

Can a 1-day clear liquid diet with a split -dose polyethylene glycol overcome conventional practice patterns during the preparation for screening colonoscopy?

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ABSTRACT

Background/Aims: A successful screening colonoscopy is closely linked to the quality of a bowel preparation. In this study, we aimed to determine the impact of a 1-day clear liquid diet (CLD) compared to a 3-day combined diet (CMD) accompanied by a split-dose regimen of polyethylene glycol and electrolyte lavage solution (PEG-ELS) for screening colonoscopy.

Materials and Methods: This was a prospective, randomized, endoscopist-blinded study. Patients referred for screening colonoscopy were randomized to four groups as a 1-day CLD+PEG-ELS vs. a 1-day CLD+sulfate free (SF)-PEG-ELS and a 3-day CMD+PEG-ELS vs. a 3-day CMD+SF-PEG-ELS. An assessment of the quality of colon cleaning, tolerability to the preparation, and symptoms related to the preparation were recorded.

Results: A total of 506 patients were enrolled in this study. The quality of bowel preparation was significantly inferior in the CMD+PEG-ELS group than CLD+PEG-ELS ($p=0.004$) and CMD+SF-PEG-ELS groups ($p=0.007$). There were no statistical differences among the groups in terms of the polyp detection rate. With respect to an easy rating of diet following and the consumption of laxative, there were no significant differences among the four groups. Gastric fullness and nausea/vomiting were pointed out much more, especially in the SF-PEG-ELS users ($p=0.008$ and $p=0.004$, respectively).

Conclusion: A 1-day CLD was not inferior to a 3-day CMD for colonoscopy preparation in terms of bowel cleaning, the polyp detection rate, and patient tolerance.

Keywords: Bowel cleaning, clear liquid diet, low-residue diet, screening for colon cancer

INTRODUCTION

Among the public, there is a growing awareness that colorectal cancer is preventable and can be diagnosed early via screening or surveillance programs (1). Colorectal cancer directly elicits the necessity of a colonoscopic examination (1). Bowel preparation is a critical quality indicator in colonoscopy (2). An adequate bowel preparation is essential in providing satisfactory visualization of the colonic mucosa, to optimize lesion detection, and to make a safe therapeutic intervention (2-4). Despite this, unfortunately, many patients cannot comply with the bowel cleaning regimens because of strict dietary modifications that affect their preprocedural quality of life and the large volume of flavorless laxative solutions (5,6). Moreover, patients having an inadequate bowel cleaning need to repeat similar preparation steps before the next examination (6,7).

This also means that the risks associated with endoscopic investigation and anesthesia increase, and the procedure cost doubles (5,7).

In studies, the dietary factor is often omitted or usually considered a component of adherence to the bowel preparation instructions, or there is only a laxative evaluation without considering diets (8). Currently, the selection of diets and their durations, as well as the strategy of preparation, have been changing according to the preference of the physician and the need of the patient (9). The clear liquid diet (CLD) and low-residue diet (LRD) are frequently prescribed diets in most bowel preparation schedules (8,9). In 2013, the European Society of Gastrointestinal Endoscopy recommended an LRD on the day preceding the colonoscopy with moderate quality evidence. However due to

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a lack of randomized controlled trials, the committee presented an open-ended approach to choosing either a CLD or an LRD with a 1-day or a 3-day regimen (10). In 2014, the guideline reviewed by the members of the Multi-Society Task Force on Colorectal Cancer in the United States offered either LRD or full liquids until the evening on the day before the colonoscopy, considering the patient's medical history, medications used, and the adequacy of bowel preparation reported from prior colonoscopies (11).

Although dietary flexibility is allowed in several bowel preparation regimens, the ideal dietary modification, to the best of our knowledge, has not yet been described. In this prospective study, considering the bowel cleaning efficacy, a detection rate of neoplastic lesions, and patient tolerance, we aimed to compare a 3-day combined diet (CMD) (2.5-day LRD followed by CLD at two meals) with a 1-day CLD in a patient population that ingested a split-dose regimen of 4 L polyethylene glycol and electrolyte lavage solution (PEG-ELS) with sulfate or without sulfate.

MATERIALS AND METHODS

Study design

This study was designed to be prospective, randomized, and investigator blinded. It was conducted between January 2018 and April 2018 at the gastrointestinal endoscopy unit of a tertiary referral single center. This study was approved by Başkent University School of Medicine, the Human Ethics Review Board (Study number: KA18/14).

Patients

Individuals aged >50 years, who applied for a screening colonoscopy under the average colon cancer risk and were healthy or without a severe or complicated systemic disease, were recruited. Patients were excluded if they had a personal history of colorectal carcinoma, inflammatory bowel disease, prior surgery of the colon, inability to move because of a neurologic or orthopedic disease, familial polyposis syndrome, or who needed colonoscopy urgently, for example, due to an acute lower gastrointestinal hemorrhage. All participants provided informed consent before the study enrollment.

Bowel preparation

The patients were randomly divided into two groups: the first group received 1-day CLD in which partic-

ipants consumed a pure liquid diet throughout 24 h, and the second group received a 3-day CMD in which participants started an LRD 72 h prior to the colonoscopy and continued for 2.5 days; then they were applied CLD at last two meals before the colonoscopy. CLD is a diet consisting of exclusively clear liquids, and it does not include any solids, fibers, vegetables, or fruit pulps. LRD limits high-fiber foods such as cereals, beans, peas, nuts, seeds, and raw or dried fruits and vegetables. All diet recipes were given to every patient in a detailed written form, including an acceptable and alternative food list for breakfast, lunch, and evening. Patients were asked to keep a food diary to verify their adherence to the prescribed diet.

The cleaning solution used in our research consisted of a total of 4 L of PEG-ELS (Golytely, Braintree Laboratories, Massachusetts, United States) or 4 L of sulfate-free-PEG-ELS (SF-PEG-ELS) (Endofalk, Dr. Falk Pharma GmbH, Freiburg, Germany), so that two subgroups were added to two different diet groups (a 1-day CLD+PEG-ELS vs. a 1-day CLD+SF-PEG-ELS and a 3-day CMD+PEG-ELS vs. a 3-day CMD+SF-PEG-ELS). Both PEG solutions were administered in a split-dose fashion. The first dose of 2 L was administered between 12 and 16 h before the scheduled time of the colonoscopy. The remaining 2 L was offered between 3 and 6 h before the scheduled time of the colonoscopy. In this way, approximately 250 mL were ingested every 10 min, and all patients completed each part of the preparation in 2 h. Due to conscious sedation, any liquid intake was prohibited 3 h before the procedure. All endoscopic procedures were performed between 8 am and 4 pm in a day following an appointment program.

Assessment of patient's tolerability and symptoms related to preparation

Before the procedure, each patient completed a questionnaire called The Mayo Clinic Bowel Prep Tolerability Questionnaire, which examined the tolerability of the preparation and willingness to take it again, taste, fullness, lack of sleep, and side effects (nausea, vomiting, bloating, and abdominal pain) (12). These were rated on a scale from 1 (easy) to 4 (extremely difficult) for tolerability, and from 1 (mild) to 4 (extremely severe) for symptoms related to the preparation. A nurse asked whether the patient had completed the prescribed diet regimen before the endoscopic procedure. If the patient consumed <50% of the laxative solution, it was described as poor compliance, and the endoscopic procedure was cancelled.

Assessment of colon cleaning

All endoscopists were blinded to the preparing regimen and instructed not to discuss the bowel preparation with the patient. After the procedure, an endoscopist recorded colonoscopic features, a total procedure time, if any therapeutic intervention was applied, and whether they would recommend an early repeat colonoscopy based on the colonoscopic findings. The quality of cleaning for each segment of the colon was rated according to the Boston Bowel Preparation Scale (BBPS) as follows: Score 0 (mucosa not visible due to solid stool, or thick liquid stool cannot be cleared); Score 1 (areas of the colon segment not seen well due to staining, residual stool, and/or opaque liquid); Score 2 (minor amount of residual staining, small fragments of stool and/or opaque liquid, but mucosa seen well); and Score 3 (entire mucosa of the colon segment seen well) (13,14). The left colon, transverse colon, and right colon segments were scored separately, and then these segment scores were summed for a total BBPS score ranging from 0 to 9. Categorical assessment for each possible total BBPS score: "excellent," 8-9; "good," 6-7; "fair," 5; "poor," 3-4; or "unsatisfactory," 0-2. All study endoscopists were trained through the video programs available at www.cori.org/bbps website to provide a reliable assessment and decrease interrater differences.

Statistical analysis

This study was designed to have an 80% power to detect a difference between the groups with good BBPS scores. We assumed that $\alpha=0.05$ and $\beta=0.20$. Considering an expected dropout rate of 10%, at least 110 patients were needed for each group.

The IBM Statistical Package for the Social Sciences 25.0 (IBM Corp.; Armonk, NY, USA) program was used in the analysis of the variables. The normal distribution of the data was evaluated with the Lilliefors corrected Kolmogorov-Smirnov and the Shapiro-Wilk tests. The Kruskal-Wallis H test was used according to the Monte Carlo simulation results for the comparison of four independent groups, according to the quantitative data (age, weight, height, and BBPS). Dunn's multiple comparison test was used for the post-hoc analyses of the BBPS variable, which was found to be significant. The Pearson chi-squared test was used with the exact and Monte Carlo simulation results, the Fisher exact test with the exact results, the Fisher-Freeman-Holton test with the Monte Carlo simulation method in the comparison of the groups according to the categorical variables, and the column ratios were compared with each other and ex-

pressed according to the Benjamini-Hochberg corrected p-value results. The quantitative data were expressed as median (percentile, 25%-75%), and the categorical variables were expressed as n (%) in Tables 1-4. The variables were analyzed at the 95% confidence level, and a p-value of less than 0.05 was accepted as significant.

RESULTS

A total of 506 patients were enrolled in this study. Of those, 124 were in the CLD+PEG-ELS group, 127 were in the CLD+SF-PEG-ELS group, 127 were in the CMD+PEG-ELS group, and 129 were in the CMD+SF-PEG-ELS group. A total of 10 patients were excluded due to nonadherence or poor compliance with the bowel preparation protocol as advised.

The demographic characteristics of the patients in the four groups are presented in Table 1. There were no significant differences among the groups in terms of their age, weight, height, gender, or comorbidity.

Overall, the BBPS and BBPS scores for each segment of the colon of the four groups are shown in Table 2. The median BBPS score was 9 for the CLD+PEG-ELS group and 8, 6, and 9 for the CLD+SF-PEG-ELS, CMD+PEG-ELS, and CMD+SF-PEG-ELS groups, respectively. The quality of the bowel preparation was significantly inferior in the CMD+PEG-ELS group than the CLD+PEG-ELS ($p=0.004$) and CMD+SF-PEG-ELS groups ($p=0.007$).

The polyp detection rate was the lowest in the CMD+PEG-ELS group (31.5%) and the highest in the CLD+SF-PEG-ELS group (41.7%), although there were no statistical differences among the groups (Table 3). However, the detection rates for an adenomatous polyp or multiple polyps were significantly lower in the CMD+PEG-ELS group than in other groups ($p=0.018$ and $p=0.039$, respectively). None of the CLD+SF-PEG-ELS, CLD+PEG-ELS, or CMD+SF-PEG-ELS groups showed superiority when compared to each other in terms of the detection rate of adenomatous polyps and detection of more than one polyp. The maximum diameter of polyps did not differ statistically among the groups ($p=0.114$).

The tolerance and compliance with diet and laxative ingestion are summarized in Table 4. The adherence to diet instructions and intake of the laxative solution was reported for at least 75% of patients before the endoscopic procedure. With respect to the easiness

Table 1. Demographic characteristics of the patients in four groups

	(CLD+PEG-ELS): A (n=124)	(CLD+SF-PEG-ELS):B (n=127)	(CMD+PEG-ELS):C (n=127)	(CMD+SF-PEG-ELS): D (n=129)	p
	Median (Q1/Q3)	Median (Q1/Q3)	Median (Q1/Q3)	Median (Q1/Q3)	
Age	61 (54/66)	61 (55/68)	60 (54/68)	58 (54/66)	0.294 ¹
Weight (kg)	75 (62/88)	74 (63/82)	79 (66/85)	74 (65/84)	0.137 ¹
Height (cm)	165 (158/171)	165 (160/172)	165 (161/174)	166 (160/173)	0.447 ¹
	n (%)	n (%)	n (%)	n (%)	
Gender					
Female	80 (64.5)	82 (64.6)	74 (58.3)	79 (63.7)	0.156 ²
Male	44 (34.5)	45 (35.4)	53 (41.7)	50 (36.3)	
Diabetes mellitus	19(14.9)	27 (21.3)	30 (23.6)	20 (15.1)	0.192 ²
Hypertension	48 (38.8)	45 (35.4)	62 (48.8)	48 (37.3)	0.120 ²
Cardiovascular disorder	17 (13.4)	19 (15.0)	22 (17.3)	18 (14.1)	0.855 ²
Thyroid dysfunction	22 (17.9)	20 (15.7)	20 (15.7)	16 (12.4)	0.683 ²
Malignancy	6 (4.5)	6 (4.7)	8 (6.3)	7 (6.3)	0.636 ³
Renal dysfunction	2 (1.5)	5 (3.9)	6 (4.7)	2 (1.6)	0.348 ³
History of abdominal surgery	57 (46.3)	47 (37.0)	63 (49.6)	52 (40.0)	0.166 ²

1-day clear liquid diet + polyethylene glycol and electrolyte lavage solution: CLD+PEG-ELS: A

1-day clear liquid diet + sulfate free polyethylene glycol and electrolyte lavage solution: CLD+ SF-PEG-ELS: B

3-day combined diet + polyethylene glycol and electrolyte lavage solution: CMD+PEG-ELS: C

3-day combined diet + sulfate free polyethylene glycol and electrolyte lavage solution: CMD+ SF-PEG-ELS: D

¹Kruskal-Wallis test (Monte Carlo), ²Pearson chi-squared test (Monte Carlo), ³Fisher-Freeman-Halton (Monte Carlo), Q1: Percentile 25%, Q3: Percentile 75%

rating of following the diet and laxative consumption, there were no significant differences among the four groups (p=0.056, p=0.611, respectively). Participants reported a willingness to perform the same preparation protocol in case of repeat colonoscopy, with the percentages of 83.6% in the CLD+PEG-ELS group, 83.5% in the CLD+SF-PEG-ELS group, 83% in the CMD+PEG-ELS group, and 89.7% in the CMD+SF-PEG-ELS group (p=0.352). Nobody discontinued the study because of bothersome symptoms during the preparation period. The most common bothersome symptoms related to bowel preparation were a bad taste in the mouth and lack of sleep due to excessive bathroom trips. However, there was no statistically significant difference among the groups (p=0.068 and p=0.760, respectively). Gastric fullness and nausea/vomiting were more frequently reported in the CMD+PEG-ELS group than the SF-PEG-ELS us-

ers (p=0.008 and p=0.004, respectively). Abdominal pain/cramps were more frequent in the CLD+PEG-ELS group than others (p=0.005).

DISCUSSION

An adequate bowel preparation is the backbone of colonoscopy. Diet control is one of the most critical factors of adequate bowel preparation. In this prospective study, a 1-day CLD was not inferior to a 3-day CMD for colonoscopy preparation in terms of bowel cleaning, the polyp detection rate, and patient tolerance. The median BBPS scores were 9 for both the CLD groups. The polyp detection rate was the highest in the CLD+SF-PEG-ELS group. None of the participants in the CLD groups abandoned the diet and consumption of laxative incomplete due to intolerance or adverse effects. However, the split-dose SF-PEG-ELS was more tolerable than the split-dose PEG-ELS.

Table 2. Overall Boston Bowel Preparation Scale scores (BBPS) and BBPS scores for each segment of the colon of the four groups

	(CLD+PEG-ELS):A (n=124)	(CLD+SF-PEG-ELS):B (n=127)	(CMD+PEG-ELS):C (n=127)	(CMD+SF-PEG-ELS):D (n=29)	p
	Median (Q1/Q3) n (%)	Median (Q1/Q3) n (%)	Median (Q1/Q3) n (%)	Median (Q1/Q3) n (%)	
BBPS total score	9 (6/9)	8 (6/9)	6 (6/9) ^{A,D}	9 (6/9)	0.001 ^{#1}
Left colon, BBPS score					
0	0 (0.0)	0 (0.0)	2 (1.6)	1 (0.5)	0.026 ³
1	4 (3.0)	4 (3.1)	6 (4.7)	3 (2.2)	
2	29 (23.9)	48 (37.8)	59 (46.5) ^A	43 (34.1)	
3	91 (73.1) ^C	75 (59.1)	60 (47.2)	82 (63.2) ^C	
Transvers colon, BBPS score					
0	0 (0.0)	0 (0.0)	2 (1.6)	1 (0.5)	0.012 ²
1	2 (1.5)	7 (5.5)	9 (7.1)	5 (3.8)	
2	41 (32.8)	53 (41.7)	64 (50.4) ^D	44 (34.6)	
3	81 (65.7) ^C	67 (52.8)	52 (40.9)	79 (61.1) ^C	
Right colon, BBPS score					
0	0 (0.0)	0 (0.0)	2 (1.6)	1 (1.1)	0.045 ³
1	7 (6.0)	12 (9.4)	14 (11.0)	7 (5.4)	
2	39 (31.3)	55 (43.3)	61 (48.0)	49 (37.8)	
3	78 (62.7) ^C	60 (47.2)	50 (39.4)	72 (55.7) ^C	

1-day clear liquid diet + polyethylene glycol and electrolyte lavage solution: CLD+PEG-ELS: A

1-day clear liquid diet + sulfate free polyethylene glycol and electrolyte lavage solution: CLD+ SF-PEG-ELS: B

3-day combined diet + polyethylene glycol and electrolyte lavage solution: CMD+PEG-ELS: C

3-day combined diet + sulfate free polyethylene glycol and electrolyte lavage solution: CMD+ SF-PEG-ELS: D

¹Kruskal–Wallis test (Monte Carlo), post-hoc test: Dunn’s test, ²Fisher–Freeman–Halton (Monte Carlo), ³Pearson chi-squared test (Monte Carlo), Q1: Percentile 25%, Q3: Percentile 75%

[#]p (A-C)=0.004, p (A-D)=0.999, p (B-C)=0.405, p (B-D)=0.999, p (C-D)=0.007

It is apparent that the restrictive characteristics of diet preparation might be a deterrent for application to colonoscopy screening (15,16). Moreover, the type of diet has not been described in the present guidelines, and the conditions for when to choose the LRD or the CLD have not been elucidated (10,11). The current strategy given in the guidelines is to leave this choice to the physician. Clinicians should ultimately make adjustment so that the diet is optimal for their population or region (17-20). Multiple factors, such as age, gender, the presence of constipation, eating habits, and kinds and quantities of food consumed, also

affect the result of the choice of diet in the clinical setting (17-20). Turkish cuisine has a wide variety of dishes, with pastries and bread taking the first place, followed by meat dishes and butter (21). Despite the regional differences, there are still common heavy meals in Turkish cuisine (21). People who were asymptomatic and older than 50 years, underwent screening colonoscopy in our study. It would make sense that the CMD would be more appropriate for our patients. However, we observed that shortening the diet duration and simplifying diet list contents might improve the compliance of the patient. Our findings confirmed

Table 3. Polyp detection rates and characteristics of polyps in four groups with different bowel preparation

	(CLD+PEG-ELS):A (n=124) n (%)	(CLD+SF-PEG-ELS):B (n=127) n (%)	(CMD+PEG-ELS):C (n=127) n (%)	(CMD+SF-PEG-ELS):D (n=129) n (%)	p
Detection of colon polyp	50 (40.3)	53 (41.7)	40 (31.5)	50 (39.0)	0.198 ²
Detection of adenomatous polyp ± High-grade dysplasia	37 (29.6)	36 (28.3)	16 (12.5) ^{A,B,D}	37 (28.5)	0.018 ¹
Number of colon polyps>1	28 (22.5)	25 (19.7)	13 (10.3) ^{A,B,D}	27 (21.0)	0.039 ²
Diameter of polyp (maximum)					
Diminutive polyp	15 (30.7)	20 (37.7)	13 (32.5)	20 (39.1)	0.114 ²
5–10 mm	28 (55.3)	25 (47.1)	19 (47.5)	21 (42.9)	
10–20 mm	6 (11.5)	8 (15.2)	7 (17.5)	7 (14.0)	
>20 mm	1 (2.5)	0 (0)	1 (2.5)	2 (4)	

1-day clear liquid diet + polyethylene glycol and electrolyte lavage solution: CLD+PEG-ELS: A

1-day clear liquid diet + sulfate free polyethylene glycol and electrolyte lavage solution: CLD+ SF-PEG-ELS: B

3-day combined diet + polyethylene glycol and electrolyte lavage solution: CMD+PEG-ELS: C

3-day combined diet + sulfate free polyethylene glycol and electrolyte lavage solution: CMD+ SF-PEG-ELS: D

¹Pearson chi-squared test (Monte Carlo), ²Fisher-Freeman-Halton (Monte Carlo), Q1: Percentile 25%, Q3: Percentile 75%

this observation; good or excellent bowel cleanness (BBPS>5) was achieved in the 1-day CLD groups. Patients from both 1-day CLD groups, regardless of their laxative choices, succeeded in achieving a high BBPS score. The consumption of a large variety and quantity of liquids on the day before the colonoscopy rendered the procedure complicated and a 3-day diet unnecessary in our patients. In the literature, it was noticed that studies specifically looking at diet showed almost no differences between the two diet types (22). Stolpman et al. (23) investigated the effect of diet on the bowel cleaning quality. These authors randomized 201 patients to either CLD the day before colonoscopy or a low-residue breakfast and lunch followed by clear liquids for the rest of the day. Sodium sulfate in a split dose was used for all patients. There were no clinically or statistically significant differences in the quality of colon cleaning. Nevertheless, minimal differences were observed in patient tolerance of the regimens, with more bloating in the LRD group and the clear liquid group experiencing slightly more hunger (23). Nguyen et al. (24) reported a meta-analysis of eight randomized controlled studies. There were no statistically significant differences between the LRD and the CLD groups for adequate bowel preparations, and 87% of patients in the LRD group had an adequate bowel

preparation compared with 83.2% (586/704) of patients in the CLD group (24). In a Polish study, Mytyk et al. (25) found that 6-18-year-old children showed no differences between the CLD group and LRD group with regard to a total BBPS score. Moreover, Megna et al. (26) recently reported that CLD was an independent predictive factor of good bowel preparation for chromoendoscopy in patients with inflammatory bowel disease. We believe that the short-term and simplified CLD will be suitable for the Turkish patient population. Although a new meta-analysis has reported that LRD is superior to CLD in terms of patient satisfaction scores, these authors were unable to detect a significant difference in the BBPS scores between the LRD and CLD groups (27). We propose that a 3-day CMD could be offered, especially in patients with previous poor bowel preparation or severe constipation.

It is known that suboptimal examination naturally decreases diagnostic accuracy, results in supererogatory repeat procedures, and yields misadjustment of the intervals of surveillance for neoplastic lesions (28-30). In our study, the polyp detection rates varied between 31.5 and 41.7%. The polyp detection rates in the 1-day CLD groups were not inferior to those in the 3-day CMD groups. Stolpman et al. (23) found that a

Table 4. Assessment of tolerability to diets and laxatives, willingness to follow the same protocol in case of repeat colonoscopy , and comparison of symptoms related to bowel preparation

	(CLD+PEG-ELS):A (n=124)	(CLD+SF-PEG-ELS):B (n=127)	(CMD+PEG-ELS):C (n=127)	(CMD+SF-PEG-ELS):D (n=129)	p
Ease of diet					
Extremely difficult	22 (17.5)	24 (18.9)	20 (15.7)	15 (11.4)	0.056 ¹
Moderately difficult	39 (31.3)	42 (33.1)	35 (27.6)	36 (27.6)	
Slightly difficult	35 (28.8)	31 (24.4)	32 (25.2)	37 (29.1)	
Easy	28 (22.4)	30 (23.6)	40 (31.5)	41 (31.9)	
Ease of laxative					
Extremely difficult	22 (17.4)	15 (11.6)	20 (15.7)	16 (12.4)	0.611 ¹
Moderately difficult	44 (35.4)	33 (26.0)	42 (33.1)	32 (25.0)	
Slightly difficult	33 (26.0)	51 (40.4)	44 (34.6)	48 (37.5)	
Easy	25 (20.2)	28 (22.0)	21 (16.6)	32 (25.1)	
Willingness to repeat colonoscopy					
No	20 (16.4)	21 (16.5)	18 (14.0)	13 (10.3)	0.352 ¹
Yes	104 (83.6)	106 (83.5)	109 (86.0)	116 (89.7)	
Symptoms related to bowel preparation					
Bad taste in the mouth	48 (38.6)	41 (32.6)	53 (41.7)	54 (42.2)	0.068 ¹
Gastric fullness	27 (21.9) ^D	13 (10.2)	30 (24.3) ^{B, D}	8 (6.2)	0.008 ²
Nausea/vomiting	28 (22.8) ^D	15 (11.5)	30 (24) ^D	7 (5.2)	0.004 ²
Bloating/gas/distension	4 (3.4)	3 (2.6)	3 (2.8)	3 (2.0)	0.186 ²
Headache	5 (4.0)	10 (7.9)	9 (7.1)	5 (3.8)	0.448 ²
Abdominal pain/cramps	19 (15.4) ^D	11 (8.7)	8 (6.3)	8 (5.9)	0.005 ²
Lack of sleep	56 (45.5)	51 (40.2)	64 (50.3)	64 (49.6)	0.760 ²

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 3-day combined diet + polyethylene glycol and electrolyte lavage solution: CMD+PEG-ELS: C
 3-day combined diet + sulfate free polyethylene glycol and electrolyte lavage solution: CMD+ SF-PEG-ELS: D
¹Pearson chi-squared test (Monte Carlo), ²Fisher-Freeman-Halton (Monte Carlo)

total of 65.4% of patients in the CLD group had polyps, compared with 68% of patients in the LRD group. This result was not significantly different between the groups (23). Walter et al. (31) reported that the adenoma detection rate was similar between the LRD group vs. clear liquid diet, that is, 35.3% vs. 44.4%, respectively. While these rates were closer to our findings, they found a significantly greater number of adenomas in the clear

liquid diet arm (31). Even though there was no statistical significance, the overall polyp detection rate and the capacity of finding of the polyps smaller than 1 cm were the highest in the 1-day CLD groups in our study. Detection rates of an adenomatous polyp or multiple polyps were significantly lower in the CMD+PEG-ELS group than other groups, which was undoubtedly associated with low-quality bowel preparation in this

group. On the contrary, patients in the 1-day CLD groups achieved higher rates in the detection of an adenomatous polyp and multiple polyps, which was consistent with a higher BBPS score. In other words, we can underline that CLD is quite convenient when it comes to detecting and following up the colon polyps.

Tolerability of the bowel preparation protocol crucially affects the results (32). When comparing the CLD and CMD groups, we detected no differences in the tolerability of diets and laxatives, as well as the willingness to take the same preparation in case of repeated colonoscopy. The CLD was too restrictive and contained insufficient calories, which might have interfered with daily activities. However, its short period and unlimited volume facilitated the patient's adherence. There was no significant difference in diet tolerance between the two diet groups. Those patients who were unwilling to repeat this procedure typically complained of a significantly greater number of adverse gastrointestinal symptoms due to the PEG solutions. Based on randomized studies, it has shown that a split-dose PEG-ELS enhances patients' compliance and tolerability of the preparation by increasing the time required to consume the entire volume of lavage solution (33-35). The consensus of the major gastrointestinal societies is that the choice of agent should be tailored to the individual patient but that a split-dose regimen can be recommended in all cases (10,11). In our study, every group had split-dose PEG-ELS. However, PEG-ELS resulted in more bothersome symptoms than SF-PEG-ELS, such as gastric fullness and nausea/vomiting. Sodium sulfate can increase the micellar properties of the ELS solution, indirectly the lavage effect of laxative. However, the taste of the solution might change to an unfavorable sense so that the tolerance and compliance of the patient might decrease (36).

There are some limitations to our study. First, we should have included the education and socioeconomic status of the patients in the initial assessment of demographic characteristics, which are important factors for optimizing the results of preparation. We could have investigated the correlation between compliance and education and socioeconomic status of the patients. Second, we could have selected just one laxative solution, which would have resulted in more homogenous groups. Yet, we had to divide the groups according to the laxative solutions beside the diet, and SF-PEG-ELS showed a difference as well. It complicated the results unavoidably. Finally, the patients

consuming less than 50% of the laxative solution or who did not adhere to the diet should not have been omitted. Then, the poor compliance might have been interpreted objectively.

In conclusion, our search found that a short-lived diet instead of a prolonged diet, split dose of laxative instead of a large volume solution at once, and more palatable formulations obtained by removing sulfate components were improved to maximize the quality of bowel preparation and patient's tolerability and adherence, and to minimize patient's discomfort. A well-defined CLD without volume restriction would be more appropriate for outpatient colonoscopy. Today, despite the pending additional studies on diet selection, colonoscopists should carefully evaluate any compromise when it comes to the efficacy and tolerability of diet based on patients' individual needs.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Başkent University School of Medicine, the Human Ethics Review Board (Study number: KA18/14).

Informed Consent: Written informed consent was obtained from all patients who participated in this study.

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