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Day before late regimen vs standard split dose of low-volume PEG-CS for early morning colonoscopy: Multicenter randomized controlled trial

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ABSTRACT

Background and study aims Despite lower patient adherence, the overnight split-dose (SD) intestinal preparation regimen is currently recommended for early morning colonoscopies. Using low-volume preparation, we compared performance of a "day before late" (DBL) regimen, with the whole preparation taken between 8.30 pm and midnight on the day before the endoscopic procedure vs the overnight SD regimen for colonoscopies scheduled between 8 am and 10 am.

Patients and methods Patients were randomized to the DBL group (n = 162) or SD group (n = 158). The SD group took the second dose 5 hours before colonoscopy. Successful bowel cleansing, defined as an overall Boston Bowel Preparation Score ≥ 3, safety, compliance and tolerability were assessed in the two groups.

Results The DBL regimen failed to demonstrate non-inferiority compared with the SD regimen in terms of successful bowel cleansing (DBL, 88.2 % vs SD, 98.1%, $P < 0.001$). Subgroup analysis on colonoscopies before 9 am showed BBPS ≥ 3 rates of 94.6% and 100% in the DBL and SD groups, respectively $P = 0.126$). The two regimens showed similar compliance and tolerability. Compared with SD patients (25.5%), a lower proportion of DBL patients (13.9%) reported fear of incontinence during the journey to the hospital ($P = 0.01$).

Conclusions Albeit more tolerable, the DBL regimen was less effective than the SD regimen with regard to successful bowel cleansing for colonoscopies between 8 am and 10 am. Subgroup analysis on colonoscopies scheduled before 9 am showed that the two regimens have similar efficacy, suggesting that the DBL regimen may be a valuable alternative to the SD regimen for very early morning colonoscopies.

Introduction

Colonoscopy, widely acknowledged as the most effective method for early detection and prevention of colorectal cancer [1], has seen increased global utilization due to advancements in endoscopic equipment, patient-specific sedation protocols, and public awareness campaigns [2, 3].

Optimal bowel preparation is crucial for successful colonoscopy and has gained considerable attention over the years [4, 5, 6]. With regard to morning colonoscopy, current international guidelines recommend a split-dose (SD) regimen with a low volume of laxatives being taken overnight in two separate doses as the standard for optimal bowel cleaning and lesion detection [7, 8, 9].

Despite the demonstrated effectiveness of the overnight SD preparation [8], adherence to this regimen remains limited, particularly when colonoscopy is scheduled in the early morning [10, 11, 12]. This may be related to the inconvenience of having to wake up very early during the night to take the second dose of preparation and also to the anxiety with regard to possible episodes of fecal incontinence on the way to the hospital [11, 13].

It has been suggested that patients would prefer taking the whole preparation on the day before when colonoscopy is scheduled in the early morning [11, 14, 15]. However, studies indicate inadequate bowel cleansing in up to 40% of patients following the same-day regimen [16, 17] due to the substantially longer time interval between preparation and colonoscopy start compared with that in patients who follow the overnight SD regimen [15, 18].

We hypothesized that for colonoscopies scheduled between 8 a.m. and 10 a.m., taking the complete intestinal preparation late on the day before would minimize inadequate cleansing by effectively shortening the time interval between the last dose of laxative and the start of the endoscopic procedure. To our knowledge, the only study comparing overnight SD with a same-day regimen taken between 8 and 11 p.m. on the day before colonoscopy scheduled in the early morning demonstrated better preparation quality with the SD regimen [19].

The Italian Society of Digestive Endoscopy (SIED) promoted a multicenter, randomized, controlled non-inferiority trial on colonoscopies scheduled in the early morning, comparing the efficacy, safety, compliance and tolerability of a "day before late" (DBL) regimen, which involved taking the whole intestinal preparation between 8.30 p.m. and midnight on the day before the endoscopic procedure, vs the standard overnight SD regimen, using low-volume polyethylene glycol-electrolyte solution with citrate and simethicone (PEG-CS) (Clensia; Alfa Sigma Pharmaceuticals, Bologna, Italy) preparation.

Patients and methods

This multicenter study, conducted in 10 Italian endoscopic units from June to December 2021, involved outpatients aged 18 to 75 years undergoing colonoscopy.

Exclusion criteria were participation in an organized colorectal cancer screening program, hypersensitivity to the study product components, suspected gastrointestinal perforation, intestinal obstruction or toxic megacolon, intestinal paralysis, previous colonic resection, history of inflammatory bowel disease, severe heart failure (New York Heart Association class III or IV), acute cardiovascular disease, severe liver cirrhosis (Child-Pugh score C), ascites, renal failure (creatinine clearance < 30 mL/minute), documented electrolyte disturbances, poorly controlled arterial hypertension (systolic pressure > 170 mm Hg, diastolic pressure > 100 mm Hg), pregnancy, and breastfeeding.

Ethics

The study was approved by the Independent Ethics Committees of each participating hospital. The study was registered on ClinicalTrials.gov, where full trial details are available, with the identifier NCT05570669. Written informed consent was obtained from all participating patients prior to enrolment. The study was conducted in accordance with the principles of the Helsinki Declaration, and with the regulations and guidelines of the Independent Ethics Committees, as well as the informed consent regulations and local regulatory requirements of each participating hospital.

Treatment allocation

Enrolled patients were randomly assigned to either the DBL or SD group using computer-generated block randomization with a block size of four in a 1:1 ratio. The allocation sequence was concealed until participants were enrolled and assigned to the intervention.

Intestinal preparation

Enrolled patients were required to follow a low-fiber diet by limiting intake of fruit and vegetables for 3 days before the colonoscopy, and to have a fiber-free normal breakfast and lunch the day before colonoscopy. During the intestinal preparation, only clear fluids were allowed until 2 hours before colonoscopy.

In the DBL group, patients took the whole PEG-CS preparation (two doses of 1 L macrogol 4000, sodium sulfate, sodium citrate, citric acid, simethicone, sodium chloride, potassium chloride) between 8.30 p.m. and midnight on the night before the colonoscopy, followed by 0.5 L of clear fluids after each 1 L of preparation. Patients in the SD group took the first dose of PEG-CS followed by 0.5 L of clear fluids on the day before the procedure between 8.30 p.m. and midnight, and the second dose of PEG-CS followed by 0.5 L of clear fluids on the day of the colonoscopy, 5 hours before the scheduled procedure time.

Study outcomes

The primary outcome of this study was to assess efficacy of the DBL regimen in comparison with the SD regimen using the Boston Bowel Preparation Score (BBPS) [20].

Secondary outcomes were to evaluate efficacy of the DBL regimen in comparison with the SD regimen using the Intraluminal Bubble Score (IBS) and the polyp detection rate, and to assess safety, compliance, and tolerability in the two groups.

Study endpoints

Evaluation of efficacy

All colonoscopies scheduled between 8 a.m. and 10 a.m. were assessed for bowel preparation quality by a blinded endoscopist. Bowel cleansing was evaluated before and after washing and aspiration using IBS [21] and BBPS [20], respectively. The BBPS [20] is a four-point (ranging from 0 to 3) scoring system based on mucosal visualization of each one of the three segments of the colon (right, transverse, and left colon) after washing and aspiration, with a total BBPS score ranging from 0 to 9 and higher values indicating better visualization. Conversely, the IBS [21] ranges from 1 (bubbles cover less than 10% of the luminal circumference) to 4 (bubbles fill more than 50% of the luminal circumference, thereby requiring extensive irrigation). In this study, we applied the IBS score to the overall colon, without separate segment analysis. The primary endpoint of our study was the rate of colonoscopies with successful (good to optimal) bowel cleansing, defined as BBPS ≥ 2 in each colonic segment, in the DBL group vs the SD group. Secondary efficacy endpoints included IBS ≥ 3, evaluated in the overall colon rather than in each colonic segment, and the colorectal polyp detection rate in the DBL group vs the SD group.

Evaluation of safety, compliance and tolerability

Safety evaluation included recording every adverse event (AE) and severe AE (SAE) in the DBL group vs the SD group.

We also assessed compliance, defined as the percentage of patients who managed to take ≥ 75% of the entire bowel preparation, and tolerability of the DBL vs the SD regimen by means of a questionnaire administered before colonoscopy by unblinded nurses, not directly involved in the study in order to maintain investigator blinding.

Statistical analysis

Assuming a 90% rate of success (i. e. good to optimal bowel preparation, defined as BBPS score ≥ 2 in each colonic segment) in the SD group, 284 patients (142 per group) were needed to establish non-inferiority of the DBL group with respect to the SD group, with a maximum allowable difference of 10%, with a one-sided significance level of $P = 0.025$ and 80% power. Allowing for 10% major protocol deviations, we predicted that a total of 316 patients (316–31.6 = 284.4) were required for the study.

Both the intention-to-treat (ITT) population, including all randomized patients, and the per-protocol population (PP), including only those patients who underwent colonoscopy without major protocol deviations, were analyzed, with PP being set as the primary analysis for efficacy outcomes.

Continuous variables were described using mean and standard deviation. Categorical variables were reported as frequencies and percentages. Continuous variables were compared using Student's *t*-test or Mann-Whitney test, if appropriate. Categorical variables were compared using chi-square tests and Fisher's test. $P < 0.05$ was considered statistically significant. All statistical analyses were performed using the statistical software Stata 17.0.

Results

Of 321 eligible patients, one was excluded for not providing signed consent. A total of 320 patients (mean age 56.8 years, 155 males and 165 females) were enrolled and randomized to the DBL group (n = 162) or to the SD group (n = 158). Baseline characteristics are shown in ▶ **Table 1**.

In the DBL group, two patients were excluded for discontinuing bowel preparation due to nausea and vomiting, whereas two did not complete the colonoscopy due to intolerance. Five additional DBL patients were excluded due to protocol deviations, including dietary non-compliance (n = 2), failure to adhere to scheduled timing for laxative intake (n = 2) and use of a different bowel preparation medicine (n = 1). In the SD group, one patient was excluded for not adhering to dietary restrictions. Consequently, 10 patients were excluded, resulting in a total PP population of 310 patients (DBL group, n = 153; SD group, n = 157). The study flow chart is summarized in ▶ **Fig. 1**.

Efficacy of DBL vs SD regimen

In the PP analysis, successful bowel preparation (BBPS ≥ 6) was achieved in 88.2% of patients in the DBL group (135/153) (95% confidence interval [CI] 82.1–92.9) and in the 98.1% of patients

▶ **Table 1** Patient characteristics.

Characteristics	Split-dose regimen (n = 158)	Day before late regimen (n = 162)
Sex (female), n (%)	80 (50.6)	85 (52.5)
Age (years), mean (SD)	57.2 (11.9)	56.4 (13.8)
Comorbidities, n (%)		
▪ Cardiovascular	54 (34.2)	55 (34.0)
▪ Metabolic	37 (23.4)	38 (23.5)
▪ Gastrointestinal	29 (18.4)	24 (14.8)
▪ Psychiatric	7 (4.4)	13 (8.0)
▪ Genitourinary	10 (6.3)	16 (9.9)
▪ Autoimmune	6 (3.8)	10 (6.2)
▪ Other	50 (31.6)	32 (19.7)
BMI, mean (SD)	25.5 (4.9)	25.8 (5.2)
Normal colonoscopy, n (%)	67 (42.7)	70 (44.3)

BMI, body mass index; SD, standard deviation

in the SD group (154/157) (95% CI 94.5–99.6), with the DBL regimen failing to demonstrate non-inferiority compared with the SD regimen ($P < 0.001$) (▶ **Table 2**). In the ITT analysis, successful bowel preparation was achieved in 83.3% of patients in the DBL group (135/162) and in 97.5% of patients in the SD group (154/158).

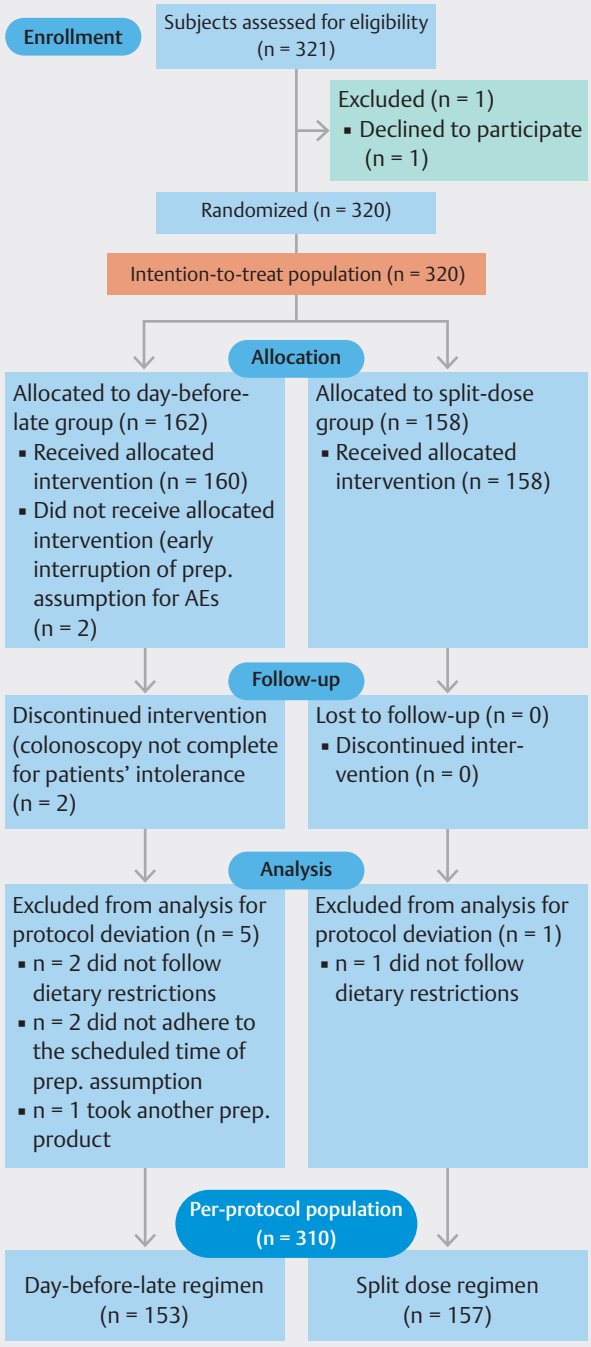
Optimal bowel preparation (BBPS 8) was reported in 35.9% of patients in the DBL group (55/153) compared with 61.1% of patients in the SD group (96/157) ($P < 0.001$).

A lower percentage of patients in the DBL group compared with the SD group achieved successful segmental colonic cleansing (BBPS 2) both in the right colon (82.4%, 126/153 vs 94.3%, 148/157, respectively, $P < 0.001$) and in the left colon (90.8%, 139/153 vs 96.8%, 152/157, respectively, $P = 0.029$).

Subgroup analysis of colonoscopies before 9 a.m. showed that BBPS 6 was achieved in 94.6% (70/74) and 100% (61/61) of patients in the DBL and SD groups, respectively ($P = 0.126$) (▶ **Table 2**).

However, when colonoscopies were scheduled between 9 a.m. and 10 a.m., a lower percentage of patients in the DBL group compared with the SD group achieved good or optimal bowel cleansing (82.3%, 65/79, CI 72.1–90.0 vs 96.9%, 93/96, CI 91.1–99.4, respectively, $P = 0.002$) (▶ **Table 2**).

Rates of successful segmental bowel cleansing (BBPS 2) in the right colon in colonoscopies performed before 9 a.m. were 87.8% (65/74) and 96.7% (59/61) in the DBL and SD groups, respectively ($P = 0.106$). Regarding colonoscopies scheduled between 9 a.m. and 10 a.m., a lower percentage of patients in the DBL group compared with the SD group achieved successful bowel cleansing in the right colon (77.2%, 61/79 vs 92.7%, 89/96, respectively, $P < 0.001$).



▶ **Fig. 1** Consolidated Standard of Reporting Trials (CONSORT) flow diagram showing enrollment and analysis. AE, adverse event

Only 5.9% of patients in the DBL group (9/153) and 2.5% in the SD group (4/157) had an IBS of 3 or 4, requiring extensive irrigation during colonoscopy ($P = 0.317$) (▶ **Table 2**).

The polyp detection rate was 41.8% in the DBL group (64/153) and 45.2% in the SD group (71/157) ($P = 0.548$) (▶ **Table 2**).

▶ **Table 2** Analysis of efficacy outcomes.

	Total, n (%)	Day before late regimen,n (%)	Split-dose regimen, n (%)	*P* value
Primary endpoint				
BBPS ≥ 6	289 (93.2)	135 (88.2)	154 (98.1)	< 0.001
Colonoscopy before 9 a.m. (n = 135)	131 (97.0)	70 (94.6)	61 (100.0)	0.126
Colonoscopy after 9 a.m. (n = 175)	158 (90.3)	65 (82.3)	93 (96.9)	0.002
Secondary endpoints				
IBS ≥ 3	13 (4.2)	9 (5.9)	4 (2.5)	0.317
Polyp detection rate	136 (43.9)	64 (41.8)	71 (45.2)	0.548

Day before late regimen (n = 153). Split-dose regimen (n = 157).
BBPS, Boston Bowel Preparation Score; IBS, Intraluminal Bubble Score.

▶ **Table 3** Analysis of safety, compliance and tolerability outcomes.

	Day before late regimen,n (%)	Split-dose regimen, n (%)	*P* value
Serious adverse events	0 (0)	0 (0)	
Adverse events			
Dysgeusia	62 (39.2)	60 (38.2)	0.852
Bloating	67 (42.4)	76 (48.4)	0.285
Abdominal pain	26 (17.1)	36 (22.9)	0.148
Headache	16 (10.1)	14 (8.9)	0.715
Nausea/vomiting	42 (26.6)	29 (18.5)	0.085
Patients who took ≥ 75% of the bowel preparation	151 (95.6)	156 (99.4)	0.181
Willingness to repeat the same regimen in the future	140 (88.6)	128 (81.5)	0.078
Fear of fecal incontinence on the way to the hospital	22 (13.9)	40 (25.5)	0.010
Perceived difficulty of preparation regimen			0.821
No difficulty	81 (51.3)	85 (54.1)	
Mild difficulty	43 (27.2)	45 (28.7)	
Medium difficulty	29 (18.4)	22 (14.0)	
High difficulty	5 (3.2)	5 (3.2)	

Day before late regimen (n = 158). Split-dose regimen (n = 157)

Safety, compliance and tolerability of DBL vs SD regimen

The safety, compliance, and tolerability analysis in the DBL group included two patients who interrupted colonoscopy due to intolerance of the procedure, two patients who did not follow dietary restrictions, and one patient who took another bowel preparation. Consequently, the analysis encompassed 158 patients in the DBL group and 157 patients in the SD group. No SAEs were reported in either the DBL or SD group. No significant differences in the rate of AEs were reported between the two groups (▶ **Table 3**).

With regard to compliance, in the DBL group 95.6% of patients (151/158) took ³75% of the entire dose of the intestinal preparation, whereas in the SD group, this percentage was 99.4% (156/157) (*P* = 0.181) (▶ **Table 3**).

In the DBL group, 88.6% of patients (140/158) expressed their willingness to undergo the same preparation regimen in the future, whereas in the SD group, this percentage was 81.5% (128/157) (*P* = 0.078). Interestingly, fear of fecal incontinence on the way to the hospital was reported by 13.9% of patients in the DBL group (22/158) compared with 25.5% in the SD group (40/157) (*P* = 0.01). Finally, in the DBL group 51.3% of patients (81/158) reported no difficulty in taking the preparation, whereas in the SD group, this percentage was 54.1% (85/157) (*P* = 0.821) (▶ **Table 3**).

Discussion

We conducted the first randomized controlled trial comparing DBL (i.e. a modified day-before regimen) with a 2-L PEG-CS preparation taken as late as possible on the day prior to colonoscopy, to the overnight SD regimen. Notably, we used a low-volume bowel preparation in accordance with the most recent evidence on the effectiveness of this type of intestinal preparation [22]. We defined the primary endpoint as the rate of colonoscopies with good to optimal bowel cleansing by using a threshold of BBPS ≥ 2 in each colonic segment, which is suitable for detecting adenomas > 5 mm [23]. Moreover, we focused most of our effectiveness analysis on the overall and right colon, given the higher occurrence of flat or sessile serrated adenomas [24, 25], missed lesions, and interval cancers [26] in the right side of the colon compared with the left side.

Consistent with comparable studies on whole-dose and SD regimens [19, 27, 28, 29, 30], our study showed that, compared with the DBL group, a higher percentage of patients in the SD group achieved good or optimal bowel cleansing throughout the entire colon and also in the right and left colon segments. Nevertheless, patients in the DBL and in the SD groups had similar IBS^{3}3 and polyp detection rates.

Interestingly, when colonoscopy was scheduled before 9 a.m., the rates of good to optimal bowel cleansing were similar between the DBL and SD groups, both in the overall colon (P = 0.126) and in the right colon (P = 0.106). Conversely, when colonoscopy was scheduled after 9 a.m., a higher rate of successful bowel cleansing was observed in the SD group compared with the DBL group. Although our study was not specifically designed for this subgroup analysis, these results suggest that the DBL regimen may be a valid option for very-early-morning colonoscopy. Although the sample size of our study may not have been powered to prove this point, our results may be valuable as hypothesis-generating data, and could provide the basis for a specifically designed subsequent prospective study. In contrast, Park et al. [19] reported improved bowel preparation, shorter cecal intubation times, reduced procedure difficulty, and increased willingness for future colonoscopies with the asymmetric SD regimen compared with the whole-dose preparation taken between 8 p.m. and 11 p.m. the day before when colonoscopy is planned between 8 and 9:30 a.m.. However, some aspects of the study by Park et al. [19] may account for this discrepancy, such as the use of a 4-L high-volume PEG solution, the asymmetric SD protocol which entailed taking a low morning dose, and stratification according to level of compliance.

Many studies support the idea of reducing the time interval between the last dose of preparation and colonoscopy; however, a definitive threshold has not been established so far. Marmo et al. [30] and Eun et al. [31], respectively, proposed that the last dose should not be taken more than 6 to 8 and 7 hours, before colonoscopy, in order to obtain optimal bowel preparation. A randomized study by Kojecky et al. [32] suggested that a time interval of 11.8 hours between the end of bowel preparation and colonoscopy is optimal regardless of preparation used. European Society of Gastrointestinal Endoscopy (ESGE) guidelines [7] recommend starting the final dose of intestinal preparation 5 hours before colonoscopy and completing it no later than 2 hours before the procedure. However, according to these indications, when the examination is planned in the very early morning, the patient would have to take the last dose of preparation in the middle of the night, and this may affect compliance and willingness to repeat the test if needed [33].

Importantly, we did not observe any significant difference between DBL and SD regimens in terms of AEs, patient compliance, or perceived difficulty of preparation regimen. Patients in the DBL group showed a slightly higher willingness to repeat this regimen (88.6%) compared with the SD group (81.5%). The lack of difficulty in taking the entire preparation on the day before the colonoscopy observed in our study may be related to the low-volume formulation, i.e. 2 L in total. As it could be expected, a lower percentage of patients in the DBL group reported fear of incontinence during travel to the hospital (P = 0.01). Accordingly, a previous study [11] identified distance from the hospital and early morning examinations as key factors negatively influencing adherence to the SD regimen.

One of the limitations of our study is that the rate of protocol deviation was not negligible. This could be attributed to heterogeneity in participant hospitals, the rural vs urban environment, and differences in education levels, thus reflecting real-life scenarios. Importantly, this issue is not unique to our study but is widespread in research conducted in other countries, as demonstrated by a study by Ton et al. [34], which reported a wide variation in colonoscopy preparation instructions provided by 201 endoscopy units across the United States. This is relatively common in open access systems, where patients often receive minimal information, usually a single sheet, when booking the test or when purchasing the preparation. There is a need for evidence-based and comprehensive guidelines for intestinal preparation, and combining written information with multimedia resources, such as videos, applications, and customer service, is essential to reduce repeated examinations due to inadequate preparation. Another limitation is that we focused on one specific intestinal preparation. Although this may have positively impacted data interpretation, it is possible that a similar randomized clinical trial using a different intestinal preparation may show better efficacy for a DBL regimen for colonoscopies between 8 a.m. and 10 a.m.

Despite these limitations, we believe that our study provides valuable insights into the efficacy and tolerability of the DBL regimen compared with the SD regimen for bowel preparation before early-morning colonoscopy. We found that the DBL regimen with low-volume PEG-CS, albeit more tolerable, is less effective than the SD regimen with regard to successful bowel cleansing for colonoscopies scheduled between 8 a.m. and 10 a.m. However, a subgroup analysis of our data on colonoscopies scheduled before 9 a.m. showed that the DBL and SD regimens have similar efficacy. This suggests that the DBL regimen may represent a valuable alternative to the SD regimen for very-early-morning colonoscopies, with the potential benefit of combining effective intestinal cleansing with enhanced patient tolerability. In light of our results, we propose further in-

vestigation about the DBL protocol as an alternative to the SD regimen for very-early-morning colonoscopies.

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Conflict of Interest

Giuseppe Grande, MD (corresponding author) is: - consultant for: Olympus, ERBE, Boston Scientific - conference speaker for: Alfa Sigma spa; Mayoly All other authors have no conflict of interest to declare.

Clinical trial

ClinicalTrials.gov (http://www.clinicaltrials.gov/)
Registration number (trial ID): NCT05570669
Type of Study: Prospective, Randomized, Multi-Center Study

References

[1] Bretthauer M, Løberg M, Wieszczy P et al. Effect of colonoscopy screening on risks of colorectal cancer and related death. N Engl J Med 2022; 387: 1547–1556 doi:10.1056/NEJMoa2208375

[2] Brown JJ, Asumeng CK, Greenwald D et al. Decreased colorectal cancer incidence and mortality in a diverse urban population with increased colonoscopy screening. BMC Public Health 2021; 21: 1280

[3] Hayman CV, Vyas D. Screening colonoscopy: The present and the future. World J Gastroenterol 2021; 27: 233–239 doi:10.3748/wjg.v27.i3.233

[4] Sharma P, Burke CA, Johnson DA et al. The importance of colonoscopy bowel preparation for the detection of colorectal lesions and colorectal cancer prevention. Endosc Int Open 2020; 8: E673–E683 doi:10.1055/a-1127-3144

[5] Dao HV, Dao QV, Lam HN et al. Effectiveness of using a patient education mobile application to improve the quality of bowel preparation: a randomised controlled trial. BMJ Open Gastroenterol 2023; 10: e001107 doi:10.1136/bmjgast-2023-001107

[6] Bennett L, Knox R, Luscombe G et al. The Colonoscopy Cookbook: Analysis of effect of a recipe resource on quality and experience of bowel preparation in colonoscopy. Endosc Int Open 2023; 11: E561–E565 doi:10.1055/a-2057-4374

[7] Hassan C, East J, Radaelli F et al. Bowel preparation for colonoscopy: European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2019. Endoscopy 2019; 51: 775–794 doi:10.1055/a-0959-0505

[8] Spadaccini M, Frazzoni L, Vanella G 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] ASGE Standards of Practice Committee, Saltzman JR, Cash BD et al. Bowel preparation before colonoscopy. Gastrointest Endosc 2015; 81: 781–794

[10] Lin OS, Schembre DB. Are split bowel preparation regimens practical for morning colonoscopies? Implications of the new American College of Gastroenterology colon cancer screening guidelines for real-world clinical practice. Am J Gastroenterol 2009; 104: 2627–2628 doi:10.1038/ajg.2009.415

[11] Radaelli F, Paggi S, Repici A et al. Barriers against split-dose bowel preparation for colonoscopy. Gut 2017; 66: 1428–1433 doi:10.1136/gutjnl-2015-311049

[12] Archer T, Shirazi-Nejad AR, Al-Rifaie A et al. Is it time we split bowel preparation for all colonoscopies? Outcomes from a national survey of bowel preparation practice in the UK BMJ Open Gastroenterol 2021; 8: e000736

[13] Altawil J, Miller LA, Antaki F. Acceptance of split-dose bowel preparation regimen for colonoscopy by patients and providers. J Clin Gastroenterol 2014; 48: e47–49 doi:10.1097/MCG.0b013e3182a9f78d

[14] Tontini GE, Prada A, Sferrazza S et al. The unmet needs for identifying the ideal bowel preparation. JGH Open 2021; 5: 1135–1141 doi:10.1002/jgh3.12653

[15] Dolovich C, Unruh C, Moffatt DC et al. Mandatory vs. optional split-dose bowel preparation for morning colonoscopies: a pragmatic noninferiority randomized controlled trial. Endoscopy 2023; 55: 822–835 doi:10.1055/a-2070-5561

[16] Bucci C, Rotondano G, Hassan C et al. Optimal bowel cleansing for colonoscopy: split the dose! A series of meta-analyses of controlled studies. Gastrointest Endosc 2014; 80: 566–576.e2

[17] Rex DK. Optimal bowel preparation – a practical guide for clinicians. Nat Rev Gastroenterol Hepatol 2014; 11: 419–425 doi:10.1038/nrgastro.2014.35

[18] Shahini E, Sinagra E, Vitello A et al. Factors affecting the quality of bowel preparation for colonoscopy in hard-to-prepare patients: Evidence from the literature. World J Gastroenterol 2023; 29: 1685–1707

[19] Park JS, Sohn CI, Hwang SJ et al. Quality and effect of single dose vs split dose of polyethylene glycol bowel preparation for early-morning colonoscopy. Endoscopy 2007; 39: 616–619 doi:10.1055/s-2007-966434

[20] Lai EJ, Calderwood AH, Doros G et al. The Boston bowel preparation scale: a valid and reliable instrument for colonoscopy-oriented research. Gastrointest Endosc 2009; 69: 620–625 doi:10.1016/j.gie.2008.05.057

[21] Matro R, Tupchong K, Daskalakis C et al. The effect on colon visualization during colonoscopy of the addition of simethicone to polyethylene glycol-electrolyte solution: a randomized single-blind study. Clin Transl Gastroenterol 2012; 3: e26

[22] Yi L-J, Tian X, Shi B et al. Low-volume polyethylene glycol improved patient attendance in bowel preparation before colonoscopy: A meta-analysis with trial sequential analysis. Front Med (Lausanne) 2019; 6: 92

[23] Clark BT, Protiva P, Nagar A et al. Quantification of Adequate Bowel Preparation for Screening or Surveillance Colonoscopy in Men. Gastroenterology 2016; 150: 396–405 doi:10.1053/j.gastro.2015.09.041

[24] Xiang L, Zhan Q, Zhao X-H et al. Risk factors associated with missed colorectal flat adenoma: a multicenter retrospective tandem colonoscopy study. World J Gastroenterol 2014; 20: 10927–10937

[25] Sawhney MS, Dickstein J, LeClair J et al. Adenomas with high-grade dysplasia and early adenocarcinoma are more likely to be sessile in the proximal colon. Colorectal Dis 2015; 17: 682–688

[26] Singh S, Singh PP, Murad MH et al. Prevalence, risk factors, and outcomes of interval colorectal cancers: a systematic review and meta-analysis. Am J Gastroenterol 2014; 109: 1375–1389 doi:10.1038/ajg.2014.171

[27] El Sayed AMA, Kanafani ZA, Mourad FH et al. A randomized single-blind trial of whole vs split-dose polyethylene glycol-electrolyte solution for colonoscopy preparation. Gastrointest Endosc 2003; 58: 36–40 doi:10.1067/mge.2003.318

[28] Abdul-Baki H, Hashash JG, Elhajj II et al. A randomized, controlled, double-blind trial of the adjunct use of tegaserod in whole-dose or split-dose polyethylene glycol electrolyte solution for colonoscopy

preparation.. Gastrointest Endosc 2008; 68: 294–300 doi:10.1016/j.gie.2008.01.044

[29] Aoun E, Abdul-Baki H, Azar C et al. A randomized single-blind trial of split-dose PEG-electrolyte solution without dietary restriction compared with whole dose PEG-electrolyte solution with dietary restriction for colonoscopy preparation. Gastrointest Endosc 2005; 62: 213–218

[30] Marmo R, Rotondano G, Riccio G et al. Effective bowel cleansing before colonoscopy: a randomized study of split-dosage vs non-split dosage regimens of high-volume vs low-volume polyethylene glycol solutions. Gastrointest Endosc 2010; 72: 313–320

[31] Eun CS, Han DS, Hyun YS et al. The timing of bowel preparation is more important than the timing of colonoscopy in determining the quality of bowel cleansing. Dig Dis Sci 2011; 56: 539–544

[32] Kojecky V, Matous J, Keil R et al. The optimal bowel preparation intervals before colonoscopy: A randomized study comparing polyethylene glycol and low-volume solutions. Dig Liver Dis 2018; 50: 271–276

[33] Shafer LA, Walker JR, Waldman C et al. Predictors of patient reluctance to wake early in the morning for bowel preparation for colonoscopy: a precolonoscopy survey in city-wide practice. Endosc Int Open 2018; 6: E706–E713 doi:10.1055/s-0044-102298

[34] Ton L, Lee H, Taunk P et al. Nationwide variability of colonoscopy preparation instructions. Dig Dis Sci 2014; 59: 1726–1732 doi:10.1007/s10620-014-3262-8