

Efficacy of single- versus split-dose polyethylene glycol electrolyte solution for morning colonoscopy: A randomized controlled study

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Abstract

Background: Split-dose (SPD) regimen has been proved more effective than a single-dose (SID) regimen for various drug preparations; however, limited data have focused on morning colonoscopy. We implemented this study to compare the bowel cleanliness and tolerability of a same-day SID versus SPD 2 L polyethylene glycol electrolyte solution (PEG) for morning colonoscopy.

Methods: Patients undergoing morning colonoscopy were randomized into two groups, SID or SPD. In the SID group, patients had to complete 2 L PEG between 4 and 6 am on the day of colonoscopy. In the SPD group, patients had to complete 1 L PEG between 8 and 9 pm on the day before followed by another 1 L PEG between 5 and 6 am on the day of colonoscopy. Colonoscopy was performed between 8 and 12 am under anesthesia. Investigators and endoscopists were blinded to the allocation. The primary end point was the effectiveness of bowel cleansing according to the Boston Bowel Preparation Scale (BBPS). The secondary outcomes were polyp detection rate, compliance, tolerability, and patient satisfaction.

Results: Overall, there were 147 and 148 patients in the SID and SPD group, respectively. The SPD group had a better quality of bowel preparation than the SID group with a total BBPS score of 7.25 ± 1.53 versus 6.71 ± 1.65 ($P = 0.005$). No difference in the polyp detection rate was noted, although more polyps were detected in the SPD group. More patients felt acceptable with the bowel preparation regimen in the SPD group compared to the SID group (76% vs. 65%, $P = 0.03$). The adverse events were more commonly observed in the SID group, presented as nausea and vomiting.

Conclusion: For morning colonoscopy, split-dose 2 L PEG is superior to single-dose 2 L PEG by improved bowel preparation, better tolerability, and patient satisfaction.

Keywords: Bowel preparation, morning colonoscopy, polyethylene glycol, split dose

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INTRODUCTION

Colonoscopy is considered the most accurate tool for the detection and prevention of colorectal cancer.^[1] However,

the sensitivity mainly depends on the quality of bowel preparation. Poor bowel preparation will lead to poor

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visualization of the colonic mucosa, thereby missing small lesions, increasing technical difficulty, inducing patient discomfort, and causing greater costs associated with colonoscopy.^[2-4]

An adequate bowel preparation regimen is not only effective in cleansing the colon but should be well tolerated by patients. The polyethylene glycol (PEG) solution, an isosmotic nonabsorbable polymer, is generally used for bowel preparation, because of its safety, effectiveness, and good tolerability.^[5] Although high-volume (4 L) PEG or 2 L (PEG or non PEG) hyperosmotic solutions are popular in North American and European countries because of a better efficacy for bowel preparation, the relatively higher incidence of adverse gastrointestinal symptoms is also noticed.^[6,7] Considering the smaller body size and lower body weight, the low-volume 2 L PEG is preferred in Asian countries.^[8] And recently several studies showed noninferior efficacy of 2 L versus 4 L PEG in bowel cleansing.^[9] 2 L PEG was used with good quality of bowel preparation for afternoon colonoscopy.^[10] However, for morning colonoscopy, 2 L PEG ingested the day before colonoscopy did not bring an adequate bowel preparation. The main reason might be due to the long interval time between the intake of PEG and the colonoscopy procedure, which has been proved to be best controlled to 4–6 h.^[11,12] To satisfy the optimal interval time, patients need to wake up at dawn to prepare for the morning colonoscopy because patients should finish the laxative at least 2 h prior to the colonoscopy. This could potentially lead to poor compliance and dissatisfaction.

Split-dose (SPD) regimen has been proved more effective than a single-dose (SID) regimen for various drug preparations; however, limited data have focused on morning colonoscopy.^[13-16] A SPD regimen can delay the intake of PEG in the early morning, which might improve compliance. Thus in this study, we performed a prospective randomized controlled trial to compare bowel cleanliness, polyp detection rate, compliance, tolerability, and patient satisfaction of a SID regimen versus a SPD regimen for morning colonoscopy.

METHODS

Study design

A prospective, single-blinded, randomized controlled trial was conducted in the third people's hospital of Chengdu between March and September, 2019. The study protocol was approved by the Human Ethics Committees of the third people's hospital of Chengdu (2019-S-51) and was conducted according to the Declaration of Helsinki.

Consecutive adult patients seen in the outpatient clinic of our department as well as hospitalized patients allocated for morning colonoscopy (8 am–12 pm) were screened for enrollment in the study. Exclusion criteria included patients under 18 years of age, severe constipation (<2 bowel movements/week), suspected bowel perforation or obstruction, previous history of colon surgery, chronic kidney disease (stages 2–5), congestive heart failure (New York Heart Association Classes II–IV), pregnancy or lactation, inflammatory bowel disease with stricture or penetrating disease, and psychiatric illness.

Written informed consent was obtained prior to enrollment if the patient was willing to participate and was able to respond to the questionnaires. Eligible patients were randomized into two bowel preparation groups, in a 1:1 manner by a nurse using a computer-generated randomization table to the SID group or the split-dose group. Investigators and endoscopists were blinded to the allocation. Figure 1 showed patient recruitment and randomization.

The primary end point was the effectiveness of bowel cleansing according to the Boston Bowel Preparation Scale (BBPS). The secondary outcomes were polyp detection rate, compliance, tolerability, and patient satisfaction.

Bowel preparation regimen

The bowel preparation regimens were PEG4000 (Shenzhen Wanhe Pharmaceutical Co. Ltd., Shenzhen, China). All patients were instructed to adhere to a low-residue diet the day before colonoscopy. The SID group was instructed to consume one packet of PEG dissolved in 2 L of water and dimeticone 5 g on the morning of the colonoscopy (4 am–6 am). The SPD group was instructed to dissolve one packet of PEG in 2 L of water and consume one-half of

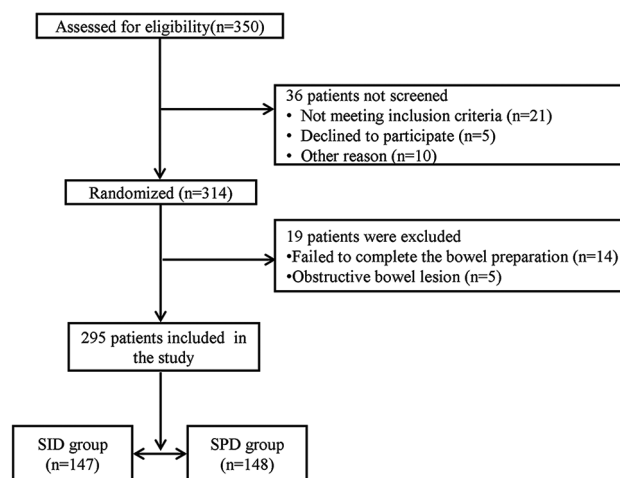


Figure 1: Flow diagram of the progress through the phases of the randomized trial (n = patients)

this the evening before the day of the colonoscopy (between 8 pm and 9 pm) and the other half plus dimeticone 5 g on the morning of the procedure (between 5 am and 6 am).

Colonoscopy

Colonoscopy was performed by experienced colonoscopists (>1000 colonoscopies/year) who were blinded to group assignment. Pentax colonoscopes EC-3890FI and EC 3870FZK, using the EPKi processor, were used to perform all procedures. All patients received anesthesia with propofol during their colonoscopy examination. Bowel cleansing quality was evaluated by the blinded colonoscopists according to the BBPS.^[17] An adequate colon preparation was defined as a BBPS score of ≥ 6 .

Assessment of compliance, tolerability, and satisfaction

All patients completed a questionnaire on compliance, tolerability, and satisfaction of the bowel preparation regimen. In relation to compliance, patients were questioned about the food they consumed the day before procedure, and if they followed the instruction for PEG intake. In terms of tolerability, patients were questioned whether the regimen interrupted sleep, and the duration of sleep. In terms of satisfaction, patients were asked about their feelings about the bowel preparation regimen, if they experienced uncomfortable symptoms during bowel cleansing, such as nausea, vomiting, bloating, abdominal discomfort, and dizziness.

Statistical analysis

On the basis of data from previous studies, a sample size of 150 patients was estimated to give an 80% power at a two-sided alpha of 0.05% to detect a 15% difference in the Boston bowel preparation quality scale.^[17] Continuous variables were expressed as the mean \pm standard deviation. Differences of continuous variables were analyzed by the independent-samples *t*-test. Categorical variables were expressed as a number (percent). These variables were analyzed using the χ^2 test and Fisher's exact test. All hypotheses were two-tailed and a *P* value < 0.05 was considered statistically significant. Statistical analyses for this study were conducted using SPSS22 (SPSS Inc., Chicago, IL, United States).

RESULTS

Patient demographics

A total of 350 patients were screened for eligibility in the study [Figure 1]. Twenty-one patients did not meet the criteria because of previous history of colon surgery ($n = 7$), severe constipation ($n = 12$), under 18 years of age ($n = 2$). Five patients declined to participate and 10 patients canceled colonoscopy before the procedure,

due to personal reasons. Of the 314 patients randomized, 19 were excluded: failure to complete bowel preparation as advised ($n = 14$; 7 in SID group and 7 in SPD group), failure to finish colonoscopy due to obstructive bowel lesions ($n = 5$; 3 in SID group and 2 in SPD group). Finally, there were 147 patients in the SID group and 148 in the SPD group.

No significant difference was observed between groups regarding age, gender, BMI, previous abdominal surgery, prior colonoscopy, smoking, alcohol consumption, medical condition, and indication for procedure [Table 1].

Comparison of quality of bowel preparation, performance of colonoscopy, and polyp detection between groups

The effectiveness of bowel cleansing between the two groups is displayed in Table 2. The SPD group showed better bowel cleansing in terms of higher adequate cleaning rate (89.9% vs. 80.3%, $P = 0.023$) and BBPS scores (7.25 ± 1.53 vs. 6.71 ± 1.65 , $P < 0.005$) compared to the SID group. The period between the last intake of assigned preparation and the colonoscopy procedure, intubation time and withdrawal times did not differ between the two groups. Polyp detection rate was similar in the two groups, although more polyps were found in the SPD group.

Comparison of the compliance, tolerability, and satisfaction of bowel preparation

Table 1: Patient characteristics

Characteristics	Single dose <i>n</i> =147	Split dose <i>n</i> =148	<i>P</i>
Age, mean (SD) (years)	48.03 \pm 12.29	46.34 \pm 11.71	0.226
Gender (<i>n</i>)			0.907
Male	68	67	
Female	79	81	0.271
BMI, mean (SD) (kg/m ²)	22.58 \pm 2.97	23.05 \pm 3.47	0.904
Previous abdominal surgery	52 (35.4%)	54 (36.5%)	1.0
Smoking ¹ (<i>n</i>)			0.862
Yes	28	28	
No	119	120	
Alcohol consumption ² (<i>n</i>)			0.384
Yes	18	20	
No	129	128	
Medical condition			0.833
Diabetes mellitus	6	4	
Hypertension	14	9	
Indication			
Screening	28	31	
Surveillance	9	10	
Abdominal discomfort	50	55	
Altered bowel habit	21	22	
Hematochezia	10	10	
Others	29	20	
Prior colonoscopy (<i>n</i>)			0.513
Yes	42	37	
No	105	111	

¹At least one cigarette/day for 1 year; ²at least 70 g/week

Table 2: Compliance, adverse event, and tolerability of bowel preparation

	Single dose n=147	Split dose n=148	P
Low-residue diet before colonoscopy, n (%)	112 (76.2%)	124 (83.8%)	0.111
Compliance with product intake, n (%)	137 (93.2%)	143 (96.6%)	0.197
Sleep disturbance, n (%)	30 (20.4%)	43 (29.1%)	0.105
Sleeping time, mean±SD (h)	3.98±1.73	4.54±1.61	0.004
Patient feeling			
Acceptable	95	113	0.03
Too much	52	35	
Adverse event			
Nausea	30	17	0.016
Vomiting	19	11	
Bloating	5	6	
Dizziness	2	3	

The data relating to compliance, tolerability, and satisfaction were collected from questionnaire surveys [Table 3]. Most patients carefully followed the instructions of product intake and adhered to a low-residue diet the day before colonoscopy, and the compliance was comparable in the SID and SPD group (93.2% vs. 96.6%, $P = 0.197$). Although sleeping time was shorter in the SPD group (4.54 ± 1.61 vs. 3.98 ± 1.73 h, $P = 0.004$), patients affected by sleep disturbance were comparable in the two groups. However, more patients felt acceptable with the bowel preparation regimen in the SPD group than the SID group (76% vs. 65%, $P = 0.03$). Adverse events were more commonly observed in the SID group, presenting as nausea and vomiting.

DISCUSSION

Traditionally, for morning colonoscopy, the entire bowel-cleansing preparation is given in the evening prior to colonoscopy. And in order to avoid sleep disturbance, it has to be given early in the evening, which results in poor bowel cleanliness reported as about 70% adequate cleaning rate,^[18] and this rate was even lower in our center at 50% as we used only low-volume 2 L PEG. The main reason for poor bowel cleanliness might be the long interval time between last preparation intake and the time of colonoscopy, which was supposed to be controlled to 4–6 h. However, for the morning colonoscopy, to satisfy the optimal interval time,

patients needed to wake up at dawn. This would lead to poor compliance and dissatisfaction. Previous studies have shown that the split preparation is better than SID preparation in terms of bowel preparation quality and patient compliance; however, whether this is still true for low-volume 2 L PEG and for morning colonoscopy is debatable, as the data are limited. As the SPD regimen can delay the intake of PEG in the early morning, we anticipated that this regimen might improve compliance and bowel cleanliness. In the present study, we compared 2 L PEG in SPD within same-morning SID preparation.

In this study, SPD regimen resulted in better bowel preparation compared to same morning SID regimen for morning colonoscopy, which was similar to the previous study.^[15] However, another study used PEG + bisacodyl which showed comparable good bowel preparation between the SPD and SID groups; we considered bisacodyl as it may assist bowel cleansing and minimize the difference.^[16] With a better bowel cleanliness, we can easily interpret the result as more polyps were found in the SPD group.

A preparation to colonoscopy (PC) interval of 4–6 h resulted in better bowel preparation compared to one greater than 6 h. A long PC interval resulted in thick secretions emptying out of the small intestine and obscuring the caecum and ascending colon at the time of colonoscopy. When we designed this study, the PC interval was taken into

Table 3: Comparison of performance of colonoscopy, quality of bowel preparation, and polyp detection between groups

	Single dose n=147	Split dose n=148	P
Interval time ¹ , mean±SD (min)	232.08±58.84	239.49±64.02	0.302
Cecal intubation time (s)	328.62±198.54	339.26±203.84	0.650
Withdrawal time (s)	421.56±138.19	409.45±128.35	0.436
Polyp detection rate	66%	60%	0.335
Number of polyps detected	125	146	0.482
Boston bowel preparation scale			
Right	2.41±0.77	2.63±0.59	0.009
Transverse	2.27±0.68	2.37±0.63	0.196
Left	2.38±0.85	2.52±0.61	0.108
Total	6.71±1.65	7.25±1.53	0.005
Adequate cleaning rate, n (%)	118 (80.3%)	133 (89.9%)	0.023

¹Period between the last intake of product and the colonoscopy procedure

consideration and the mean interval time was comparable in the two groups, at around 4 h. Thus, we got a good bowel preparation in most patients even in low-volume 2 L PEG (adequate cleaning rate >80%), which was similar to a previous study.^[17] This result further proved that 2 L PEG was suitable for Chinese people as long as the optimal interval time was promised. But it should be noticed that patients with severe constipation were excluded in this study.

More importantly, SPD regimen can be better tolerated and preferred by patients, compared to the SID regimen. Although sleep disturbance was not significantly different in the two groups, patients in the SPD group experienced less adverse gastrointestinal symptoms and found the regimen more acceptable. This was in accordance with previous studies.^[10]

There were some concerns with the PEG intake in the morning as only a 2-h interval was given between the last intake and the colonoscopy. As all colonoscopies were under anesthesia, aspiration of bowel preparation solution from the stomach into the lung was of concern. However, a randomized study found no difference in residual gastric volume between patients who fasted for 2 h and patients who fasted for 6–23 h.^[19]

In conclusion, split dose of 2 L PEG is superior to single dose for colon cleansing if the procedure is slated in the morning. Patients in SPD group experienced less nausea and vomiting and were more accepting of the regimen.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Sung JJ, Lau JY, Young GP, Sano Y, Chiu HM, Byeon JS, *et al.* Asia

2. Pacific consensus recommendations for colorectal cancer screening. *Gut* 2008;57:1166-76.
3. Leaper M, Johnston MJ, Barclay M, Dobbs BR, Frizelle FA. Reasons for failure to diagnose colorectal carcinoma at colonoscopy. *Endoscopy* 2004;36:499-503.
4. Froehlich F, Wietlisbach V, Gonvers JJ, Burnand B, Vader JP. Impact of colonic cleansing on quality and diagnostic yield of colonoscopy: The European Panel of Appropriateness of Gastrointestinal Endoscopy European multicenter study. *Gastrointest Endosc* 2005;61:378-84.
5. Burke CA, Church JM. Enhancing the quality of colonoscopy: The importance of bowel purgatives. *Gastrointest Endosc* 2007;66:565-73.
6. Johnson DA, Barkun AN, Cohen LB, Dominitz JA, Kaltenbach T, Martel M, *et al.* Optimizing adequacy of bowel cleansing for colonoscopy: Recommendations from the US multi-society task force on colorectal cancer. *Gastroenterology* 2014;147:903-24.
7. Hassan C, East J, Radaelli F, Spada C, Benamouzig R, Bisschops R, *et al.* Bowel preparation for colonoscopy: European Society of Gastrointestinal Endoscopy (ESGE) guideline-Update 2019. *Endoscopy* 2019;51:775-94.
8. Spadaccini M, Frazzoni L, Vanella G, East J, Radaelli F, Spada C, *et al.* Efficacy and tolerability of high- vs low-volume split-dose bowel cleansing regimens for colonoscopy: A systematic review and meta-analysis. *Clin Gastroenterol Hepatol* 2020;18:1454-1465.e14.
9. Endoscopy CSfG. Chinese consensus on bowel preparation before endoscopy. *Chin J Pract Int Med* 2013;33:705-7.
10. Ell C, Fischbach W, Bronisch HJ, Dertinger S, Layer P, Runzi M, *et al.* Randomized trial of low-volume PEG solution versus standard PEG + electrolytes for bowel cleansing before colonoscopy. *Am J Gastroenterol* 2008;103:883-93.
11. Avalos DJ, Castro FJ, Zuckerman MJ, Keihanian T, Berry AC, Nutter B, *et al.* Bowel preparations administered the morning of colonoscopy provide similar efficacy to a split dose regimen: A meta analysis. *J Clin Gastroenterol* 2018;52:859-68.
12. Tan JJ, Tjandra JJ. Which is the optimal bowel preparation for colonoscopy-A meta-analysis. *Colorectal Dis* 2006;8:247-58.
13. Parra-Blanco A, Nicolas-Perez D, Gimeno-Garcia A, Grosso B, Jimenez A, Ortega J, *et al.* The timing of bowel preparation before colonoscopy determines the quality of cleansing, and is a significant factor contributing to the detection of flat lesions: A randomized study. *World J Gastroenterol* 2006;12:6161-6.
14. El Sayed AM, Kanafani ZA, Mourad FH, Soweid AM, Barada KA, Adorian CS, *et al.* A randomized single-blind trial of whole versus split-dose polyethylene glycol-electrolyte solution for colonoscopy preparation. *Gastrointest Endosc* 2003;58:36-40.
15. Park JS, Sohn CI, Hwang SJ, Choi HS, Park JH, Kim HJ, *et al.* Quality and effect of single dose versus split dose of polyethylene glycol bowel preparation for early-morning colonoscopy. *Endoscopy* 2007;39:616-9.
16. Shah H, Desai D, Samant H, Davavala S, Joshi A, Gupta T, *et al.* Comparison of split-dosing vs non-split (morning) dosing regimen for assessment of quality of bowel preparation for colonoscopy. *World J Gastrointest Endosc* 2014;6:606-11.
17. Chan WK, Azmi N, Mahadeva S, Goh KL. Split-dose vs same-day reduced-volume polyethylene glycol electrolyte lavage solution for morning colonoscopy. *World J Gastroenterol* 2014;20:14488-94.
18. Zhang S, Li M, Zhao Y, Lv T, Shu Q, Zhi F, *et al.* 3-L split-dose is superior to 2-L polyethylene glycol in bowel cleansing in Chinese population: A multicenter randomized, controlled trial. *Medicine* 2015;94:e472.
19. Jung YS, Lee CK, Eun CS, Park DI, Han DS, Kim HJ. Low-volume polyethylene glycol with ascorbic acid for colonoscopy preparation in elderly patients: A randomized multicenter study. *Digestion* 2016;94:82-91.
20. Phillips S, Hutchinson S, Davidson T. Preoperative drinking does not affect gastric contents. *Br J Anaesth* 1993;70:6-9.