Original Article

A Randomized Study Comparison between Split Dosage and Non-Split Dosage PEG-Electrolyte Solution Preparation Methods for Elective Colonoscopy

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Background: A two liters low volume polyethylene glycol (PEG) electrolyte solution preparation was proposed for improving patients' tolerability with either split or non-split dosage cleansing method. Patient compliance, adverse experiences, and cleansing efficacy of each anatomical segment of the colon using both methods should be determined.

Objective: To assess the cleansing efficacy of split dosage versus non-split dosage PEG-electrolyte solution for each anatomical segment of the colon according to the inverted Ottawa bowel preparation scale.

Materials and Methods: The present study was a prospective, randomized, endoscopist-blinded study. Volunteers that underwent elective screening colonoscopy were eligible for recruitment into the present study. Patients having any contraindication for colonoscopy, or the use of PEG-electrolyte solution such as bowel obstruction, intestinal perforation, or toxic megacolon were excluded. Cleansing efficacy was evaluated by the inverted Ottawa bowel preparation scale for each anatomical segment of the colon. Medical adherence and compliance were evaluated. Participants were asked to rate their satisfaction and inform the presence of any adverse experiences related to the bowel preparation method.

Results: Ninety-four volunteers were randomly assigned to two groups. Of these, 46 received the split dosage cleansing method and 48 received the non-split dosages cleansing method. Overall compliance was approximately 94%, comparable for both preparation methods. Average age was 61.5 years for non-split dosage and 60.4 for split dosage group. Satisfaction score in the non-split dosage group was 8.46, which was not significantly different from 8.56 of the split dosage group (p=0.934). Split dosage PEG-electrolyte solution provided comparable degree of cleansing as standard non-split dosages preparation for transverse, descending, sigmoid, and rectum. However, split dosage provided significantly superior cleansing results over the non-split dosages method for ascending colon at good or excellent with 84.7% versus 47.9% (p<0.01), and caecum at good or excellent for 76.1% versus 41.7% (p<0.01) based on the inverted Ottawa bowel preparation scale.

Conclusion: Split dosage PEG-electrolyte solution method provided significantly superior cleansing results over the non-split dosages method for right-side colon with comparable satisfaction score and rate of adverse events.

Keywords: Bowel preparation; Split dosage cleansing; Quality of bowel preparation

Received 30 October 2018 | Revised 24 November 2021 | Accepted 26 November 2021

J Med Assoc Thai 2022;105(1):1-5

Website: http://www.jmatonline.com

Routine screening for colorectal cancer is recommended to start at age 50 years for general population at average risk with reference to the American College of Gastroenterology Guidelines for Colorectal Cancer Screening[1]. Adequate bowel preparation is important in assuring completion of visualization and accuracy of the colonoscopy. Mechanical bowel cleansing is an essential step of preparation for elective colonoscopy and colorectal surgery. Poor visualized mucosa from inadequate bowel preparation may lead to a higher chance of complication and missing small mucosal lesions. Inadequate bowel preparation also results in wasting time and resources due to the need to reschedule the procedure. The conventional polyethylene glycol (PEG) regimen has demonstrated a good cleansing efficacy however, patients have poor compliance due to the large volume consumption and the unpleasant taste of this solution. PEG is an osmotic balance solution that has been used worldwide. A large volume of four liters of PEG solution has

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How to cite this article:

Anannamcharoen S, Muchchimdamrong K. A Randomized Study Comparison between Split Dosage and Non-Split Dosage PEG-Electrolyte Solution Preparation Methods for Elective Colonoscopy. J Med Assoc Thai 202;105:1-5.

DOI: 10.35755/jmedassocthai.2022.01.9436

been recommended for achieving an adequate colon cleansing. However, elderly patients may have poor tolerance and may be unable to complete this entire large volume consumption due to the unpleasant taste and the related gastrointestinal symptoms. For this reason, low-volume consumption with a better tolerability colon cleansing regimen were required. Recently, an alternative low-volume PEG preparation of two liters was proposed to improve patients' tolerability with either a split or non-split dosage cleansing method. The split dosage cleansing method is recommended to improve patient compliance[2]. In the present study, authors aimed to compare cleaning efficacy, tolerability, unintended medical event, and compliance between these two cleansing methods, split dosage and non-split dosage.

Materials and Methods

Study design and randomization

The present study was conducted as a prospective randomized parallel group study with blind assessor design. Patients were allocated to the two groups by block of four randomization, in a ratio of 1:1. Computer generated random number was used to generate the random allocation sequence. One research assistant was responsible for providing the solution and explanation of the bowel preparation method to participants according to the allocation sequence.

Patients

Average-risk patients who were scheduled for screening colonoscopy in the Division of Coloproctology, Department of Surgery, Phramongkutklao Hospital between May 2013 and November 2014 were included in this study. Patients must be 18 years of age or older without signs and symptoms that indicated colorectal cancer. Patients volunteered to participate in the present study with signed informed consent. Patients with bowel habit changed, severe comorbidities, massive or ongoing lower gastrointestinal bleeding, prior abdominal surgery, presenting with signs and symptoms of mechanical bowel obstruction or intra-abdominal inflammation were excluded.

Methods

The Institutional Review Board of the Royal Thai Army, Medical Department approved the present study before the start of the investigation (R110h/55). All eligible patients were allocated to either the non-split dosage group or the split dosage group by block randomization by block of 4. PEG-electrolyte solution (Niflec®; Ajinomoto Pharmaceuticals Co., Ltd., Tokyo, Japan) was selected to be the bowel preparation solution in the present study. One sachet of Niflec® was diluted into two liters water to make the cleansing solution. The patients were instructed to drink the solution one glass or 250 mL, every 15 minutes starting at 6.00 p.m. the day before the procedure. For the non-split dosage group, the patients drank the two liters during the evening. For the split dosage group, the patients drank half of the solution, or one liter during the evening. Then, the patients were instructed to drink the other half, or 1 liter starting at 5:00 AM on the examination day and complete drinking the solution at least four hours before the procedure. Example images of colon segments with various degree of bowel preparation qualities were used for four endoscopists to practice before actual assessment until they were capable to assess the quality of bowel preparation according to the inverted Ottawa bowel preparation scale. Prior to starting colonoscopy, patients were asked to rate their satisfaction with the allocated preparation method by using visual analogue scale. Compliance of individual patient was also assessed. All unintended medical occurrences related to the preparation regimens were recorded. During colonoscopy, endoscopists, not knowing to which group subjects were allocated, evaluated the quality of bowel preparation for each anatomical segment of colon according to the inverted Ottawa bowel preparation scale with 4 as excellent or colon empty and clean, 3 as good or presence of clear liquid in the colon easy to aspirate, 2 as fair or presence of brown liquid or small amounts of semisolid residual stool that partially removable by suction to adequately visualize the underlying colonic mucosa, and 1 as poor or large amounts of fecal residue, removable, with hampered visualization of the underlying mucosa.

Statistical analysis

Statistical analysis was performed with IBM SPSS Statistics, version 19.0 (IBM Corp., Armonk, NY, USA). All outcomes were analyzed based on intention to treat principles. Patients' demographics data, compliance, and satisfaction rating were tested for normality with Kolmogorov-Smirnov (KS) test. Statistical analysis was performed for comparison between groups with independent t-test for normally distributed variables or Mann-Whitney U test for non-normally distributed variables. Chi-square test was used for categorical data. Comparison number

of patients who were experienced adverse events of both groups by using logistic regression analysis. Cleansing efficacies were evaluated according to inverted Ottawa scale of both groups for each anatomical segments by using chi-square test. A p-value of less than 0.05 was considered statistically significant.

Results

Ninety-four subjects volunteered to participate in the present study randomly divided with 48 in the non-split dosage group and 46 in the split dosage group. The average age was 61.5 years for non-split dosage and 60.4 for split dosage group. There were 22 males (45.8%) and 26 females (54.2%) in non-split dosage groups, meanwhile 24 males (52.2%) and 22 females (47.8%) were in split dosage group. Satisfaction score in non-split dosage group was 8.46, which did not significantly differ from 8.56 of split dosage group (p=0.934). Overall compliance was comparable as shown in Table 1.

Abdominal bloating, nausea, vomiting, and sleep disturbance were the common adverse experiences, which tended to be higher in the non-split dosage group, but did not reach statistical significance. Six subjects (12.2%) experienced headaches, which was found only in the non-split dosage group, as shown in Table 2.

In term of quality of bowel cleansing, cleansing efficacies were evaluated according to the inverted Ottawa scale of both groups for each anatomical segments of colon. The two dosage preparation methods provided a comparable degree of cleansing quality for transverse, descending, sigmoid, and rectum. The present study revealed that the split dosage group had a better cleansing result for ascending colon at good or excellent with 84.7% versus 47.9% (p<0.01) and caecum at good or excellent with 76.1% versus 41.7% (p<0.01) as shown in Figure 1 and 2, and Table 3.

Table 1. Patients' demographic data, satisfaction score for preparation methods and compliance

	Preparation methods		p-value
	Non-split dosage (n=48)	Spilt dosage (n=46)	
Sex; n (%)			0.784
Male	22 (45.8)	24 (52.2)	
Female	26 (54.2)	22 (47.8)	
Age; mean±SD	61.5±12.0	60.4±12.3	0.586
Rating of satisfaction; mean±SD	8.46±1.41	8.56±1.22	0.934
Overall compliance; n (%)	45 (93.8)	43 (93.5)	0.641

SD=standard deviation

Discussion

A large volume consumption to complete the entire solution of conventional PEG regimen often leads to a poor compliance in many patients. For this reason, low-volume bowel preparation regimens are required. The aqueous sodium phosphate is an alternative low-volume hyperosmotic solution available worldwide. However, the risk of phosphate nephropathy after using this solution had been reported in patients with compromised renal function, and in patients who were treated with angiotensin-converting enzyme inhibitors or angiotensin receptor blockers[3]. Studies revealed that approximately 40 percent of healthy patients experience hyperphosphatemia after completing this preparation. Even though they are usually asymptomatic, this may have a significant impact in patients with renal failure[4,5]. Sodium phosphate can also cause a significant fluid and electrolyte shift and the propensity for salt and water retention that is contraindicated in patients with cirrhosis, renal impairment, or heart failure[6].

Studies have revealed that split dose regimens provided a better tolerability and compliance than the

Table 2. Adverse effects

Types of complication	Non-split dosage (n=48); n (%)	Spilt dosage (n=46); n (%)	Odd ratio (95% CI)	p-value
Bloating	12 (25.0)	8 (17.4)	1.583 (0.580 to 4.321)	0.259
Nausea	10 (20.8)	6 (13.0)	1.754 (0.581 to 5.298)	0.233
Vomiting	3 (6.3)	1 (2.2)	3.000 (0.301 to 29.940)	0.325
Cramp/pain	3 (6.3)	4 (8.7)	0.700 (0.148 to 3.314)	0.476
Headache	6 (12.5)	0 (0.0)	0.875 (0.786 to 0.974)	0.015*
Faecal incontinent	8 (16.7)	4 (8.7)	2.100 (0.586 to 7.522)	0.199
Sleep discomfort	14 (29.2)	9 (19.6)	1.693 (0.649 to 4.413)	0.200

CI=confidence interval

* Statistically significant

Table 3. Quality of bowel cleansing

Segment of bowel	Quality	Non-split dosage (n=48); n (%)	Spilt dosage (n=46); n (%)	p-value
Rectum	Poor	1 (2.1)	1 (2.2)	0.416
	Fair	5 (10.4)	1 (2.2)	
	Good	8 (16.7)	10 (21.7)	
	Excellent	34 (70.8)	34 (73.9)	
Sigmoid colon	Poor	1 (2.1)	2 (4.3)	0.724
	Fair	7 (14.6)	4 (8.7)	
	Good	14 (29.2)	16 (34.8)	
	Excellent	26 (54.2)	24 (52.2)	
Descending colon	Poor	1 (2.1)	1 (2.2)	0.752
	Fair	10 (20.8)	6 (13.0)	
	Good	19 (39.6)	22 (47.8)	
	Excellent	18 (37.5)	17 (37.0)	
Transverse colon	Poor	2 (4.2)	0 (0.0)	0.135
	Fair	16 (33.3)	8 (17.4)	
	Good	18 (37.5)	23 (50.0)	
	Excellent	12 (25.0)	15 (32.6)	
Ascending colon	Poor	7 (14.6)	0 (0.0)	0.001*
	Fair	18 (37.5)	7 (15.2)	
	Good	17 (35.4)	29 (63.0)	
	Excellent	6 (12.5)	10 (21.7)	
Cecum	Poor	9 (18.8)	0 (0.0)	0.001*
	Fair	19 (39.6)	11 (23.9)	
	Good	17 (35.4)	27 (58.7)	
	Excellent	3 (6.3)	8 (17.4)	

* Pearson chi-square

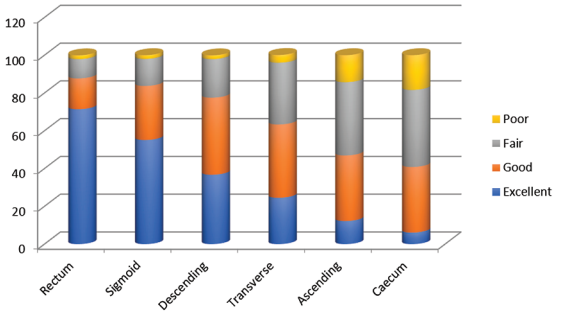

Figure 1. The quality of bowel preparation in non-split dosage group evaluated by inverted Ottawa bowel preparation scale for each anatomical segment of colon.

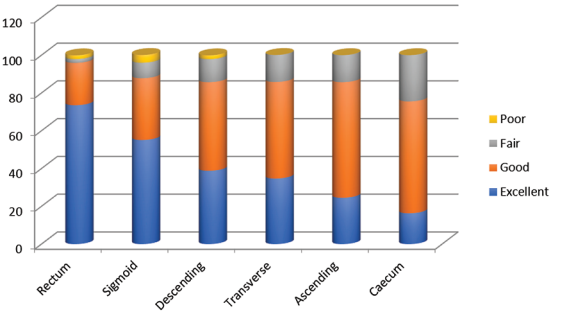

Figure 2. The quality of bowel preparation in split dosage group evaluated by inverted Ottawa bowel preparation scale for each anatomical segment of colon.

conventional total volume preparation regimen the day before the procedure[2,7-9]. However, sleep disturbance and urge to go to toilet during transportation are two main unintended problems for practical application of the split dosage method. El Sayed AM, et al[10] conducted a study to compare patients' compliance and cleansing efficacy between a 3-liters non-split dose and split dose polyethylene glycol electrolyte solution plus one Bisacodyl tablet. The study found that participants in the split dose plus one Bisacodyl tablet group had better compliance and quality of bowel cleansing with less dietary restriction.

Data gathering from the present study revealed that split dosage low volume PEG solutions was an effective and well-tolerated preparation method. Sleep disturbance and urge to go to toilet during transportation was still found in a high proportion in the present study. For a better outcome, arrangement

for more flexible schedule may be beneficial to optimize the split dosage preparation method such as the procedure should not be started until at least six hours after completing the remaining one-liter solution on the examination date. The present study also found that the split dosage method significantly provided superior cleansing results over the non-split dosage method for the right-side of the colon, while comparable cleansing quality for other parts of the colon. Under certain circumstances, split dosage method may be useful, such as when preoperative imaging suggests suspicious lesions located in the right side of the colon. Split dosage preparation may be a favorable choice over same day non-split dosage method.

Conclusion

Split dosage PEG-electrolyte solution method provided a comparable overall compliance with non-split dosage method but superior cleansing efficacy for the right-side of the colon.

What is already known on this topic?

Split dosage low volume PEG solutions is an effective and well-tolerated preparation method. Split dose regimens provided a better tolerability and compliance than the conventional total volume preparation regimen on the day before procedure.

What this study adds?

Split dosage method provided a significant superior cleansing result over the non-split dosage method for right side colon. For patients with suspected lower chance of missing small mucosal lesions.

Conflicts of interest

The authors declare no conflict of interest.

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