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Efficacy of morning-only dose compared with split-dose polyethylene glycol electrolyte solution in bowel cleansing for afternoon colonoscopy

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Abstract

Introduction: The efficacy of colonoscopy in detecting abnormalities within the colon is highly dependent on the adequacy of the bowel preparation. The objective of this study was to compare the efficacy and tolerability of morning-only dose vs split-dose administration of polyethylene glycol (PEG) solution for colon cleansing in patients undergoing afternoon colonoscopy.

Method: This was a comparative study conducted in Department of Medicine, Patan Academy of Health Sciences (PAHS), Patan Hospital, Nepal from November 2021 to June 2022. The ethical clearance was obtained from the Institutional Review Committee. Informed consent was taken from the patients. Patients aged >18 y undergoing elective colonoscopy were randomly assigned to one of the two bowel preparation regimens- morning-only or split-dose of PEG. The adequacy of bowel preparation was assessed by the endoscopist using Boston Bowel Preparation scale. Preparation to colonoscopy (PC) interval, adverse events and risk factors for poor bowel preparations were noted.

Result: In this study, 110 patients were included in the final analysis-55 received morning only regimen and 55 received split-dose. Mean Boston bowel preparation scales of Morning-only and Split-dose regimen were 7.60 and 7.09 respectively ($p=0.019$). Split-dose group had significant sleep disturbances compared to Morning only regimen ($p<0.001$), whereas nausea occurred significantly more often in Morning only regimen ($p=0.012$). Preparation to colonoscopy interval between 4-6 hours resulted in better bowel cleansing compared to PC interval of greater than 6 hours.

Conclusion: Morning-only bowel preparation is more effective than Split-dose for achieving adequate colon cleansing for afternoon colonoscopy.

Keywords: bowel preparation, colonoscopy, efficacy, morning, split dose

Introduction

A successful colonoscopy requires an adequate preparation of the large bowel that facilitates clear visualization of the mucosal surface¹. The effectiveness of the bowel preparation is a critical factor related to the safety, diagnostic accuracy, quality, difficulty, and speed of the examination².

Bowel preparation has evolved from previous evening regimen to split dose regimen. Majority of the studies³⁻⁵ done previously showed superior cleansing when whole or part of the bowel preparation was given in the morning of the scheduled colonoscopy.

However, colonoscopies are often scheduled in the afternoon, and split dosing may not leave a clean colon by afternoon. A study by Matro et al⁶ showed equal cleansing efficacy and tolerability of a morning dosing and split preparation when procedures are slated for the afternoon.

Recent guidelines^{2,7} suggest using the split preparation for colonoscopy for its higher cleaning rate; however, concerns on tolerability, sleep disturbance and the optimal bowel preparation still remain as some patients have an inadequate bowel cleansing after this type of preparation.

The primary aim of this study was to evaluate the efficacy of colon cleansing in patients undergoing colonoscopy, comparing morning-only dose vs split-dose, using the Boston Bowel Preparation Scale

Method

This was a comparative study conducted in Department of Medicine, Patan Academy of Health Sciences (PAHS), Patan Hospital, Nepal from November 2021 to June 2022. The ethical clearance was obtained from the Institutional Review Committee - PAHS (Reference No. drs2111021577). Informed consent was taken from the patients.

Patients seen in the outpatient clinic as well as in-patients undergoing colonoscopy were screened for enrolment in the study. Inclusion Criteria were patients age >18 y and patients undergoing elective colonoscopy. Exclusion Criteria were suspected or established Severe congestive heart failure (NYHA III or IV), suspected or established mechanical bowel obstruction, history of large bowel resection, severe renal impairment (creatinine clearance < 30ml/min) or on hemodialysis, suspected or established severe inflammatory or infectious colitis, known allergies to polyethylene glycol (PEG), refusal of consent for the study and patients who are inconvenienced by the timing of bowel preparation.

The analysis of the end points of bowel preparation quality and findings were evaluated by non-inferiority of the morning-only regimen compared with the split-dose regimen, with pre-specified margins.

According to a study by Matro, et al.⁶ 90% of the cases in the split-dose regimen will be adequate, and the non-inferiority margin will be set at – 15% (that is, the adequacy rate of the morning dose-only preparation should not be lower than that of the split-dose regimen by more than 15%).

The study was designed to have 80% power to establish non-inferiority (using a one-sided test with $\alpha=0.05$ and $\beta=0.2$).

The following formula was used to calculate sample size:

$$N=2 \times \left(\frac{z_{1-\alpha} + z_{1-\beta} \times p \times (1-p)}{\delta_0} \right)^2$$

where,

N=size per group

$z_{1-\alpha}=1.645$ $z_{1-\beta}=0.845$

δ_0 (clinically acceptable margin) = 0.15

p (adequacy rate of split-dose) = 0.9.

Thus, the minimum sample size for each group would be 50. The calculated sample size was increased to 10 percent to mitigate the risk of drop out. The final sample size was 110 (55 for each group).

Preparation to colonoscopy interval

It was defined as the time interval between the last dose of bowel preparation and the start of colonoscopy. Preparation to colonoscopy interval affects the quality of bowel preparation. A long interval results in thick secretions emptying out of the small intestine and obscuring the caecum and ascending colon at the time of colonoscopy.

Adverse events of bowel preparation

The adverse events of the bowel preparation were defined as occurrence of nausea, vomiting, bloating, abdominal pain, light headedness or sleep disturbance.

Risk factors for poor bowel preparation

The risk factors for poor bowel preparation were defined as history of constipation, use of medications associated with constipation eg, tricyclic antidepressants (amitriptyline or imipramine), opioids (codeine, tramadol, morphine or pethidine), dementia or Parkinson's disease, male sex, obesity(BMI>25), Diabetes Mellitus or Liver Cirrhosis.

Efficacy

Efficacy of the bowel preparation was defined as adequacy of bowel preparation as assessed by Boston Bowel Preparation scale (higher the score higher is the efficacy).

Procedure Details

Bowel Preparation

During the appointment for the procedure all patients were instructed to adhere to a low residue diet (avoid foods that are high in fiber such as fruits, vegetables, and whole grains) at least 2 d before the procedure and liquid diet a day before their colonoscopy, and only clear liquids orally after midnight until the procedure time.

The morning preparation group were instructed to consume one packet of PEG (Polyethylene Glycol) dissolved in 2 L of water on the morning of the colonoscopy (between 6 am and 8 am).

The split-dose group were instructed to dissolve one packet of PEG in 2 L of water and consume one-half of this in the evening before the day of the colonoscopy (between 8 pm and 9 pm) and the other half on the morning of the procedure (between 7 am and 8 am).

Drinking at least 75% of the preparation volume was regarded as proper amount of PEG taken for bowel preparation, which was ensured by asking patient how much PEG (dissolved in 2 L) was left. And patients who did not finish 2 L of peglec were asked to bring the remaining peglec during the procedure to confirm how much peglec they consumed.

All patients were advised to take 2 L of Oral Rehydration Solution (if no contraindication) after finishing the bowel cleansing regimen. Patients were instructed to report to the endoscopy unit at 10 AM on the day of the procedure. Patients also were provided written instruction that was simple, easy to follow, and in Nepali language that the patient understood.

Colonoscopy

Colonoscopies were performed by experienced endoscopists (gastroenterologists and surgeons) with at least 5 y of experience in the field of diagnostic endoscopy with 1000 minimum number of colonoscopies performed. All colonoscopies were done in the afternoon after 12 PM. Only patients who had a complete colon examination from anal verge up to the cecum were included in the analysis. In uncooperative patients, colonoscopies were performed under conscious sedation (combination of intravenous fentanyl 50 mcg and midazolam 2 mg) with close hemodynamic during and after the procedure.

Efficacy of Bowel cleansing was evaluated by using Boston bowel preparation scale⁸. The score ranges from 0 to 3 for individual colonic segments: the right side of the colon (including the cecum and ascending colon), the transverse section of the colon (including the hepatic and splenic flexures), and the left side of the colon (including the descending colon, sigmoid colon, and rectum).

- **Score 0:** Unprepared colon with mucosa not seen because of solid stool that cannot be cleared.
- **Score 1:** Portion of the mucosa of the colon segment seen, but other areas of the colon segment not seen well because of staining, residual stool, and/or opaque liquid.
- **Score 2:** Minor amount of residual staining, small fragments of stool and/or opaque liquid, but most mucosa of the colon segment seen well.
- **Score 3:** Entire mucosa of colon segment seen well with no residual staining, small fragments of stool, and/or opaque liquid.

BBPS		3	2	1	0
3=Excellent					
	2=Good				
1=Poor					
0=Inadequate					
LC	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
TC	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
RC	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
BBPS= <input type="checkbox"/>					

Note: LC- Left Colon, TC- Transverse Colon, RC- Right Colon; Source: Lorenzo-Zúñiga V, Moreno-de-Vega V, Boix J. Preparation for colonoscopy: types of scales and cleaning products. Rev Esp Enferm Dig. 2012;104(8):426-31.

Figure 1. Boston Bowel Preparation Scale (BBPS)⁹

The scores of each of the 3 segments were added to obtain the total Boston bowel preparation scale score, which ranges from 0 (poor) to 9 (excellent). The sum total of the three segments represents the degree of soiling, so that a total ≤ 5 points indicates poor bowel preparation, while 6–7 indicates good bowel preparation, and ≥ 8 very good bowel preparation.

The quality of preparation was assessed at the time of insertion of the colonoscope before any cleansing maneuvers. Each patient’s bowel-preparation quality was rated by the endoscopist by the Boston Bowel Preparation Scale, and the results were recorded on a standardized form.

Statistical analysis

All data were filled into a predesigned proforma and compiled and entered into Microsoft Excel. The data was uploaded and analyzed using Statistical Package for the Sciences version 16.0. Continuous variables

like Boston Bowel preparation scale score, time interval between the last dose of bowel preparation and the start of colonoscopy etc. were expressed as mean, and categorical variables such as sex, age group, and history of constipation, use of medications associated with constipation (i.e., tricyclic antidepressants and opioids), dementia or Parkinson’s disease, obesity, diabetes mellitus, cirrhosis were expressed as count with percentage. Comparison of efficacy of Morning-only dosing and Split-dosing regimen assessed by Boston Bowel Preparation Scale scores was done by chi squared test and comparison of adverse events in Morning-only dosing and Split-dosing groups was done by odd’s ratio. A value of $p \leq 0.05$ was considered statistically significant.

Result

In this study, a total of 120 patients were screened for the inclusion in the study, out of

which 10(8.33%) were excluded as they did not meet the inclusion criteria: 5 patients had suspected bowel obstruction 3 had history of large bowel resection and 2 declined to participate (Figure 2). Fifty-five patients received morning-only regimen of bowel preparation and 55 patients received split-dose. There were 32(58.2%) females in morning only regimen and 29(52.7%) females in split-dose, and mean age was 45.02±16.63 y and 53.35±18.74 y in morning only and split-dose group respectively. Mean preparation to colonoscopy interval was 6.29±1.5 h in morning only group and 6.82±1.72 h in split-dose group (Table 1). The caecal intubation rate was 100% in both groups. Only patients who had a complete colon examination from anal verge up to the cecum were included in the analysis.

Quality of bowel preparation

The morning only regimen had better bowel efficacy compared to the split-dose with the statistical significance ($p=0.019$). The mean BBPS was 7.60 with the morning only regimen and 7.09 with split preparation (Figure 2). Overall, 13(11.8%) patients had BBPS 5 or less indicating poor bowel preparation, 40(36.3%) had good bowel preparation with score 6 and 7, and 57(51.8%) patients had very good bowel preparation with score 8 and 9 (Table 2).

PC Interval

A gap of at least 4 h was kept for every patient between the last preparation intake and the time of colonoscopy. Forty-three colonoscopies were performed within 4-6 h of interval, 48 were performed between 6 to 8 h interval and rest 19 were performed after 8 h interval. Bowel preparation was adequate (good or very good) in 42(97.6%) when colonoscopies were performed within 4-6 hours interval, 40(89.5%) had adequate preparation when performed between 6-8 hours and 15(78.9%) when performed after more than 8 hours of interval. However, there was no statistical significance in efficacy of bowel preparation with PC interval (Table 3).

Tolerability of the preparation and sleep disturbance

Nausea was complained of by 21.8% of patients with the morning only regimen and 5.45% with split-dose ($p=0.012$), abdominal discomfort by 9.09% and 1.81%, ($p=0.093$), vomiting by 9.09% and 7.27% ($p=0.728$), bloating by 10.90% and 10.90% ($p=1$), and light headedness by 5.45% and 7.27% ($p=0.696$). Sleep was disturbed in 1(1.81%) patients receiving the morning only regimen and in 25(45.45%) patients receiving the split-dose ($p<0.001$) (Table 4).

Table 1. Baseline characteristics of patients undergoing colonoscopy in two study groups.

	Morning only regimen(N=55)	Split-dose regimen(N=55)
Age, mean(y)±SD	45.02±16.63	53.35±18.74
Sex, N(%)		
Male	23(41.82%)	26(47.27%)
Female	32(58.18%)	29(52.73%)
PC Interval time (hours±SD)	6.29±1.5	6.82±1.72
Risk Factors, N(%)		
History of constipation	24(43.63%)	16(29.09%)
Use of medications	0	2(3.63%)
Dementia or Parkinson`s disease	1(1.81%)	0
Male sex	23(76.03%)	26(47.27%)
Diabetes Mellitus	0	2
Cirrhosis	0	0
Obesity	22(40%)	22(40%)

Note- PC: Preparation to Colonoscopy

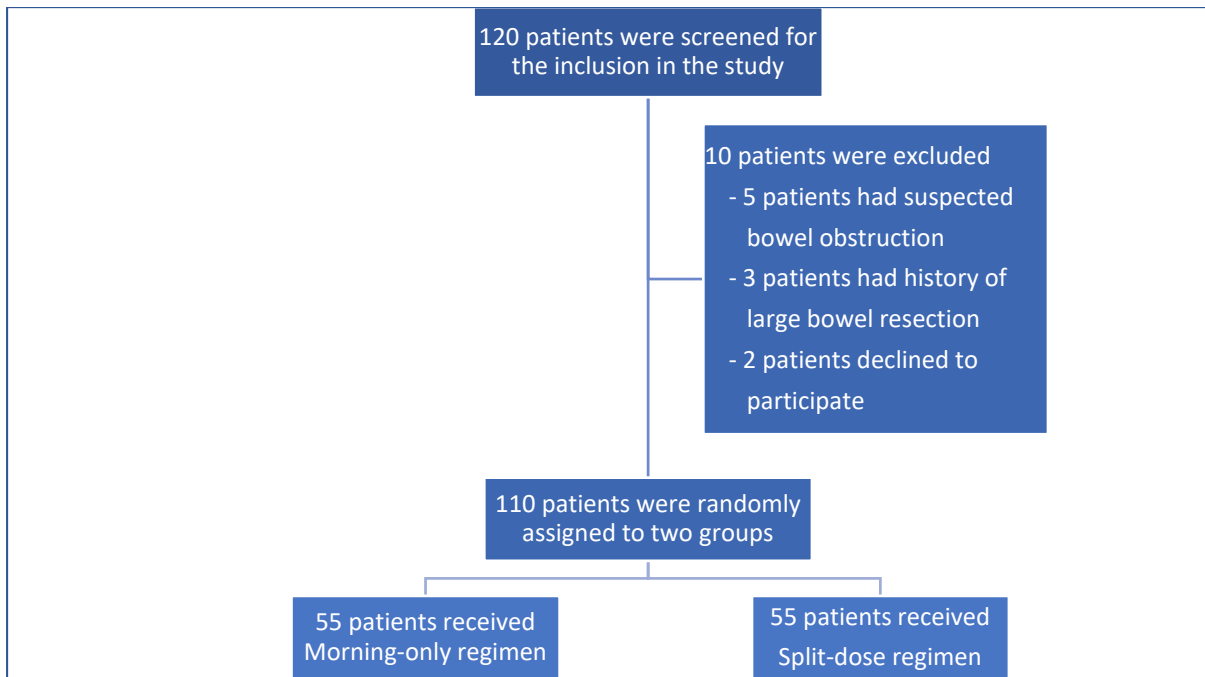


Figure 2. Patient assignment and disposition flow diagram

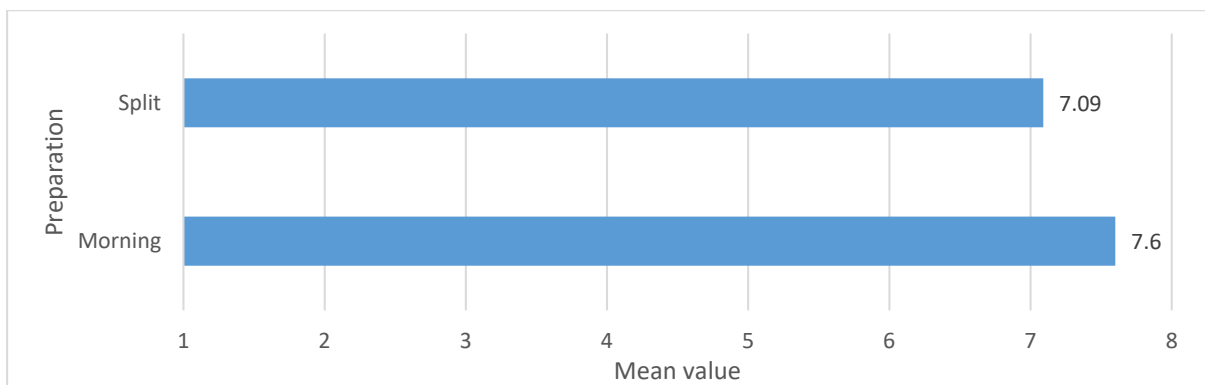


Figure 3. Comparison of Morning-only and Split-dose using Boston Bowel Preparation scale

Table 2. Measures of bowel preparation quality in study patients

BBPS	Morning only regimen(N=55)	Split-dose regimen(N=55)
Poor (≤ 5)	7(12.72%)	6(10.9%)
Good (6-7)	13(23.64%)	17(30.9%)
Very Good (8-9)	35(63.64%)	32(58.2%)

Table 3. Relationship between PC Interval and bowel preparation quality in two groups.

PC Interval	Bowel Preparation Quality			Total	p-value
	Poor	Good	Very good		
4-6 hours	1(2.33%)	20(46.51%)	22(51.16%)	43	0.103
6-8 hours	8(16.66%)	15(31.25%)	25(52.08%)	48	
More than 8 hours	4(21.05%)	5(26.32%)	10(52.63)	19	
Total(N)	13	40	57	110	

Table 4. Adverse events of bowel preparation in study groups

	Morning-only regimen(N=55)	Split-dose regimen(N=55)	p-value
Nausea	12(21.8%)	3(5.45%)	0.012
Vomiting	5(9.09%)	4(7.27%)	0.728
Abdominal Pain	5(9.09%)	1(1.81%)	0.093
Bloating	6(10.90%)	6(10.90%)	1
Light Headedness	3(5.45%)	4(7.27%)	0.696
Sleep Disturbances	1(1.81%)	25(45.45%)	0.000

Discussion

In our study patients who received the morning-only preparation had better overall bowel cleansing compared with those who received split-dosing, and the difference in bowel cleansing between the two groups was statistically significant ($p=0.019$). In the morning only preparation group, bowel cleansing was graded as very good, good, or poor in 35(63.6%), 13(23.6%), and 7(12.7%) of patients, respectively, and the rates were 22(40%), 27(49%), and 6(10.9%), respectively in split-dose group. Similarly, in a study by Longcroft-Wheaton G, et al.¹⁰ morning only preparation resulted in better bowel cleansing compared to split-dose regimen. In their study bowel cleansing was graded as excellent, average, or poor in 47%, 52%, and 1.5%, respectively in morning-only preparation, and the rates were 50%, 40%, and 11%, respectively in split-dose group. On the other hand, a study by Matro, et al.⁶ who compared the efficacy and tolerability of morning-only PEG to split dose PEG for afternoon colonoscopy found both regimen equivalent with respect to cleaning efficacy and polyp detection. Similarly, a study by Shah H et al¹¹ also reported that split dosing and morning only regimen of bowel preparation are equally effective for afternoon procedures, and morning preparation may be more convenient to the patients.

This discrepancy in results may be because the patients in morning only group in our study were relatively young with mean age of 45.02 y, whereas in a study by Matro, et al.⁶ morning only group had mean age of 53 y. Many studies^{12,13} have also confirmed that old age is an important predictor of inadequate bowel

preparation. This may be due to the weaker colonic motility in elderly patients. Further, patients in this population are likely to have chronic comorbid diseases and take multiple medications, which may increase the risk of inadequate bowel preparation.

Results on several adverse events in our study showed nausea to be more common in patients with morning only dose ($p=0.012$), whereas sleep disturbance occurred significantly more often with split-dose regimen ($p<0.001$). In a study by Shah H et al¹¹, nausea was complained of by 29.1% of patients with the morning preparation and 19.6% with split preparation ($p=0.161$). Sleep was disturbed in 8(7.8%) patients receiving the morning preparation and in 14(14.4%) patients receiving the split preparation ($p=0.201$). These findings are consistent with our study. The advantage of the morning preparation is it interferes less with the patient's routines and work schedules; patients often complain about trouble sleeping after taking the evening preparation. Whereas, in a study by Matro, et al.⁶ abdominal pain occurred significantly less often with morning-only dosing. This study failed to establish superiority of the morning-only dosing on other side effects, although some of those were somewhat less common in the morning-only group. On the other hand, in a study by Mohamad, et al.¹⁴ the split-dose preparation was well tolerated and associated with fewer side effects than the single-dose preparation.

In our study interval between preparation and procedure greater than 6 hours resulted in inferior bowel preparation compared to PC interval of 4-6 hours (97.6% vs 82%, $p=0.103$), although this was not statistically significant.

Whereas, in a study by Seo, et al.¹⁵ PC interval 3 to 5 hours had the best bowel preparation quality. We assume that this difference is most likely due to the difference in the patient groups or PEG intake methods and timing. A long interval results in thick secretions emptying out of the small intestine and obscuring the caecum and ascending colon at the time of colonoscopy.

The rate of poor bowel preparation was 11.81% in our study, whereas in a Nepalese study by Parajuli A, et al.¹⁶ rate of poor bowel preparation was 13.8%. The reported rate of poor bowel preparation in other studies¹⁷⁻¹⁹ is 5% to 60% (median about 25%). Such discrepancy in the results may be due to difference in preparation regimen and patient population.

Several factors have been reported to predict inadequate bowel preparation for colonoscopy and include male sex, a high body mass index, older age, previous colorectal surgery, cirrhosis, Parkinson disease, diabetes, and positive results in a fecal occult test.²⁰ In our study, these factors were not significantly related with inadequate bowel preparation. Whereas in a study²¹ from Africa the educational status of patients was the strongest contributor to inadequate bowel preparation for colonoscopy, apparently as a result of language and communication gaps. However, we did not include the educational background of our study patients, and this could be a risk factor in our patients in view of poor literacy rate of our country. Future studies with larger sample size should identify patients at risk for poor bowel preparation and develop interventions to improve efficacy of bowel preparation.

Conclusion

Morning-only bowel preparation is more effective than Split-dose for achieving adequate colon cleansing for afternoon colonoscopy. Morning only regimen may be more convenient to the patient as it has the benefit of less sleep disruption.

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Conflict of Interest

None

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None

Author Contribution

Concept, design, planning: RS, SK, YRS; Literature review: RS; Data collection: RS, SK; Data analysis: RS, SK; Draft manuscript: RS; Revision of draft: YRS; Final manuscript: RS, SK, YRS; Accountability of the work: RS, SK, YRS; Guarantor: RS.

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