-dose PEG. Split-dose PEG also significantly decreased the number of preparation discontinuations (OR 0.53; 95% CI, 0.28-0.98; $P = .04$) and nausea (OR 0.55; 95% CI, 0.38-0.79; $P < .01$) compared with full-dose PEG.

Limitations: Limited number of studies.

Conclusions: The use of a split-dose PEG for bowel preparation before colonoscopy significantly improved the number of satisfactory bowel preparations, increased patient compliance, and decreased nausea compared with the full-dose PEG. (Gastrointest Endosc 2011;73:1240-5.)

Colonoscopy remains the preferred procedure for investigation of large-bowel and distal terminal ileum diseases in adults. Adequate colon preparation is essential for optimal visualization of the colonic mucosa. A good colon preparation is one that is palatable to the patient, effective in cleansing quality, relatively small in volume, and tolerated well by patients with minimal adverse GI symptoms. Multiple bowel preparations have been used throughout the years, with the 2 most common being sodium phosphate preparations and polyethylene glycol (PEG) solutions.

Abbreviations: OR, odds ratio; PEG, polyethylene glycol; RCT, randomized, controlled trial.

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Since its introduction in 1980, PEG solutions have become the most commonly used preparation for colon cleansing.[1] The main advantage of PEG solutions is the minimal fluid and electrolyte shifts that can be seen with other preparations; however, a major disadvantage is the large volume required to produce adequate mucosal cleansing. This large volume taken over a short period of time may result in patient intolerance and poor compliance, leading to poor colon preparation, missed lesions, and potentially increased overall cost because of the need for repeat procedures.

Take-home Message

- Split-dose polyethylene glycol (PEG) bowel preparation is superior to full-dose PEG with respect to colon cleansing, patient compliance, and patients' willingness to repeat the same bowel preparation.
- Significant alterations should be made worldwide in bowel preparation before colonoscopy.

BACKGROUND

Given the already-established efficacy of PEG solutions and limited side effects, recent studies have explored new approaches in the administration of PEG solutions to enhance patient tolerability and improve efficacy. Three such strategies involve a lower-volume PEG solution with an adjunct therapy, such as a laxative or additive,[2-4] splitting the large volume of PEG solution with an adjunct therapy (bisacodyl),[5] or splitting the large volume of PEG solution into 2 rounds, 1 (2 L or 3 L) the night before and 1 (2 L or 1 L) the day of colonoscopy.[6-10] Patient compliance, quality of bowel preparation, and side effects have differed among randomized trials evaluating the split-dose PEG preparations. Therefore, we conducted a meta-analysis to assess the role of split-dose PEG versus full-dose PEG (4 L) for bowel preparation before colonoscopy.

METHODS

Study selection criteria

All randomized, controlled trials (RCTs) on adult patients comparing large-volume PEG solutions with split-dose PEG solutions were included in our analysis.

Data collection and extraction

MEDLINE, Cochrane Central Register of Controlled Trials & Database of Systematic Reviews, CINAHL, PubMed, and recent abstracts from major conference proceedings (Digestive Disease Week and American College of Gastroenterology National Meeting from 1999 to 2010) were searched through January 2011. The search terms used were bowel preparations, polyethylene glycol, and split-dose. All references from selected RCTs were reviewed to ensure that no additional trials were omitted from the primary searches. Only RCTs comparing full-dose PEG solution (4 L) with split-dose PEG solution (2 L or 3 L on the night before and 2 L or 1 L the day of procedure, respectively) without an adjunct therapy (bisacodyl, magnesium citrate) were included. Standard forms were used to extract the data by 2 independent reviewers (T.W.K., M.L.B.), with any differences resolved by mutual agreement. Data were extracted that directly compared only full-dose PEG solution (4 L) with split-dose PEG solution (2 L or 3 L on the night before and 2 L or 1 L the day of procedure, respectively) without any adjuncts medications for the measured outcomes. If adjunct medications were used, the data were excluded from the analysis. This exclusion of adjunct therapy strengthens the significance of the comparison of the 2 PEG groups. Each study was evaluated by a Jadad score[11] (5 = excellent quality, 0 = poor quality) and criteria based on Jüni et al[12] to assess the quality of the study. The Jadad score is a statistical point system based on 5 components to evaluate the quality of studies: randomization, method of randomization being appropriate and described, double-blinding, double-blinding being appropriate and described, and description of withdrawal and dropouts.[11] If the methods of double-blinding or randomization were inappropriate, a point may be deducted for each inappropriate criterion.[11]

Statistical analysis

A meta-analysis was performed comparing split-dose PEG and full-dose PEG for bowel preparation before colonoscopy by calculating pooled estimates of quality of bowel preparation, compliance with the preparation, willingness to repeat the same preparation, and side effects by using odds ratio (OR) with fixed and random-effects models. Publication bias was assessed by funnel plots and Egger[13] and Begg-Mazumdar[14] bias indicators. Heterogeneity among studies was assessed by calculating I^2 measure of inconsistency, which was considered significant if $P < .10$ or $I^2 > 40\%$. RevMan 5 was used for the statistical analysis.

RESULTS

The initial search identified 386 articles and trials (Fig. 1). Five studies satisfied the inclusion criteria (N = 1232) with a mean age ranging from 47.8 to 58.2 years (Table 1). All studies were RCTs of adequate quality (Jadad score ≥2) in English (Table 2). Table 3 shows the diets on the day before the procedure for the various studies. All studies used 4 L for the full-dose PEG and 2 L the night before and 2 L the day of the procedure for the split-dose PEG except one. Park et al[6] used 4 L PEG for the full-dose PEG and 3 L the night before and 1 L the day of procedure for the split-dose PEG.

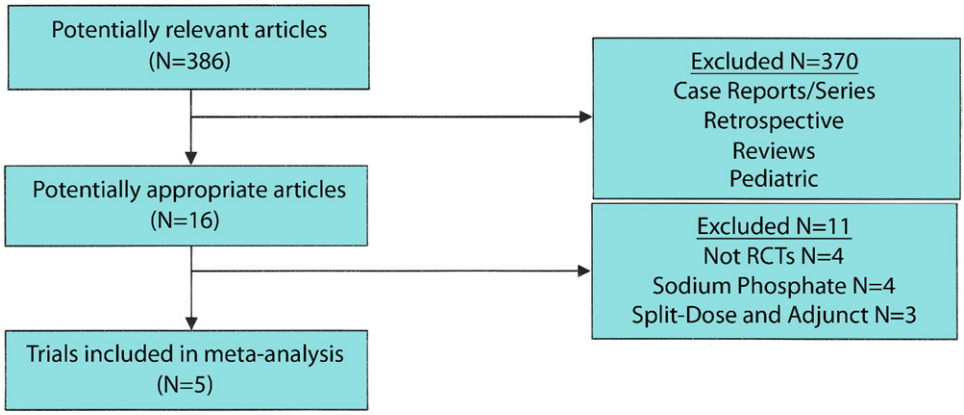

Figure 1. Article search results for this meta-analysis.

TABLE 1. Details of studies included in the meta-analysis

Author	Type of study	Blinding	Location	No. of patients	Bowel preparation scale	Split-dose (evening before day of procedure)	Split-dose PEG ingestion times (dose 1/dose 2)	Full-dose PEG ingestion times (dose 1)	Jadad score (0-5)
Aoun et al, 2005[7]	RCT	Single	Lebanon	141	Aronchick	2 L–2 L	7:00 PM/complete 1.5 h before colonoscopy	6:00 PM	3
Abdul-Baki et al, 2008[8]	RCT	Single	Lebanon	196	Aronchick	2 L–2 L	7:00 PM/complete 2 h before colonoscopy	7:00 PM	3
Park JS et al, 2007[6]	RCT	Single	South Korea	303	Ottawa	3 L–1 L	8:00 PM/complete 2 h before colonoscopy	8:00 PM	2
Park SS et al, 2010[9]	RCT	Single	South Korea	159	Aronchick	2 L–2 L	8:00 PM/5:00 AM	10:00 PM	3
Marmo et al, 2010[10]	RCT	Single	Italy	433	Ottawa	2 L–2 L	Afternoon before colonoscopy/early morning before colonoscopy	6:30 PM	3

PEG, Polyethylene glycol; *RCT*, randomized, controlled trial.

Satisfactory bowel preparations

Four studies examined the number of satisfactory bowel preparation (N = 929) by using similar scales.[7-10] Of these 929 patients, 582 had satisfactory bowel preparations with 365 in the split-dose group and 217 in the full-dose group. Split-dose PEG significantly increased the number of satisfactory bowel preparations compared with full-dose PEG (OR 3.70; 95% CI, 2.79-4.91; $P < .01$). Figure 2 shows the Forest plot for the satisfactory bowel preparations. No statistically significant heterogeneity was noted ($I^2 = 39\%$, $P = .18$).

Preparation discontinuations

Three studies evaluated the number of preparation discontinuations (N = 733).[7,9,10] Of the 733 patients, 48 patients discontinued their colon preparation at some point; 17 in the split-dose group and 31 in the full-dose group. Split-dose PEG significantly decreased the number of preparation discontinuations compared with full-dose PEG (OR 0.53; 95% CI, 0.28-0.98; $P = .04$). Figure 3 shows the Forest plot for the bowel preparation discontinuations. No statistically significant heterogeneity was observed ($I^2 = 26\%$, $P = .26$).

Willingness to repeat bowel preparation

Two studies evaluated the patient's willingness to repeat the same bowel preparation for future colonoscopies (N = 300).[7,9] Of these patients, 107 patients in the split-dose group and 93 in the full-dose group were willing to repeat their respective preparation. Split-dose PEG significantly increased the willingness to repeat the same bowel preparation compared with full-dose PEG (OR 1.76; 95% CI, 1.06-2.91; $P = .03$). Figure 4 shows the Forest plot for willingness to repeat the same bowel preparation. No significant heterogeneity was noted ($I^2 = 0\%$, $P = .91$).

TABLE 2. Quality assessment of RCTs analyzed in meta-analysis

Criteria	Aoun et al[7]	Abdul-Baki et al[8]	Park JS et al[6]	Park SS et al[9]	Marmo et al[10]
Jadad score	3	3	2	3	3
Randomization	+	+	+	+	+
Allocation sequence	+	+	−	+	+
Allocation concealment	Not described	+	Not described	+	Not described
Blinding	Single blind	Single blind	Single blind	Single blind	Single blind
Definition of outcome measures	+	+	+	+	+
Adequate power	+	+	+	+	+
Intent-to-treat analysis	+	+	+	+	+
Baseline assessment of treatment group	+	+	+	+	+
Description of follow-up	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable

+, performed in RCT; −, not described or performed in RCT; *RCT*, Randomized, controlled trial.

TABLE 3. Details regarding preprocedure diets on the day before colonoscopy

Author	Split-dose PEG	Full-dose PEG
Aoun et al, 2005[7]	Regular diet until 6:30 PM, water only after 6:30 PM	Liquid diet, water only after midnight
Abdul-Baki et al, 2008[8]	Regular diet until 6:00 PM (last meal to be a light meal)	Liquid diet, water only after 6:00 PM
Park JS et al, 2007[6]	Soft diet	Soft diet
Park SS et al, 2010[9]	Regular diet until 6:00 PM (last meal a thick liquid dinner), nothing by mouth after 6:00 PM	Regular diet until 6:00 PM (last meal a thick liquid dinner), nothing by mouth after 6:00 PM
Marmo et al, 2010[10]	No fruit, vegetables, legumes for 3 days, light breakfast and lunch, semiliquid dinner	No fruit, vegetables, legumes for 3 days, light breakfast and lunch, semiliquid dinner

PEG, Polyethylene glycol.

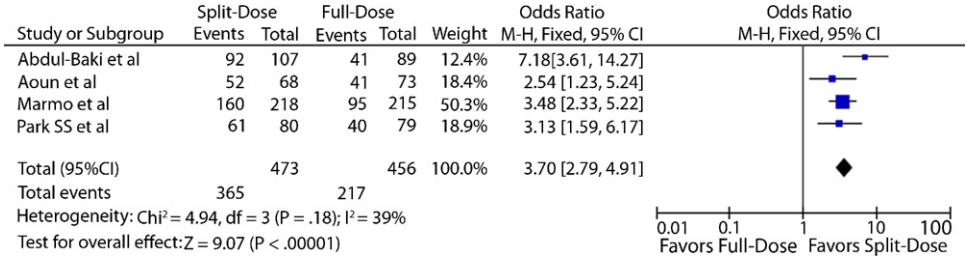

Figure 2. Forest plot demonstrating a significant improvement in the number of satisfactory bowel preparations with split-dose PEG before colonoscopy.

Side effects

Multiple side effects were analyzed including nausea, vomiting, abdominal cramping, abdominal bloating, sleep disturbance, and missing work or school (Table 4). Split-dose PEG resulted in a statistically significant reduction in nausea (OR 0.55; 95% CI, 0.38-0.79; $P < .01$) compared with the full-dose PEG. Figure 5 shows the Forest plot for nausea for the 2 preparations. However, no statistically significant difference was noted between the 2 groups for abdominal cramping ($P = .14$), abdominal bloating ($P = .84$), vomiting ($P = .17$), sleep disturbance ($P = .18$), and missing work or school ($P = .32$) (Table 4).

Publication bias

No significant publication bias was found for any of the outcomes by the funnel plot (Fig. 6) or by Egger (1.09 with

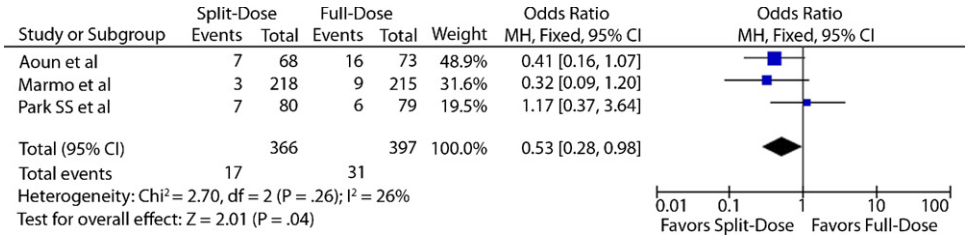

Figure 3. Forest plot demonstrating a significant decrease in the number of bowel preparation discontinuations with split-dose PEG before colonoscopy.

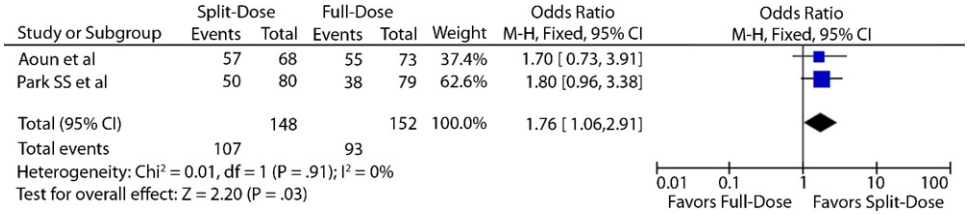

Figure 4. Forest plot demonstrating a significant improvement in the patients' willingness to repeat the same preparation with split-dose PEG before colonoscopy.

TABLE 4. Outcomes of the various side effects analyzed between split-dose PEG and full-dose PEG before colonoscopy

Side effect	OR	95% CI	*P* value	Significance
Abdominal cramping	0.75	0.52-1.10	.14	NS
Abdominal bloating	0.92	0.42-2.01	.84	NS
Vomiting	0.51	0.20-1.34	.17	NS
Sleep disturbance	0.78	0.55-1.12	.18	NS
Missing work or school	0.72	0.38-1.38	.32	NS

PEG, Polyethylene glycol; *OR*, odds ratio; *CI*, confidence interval; NS, not significant.

95% CI: −6.06 to 8.24; $P = .58$) or Begg-Mazumdar (Kendall's $\tau = 0.33$; $P = .75$) bias indicators.

DISCUSSION

Colonoscopy remains an extremely important procedure for diagnosing colonic and terminal ileal disease. Colon preparations have long been limited by their tolerability, mostly attributed to their large volumes. Some studies have shown that as many as 38% of patients do not complete the preparation because of poor palatability and/or intolerance of such a large volume of solution to consume.[2,15] Other more recent studies have used lower volume 2-L PEG solutions in conjunction with senna, bisacodyl, or magnesium citrate and evaluating for efficacy, tolerability, and acceptability. Generally, these studies showed good tolerability but poor efficacy.[2-4] Given the need for further improvements in bowel preparation because of its inherent limitations, split-dosing of the PEG solutions was introduced and studied.[6-10] However, results have varied, making the overall effect controversial.

Our meta-analysis was performed to clarify the overall effects of split-dose PEG compared with full-dose PEG by examining only RCTs in adult patients. Based on our results, split-dose PEG offers major benefits in clinical practice because it relates to better satisfactory bowel preparations (which leads to a more thorough examination of the mucosa and potentially decreases the potential for missed lesions), and patient compliance (which potentially could improve bowel preparation quality). Patients receiving the split-dose PEG bowel preparation also had an increased willingness to repeat the same preparation (which may improve follow-up colonoscopy compliance) and decreased nausea.

The strengths of this meta-analysis include the use of only RCTs in varying populations and significant endpoints that are applicable to clinical practice. This represents the first meta-analysis to date on the subject of split-dose bowel preparations. Limitations of the study are as follows. First, this meta-analysis only addressed split-dose PEG compared with full-dose PEG. Other unique combinations of bowel preparations are available and studies, such as PEG with an adjunct, were beyond the scope of this analysis. Second, a limited number of studies were available to be included in the analysis; however, these are the only studies to date on the subject. The addition of future trials may affect certain outcomes (such as willingness to repeat bowel preparation, vomiting, and missing school or work) because only 2 studies were

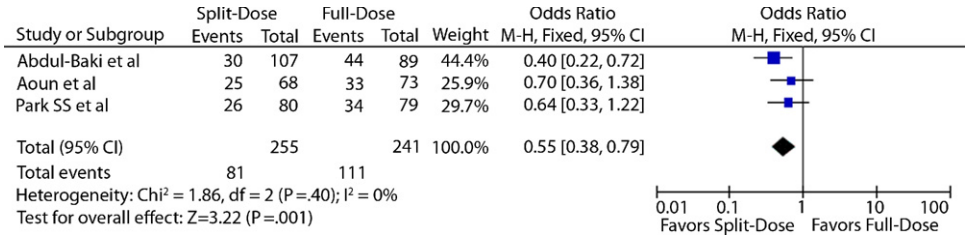

Figure 5. Forest plot demonstrating a significant reduction in patients' nausea with split-dose PEG before colonoscopy.

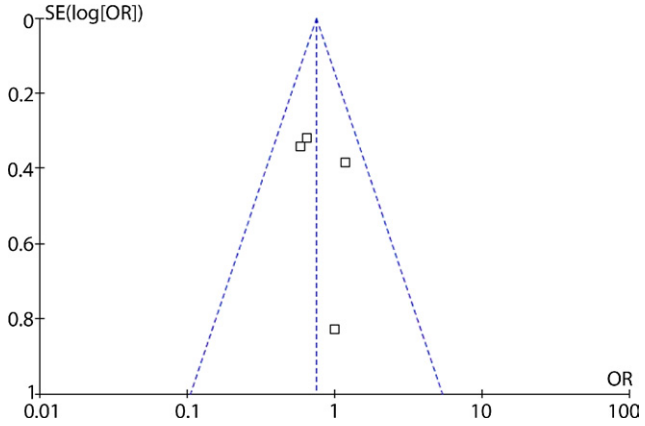

Figure 6. Funnel plot demonstrating no significant publication bias. SE, standard error.

analyzed. Third, abdominal bloating analysis did reveal statistically significant heterogeneity, likely attributed to extensive variation in results from the included studies. To compensate for this, a random-effects model was used and still demonstrated no statistical difference between the split-dose and full-dose bowel preparation. Finally, the PEG bowel preparations between studies varied slightly because of different manufacturers. This likely had little impact on the overall results given that all studies used the same PEG solution for split-dose and full-dose.

In conclusion, our meta-analysis found that split-dose PEG solution for bowel preparation before colonoscopy improved the quality of bowel preparation and patients' willingness to repeat the same bowel preparation while decreasing the amount of nausea experienced by patients and patient-induced bowel preparation discontinuation compared with the full-dose PEG solution. Therefore, split-dose PEG appears to be superior to full-dose PEG for bowel preparation before colonoscopy.

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