Article published online: 2021-11-12

Bowel cleansing efficacy for colonoscopy: prospective, randomized comparative study of same-day dosing with 1-L and 2-L PEG + ascorbate

OPEN ACCESS

Authors

Cátia Arieira[1,2,3], Francisca Dias de Castro[1,2,3], Pedro Boal Carvalho[1,2,3], Joana Magalhães[1,2,3], Sofia Xavier[1,2,3], Carla Sousa[1], Bruno Rosa[1,2,3], José Cotter[1,2,3]

Institutions

1 Gastroenterology Department, Hospital da Senhora da Oliveira, Guimarães, Portugal
2 Life and Health Sciences Research Institute, School of Medicine, University of Minho, Braga/Guimarães, Portugal
3 Life and Health Sciences Research Institute (ICVS)/3B's Research Group, PT Government Associate Laboratory, Braga/Guimarães, Portugal

submitted 27.10.2020
accepted after revision 10.5.2021

Bibliography
Endosc Int Open 2021; 09: E1602–E1610
DOI 10.1055/a-1520-4596
ISSN 2364-3722

Georg Thieme Verlag KG, Rüdigerstraße 14,
70469 Stuttgart, Germany

Corresponding author
Professor José Cotter, Gastroenterology Department, Hospital da Senhora da Oliveira – Guimarães, Rua dos Cutileiros, Creixomil – 4835-044 Guimarães, Portugal
Fax: +0207-837-3000
jabcotter@gmail.com

Supplementary material is available under https://doi.org/10.1055/a-1520-4596

ABSTRACT

Background and study aims Polyethylene glycol (PEG) bowel preparations are effective but associated with high ingestion volume. In this study, 1-L PEG and 2-L PEG preparations were compared in a randomized, colonoscopist-blinded, single-center trial.

Patients and methods Patients were aged >18 years, required colonoscopy, and provided informed consent. Randomization was 1:1 to 1-L PEG or 2-L PEG, based on hospital identification number (odd or even). Preparations were administered using same-day dosing adjusted for colonoscopy start time. The primary endpoint was successful bowel preparation on the Boston Bowel Preparation Scale (BBPS) (no segment scored <2).

Results A total of 852 patients were randomized. In the intention-to-treat (ITT) population, significantly more patients had diabetes in the 2-L PEG arm, resulting in the creation of the modified-ITT population (mITT) that excluded diabetic patients to correct the imbalance (1-L PEG, n = 239; 2-L PEG, n = 238). In the mITT, there was no significant difference in successful cleansing between 1-L PEG and 2-L PEG (88.3 % vs. 82.4 %; $P = 0.067$). Excellent cleansing (BBPS 7–9; no segment <2) was significantly improved with 1-L PEG (60.7 % vs. 50.4 %; $P < 0.024$), as were mean scores in the right and left colon (right: 2.47 vs. 2.30; $P < 0.008$; left: 2.55 vs. 2.39; $P = 0.008$). Adverse events were mild to moderate in intensity and none resulted in discontinuation. Rates of nausea and vomiting were significantly higher with 1-L PEG, but that did not affect successful cleansing.

Conclusions The lower-volume 1-L PEG was associated with higher levels of excellent bowel cleansing and greater mean segmental scores on the BBPS than 2-L PEG.

Introduction

Colonoscopy for colorectal cancer (CRC) screening has been proven to reduce the mortality of CRC, leading to its introduction in many countries as part of national screening programs [1–3]. Visualization of cancerous and pre-cancerous lesions during colonoscopy is dependent on being able to inspect the whole colonic mucosa. This requires effective pre-procedural bowel preparation, which is critical to the success of the procedure and the overall cost-effectiveness of colonoscopy [4–6].

The importance of bowel preparation for successful procedures is highlighted across clinical colonoscopy guidelines and is a key performance measure for the improvement of the quality of colonoscopy procedures [7–9].

Several studies suggest that the success of bowel preparation is influenced by a number of factors, such as the bowel preparation selected, the dosing regimen used, the time between completion of the preparation, and the procedure and patient education (e. g., telephone re-education the day before a colonoscopy) [10–15]. Despite advances in this area, inadequate preparation remains a problem during colonoscopies [7, 8]. According to guidelines from the US Colonoscopy Taskforce, an adequate level of bowel cleansing is one that allows the detection of adenomas > 5 mm in size [9, 16]. For the detection of > 5-mm adenomas, a score of ≥ 6 on the Boston Bowel Preparation Scale (BBPS), with no individual segment scoring < 2, has been shown to be adequate and noninferior to higher levels of cleansing [17]. However, for lesions with a different morphological appearance, such as sessile serrated adenomas, higher than adequate or excellent levels of cleansing may be required for sufficient detection [18]. These flat lesions have been shown to occur more frequently in the right colon than the left, and the right colon is associated with a greater frequency of missed lesions and interval cancers [19–22]. As such, right colon cleansing performance is an important consideration when selecting a bowel preparation for colonoscopy.

Polyethylene glycol (PEG) bowel preparations, commonly combined with ascorbate components, are widely used for bowel preparation due to their consistent efficacy and safety [7]. However, despite their effectiveness, PEG-based bowel preparations may require a high volume of preparation ingestion and thus be limited by patient tolerability and acceptability [23, 24]. 2-L PEG + ascorbate (2-L PEG, MOVIPREP®, Norgine Ltd) has shown superior rates of right colon cleansing efficacy and high rates of excellent cleansing (on the Harefield Cleansing Scale) compared with comparator preparations in studies [25, 26]. A 1-L PEG + ascorbate preparation (1-L PEG, PLENVU, Norgine Ltd) is now also approved for use in Europe and the USA and involves the patient only consuming 1 L of preparation volume plus additional mandatory water [27]. In a clinical trial, 1-L PEG has shown superior levels of right colon cleansing compared with 2-L PEG [28].

In this study, the cleansing efficacy, safety and patient satisfaction of 1-L PEG and 2-L PEG bowel preparations were compared in a randomized, prospective, colonoscopist-blinded, single-center, active-controlled trial. The influence of telephone re-education on how to take the preparations, in addition to usual oral and written communications, was also assessed.

Patient and methods

Trial design and participants

This trial was a prospective, comparative, single-center, randomized, colonoscopist-blinded study conducted at the Gastroenterology Department of the Hospital da Senhora da Oliveira, a university hospital based in Guimarães, Portugal (ClinicalTrials.gov identifier: NCT04497935). Institutional review board approval was granted on November 23, 2018 by the Comissaõ de Ética para a Saúde. The study then ran over a 6-month period beginning on January 1, 2019 with the first patient enrolling on January 7, 2019. The full protocol for the study is available in the supplementary materials.

Eligible participants were any patients aged > 18 years old for whom colonoscopy was requested at the gastroenterology department of the hospital and who provided informed consent to participate. Patients who were excluded from the study were: pregnant or breastfeeding women; patients with gastric obstruction, psychiatric disorders, severe renal impairment (creatinine clearance < 30 mL/min), heart failure (class III-IV), laxative use or dependence, chronic constipation (< 3 stools/week), uncontrolled hypertension (systolic blood pressure, > 170 mm Hg or diastolic blood pressure > 100 mm Hg), intestinal obstruction, any previous intestinal surgery, or severe ascites; and those who refused to participate in the study. Once informed consent was obtained, patients' demographic data were collected, namely, age, sex, weight, height, comorbidities, concomitant medication use, marital status, education level, and area of residence.

Patients were randomized in a 1:1 ratio to receive either 1-L PEG or 2-L PEG for bowel preparation prior to receiving a colonoscopy. Randomization was done by hospital identification number, with even numbers being assigned to 1-L PEG and odd numbers assigned to 2-L PEG. All patients received instructions on how to take the bowel preparation and the associated dietary restrictions during the initial appointment (oral) and also in writing by mail. A low-fiber diet was followed on the day before the colonoscopy, with consumption of clear liquids permitted from starting the first dose of the bowel preparation up until 3 hours before the procedure. Patients were instructed to report all adverse events (AEs) occurring during bowel preparation, including specific mention of headache, abdominal distension, nausea, or vomiting.

Patients in both treatment arms were randomly assigned to receive telephone re-education 2 days before a colonoscopy or no telephone re-education (control group). Telephone re-education was performed by an experienced endoscopy nurse and consisted of a phone call, which was on average 10 minutes long, in which an explanation of the steps required to administer the preparation was given, and any questions the patient had were answered. Patient satisfaction surveys to assess bowel preparation experience were conducted in the clinic prior to the colonoscopy (patient satisfaction survey provided in supplementary materials). All colonoscopy procedures were performed in line with the standard clinical practice protocol of the hospital, with all clinical data, including cleansing data, being recorded during the procedure. Once the colonoscopy was completed, patients were instructed to report any possible AEs for up to 1 month after the procedure.

Treatments

Patients randomized to either 1-L PEG or 2-L PEG were given same-day dosing schedules starting at different times depending on whether their colonoscopy was in the morning or the afternoon, in line with the department's standard protocol.

Overnight split-dosing was not used with any preparation in this study due to local experience of non-adherence from patients with overnight split-dosing for cultural and social reasons.

Patients receiving 1-L PEG who had a colonoscopy in the morning were advised to follow a day-before dosing regimen, where, at 19:00 the day before the colonoscopy, they prepared the Dose 1 sachet in 500 mL of water and consumed it over a period of 30 minutes, followed by 500 mL of clear liquids. The second dose was then taken at 23:00 by mixing the two Dose 2 sachets in a single glass of 500 mL of water and consuming them over 30 minutes, followed by 500 mL of clear liquids. If the colonoscopy was scheduled for the afternoon, the same dosing instructions were given, but the first dose was taken at 07:00 on the day of the procedure, and the second dose began at 10:00.

Patients receiving 2-L PEG who had a colonoscopy in the morning were asked to follow a similar day-before dosing regimen, where, at 19:00 the day before the colonoscopy, the first 1 L dose was consumed over a 1-hour period, followed by the second dose at 23:00. For 2-L PEG patients with procedures in the afternoon, they took Dose 1 at 07:00 and Dose 2 at 10:00. Any patient receiving 2-L PEG was also told to consume 1 L of clear liquids during the preparation procedure.

Outcomes

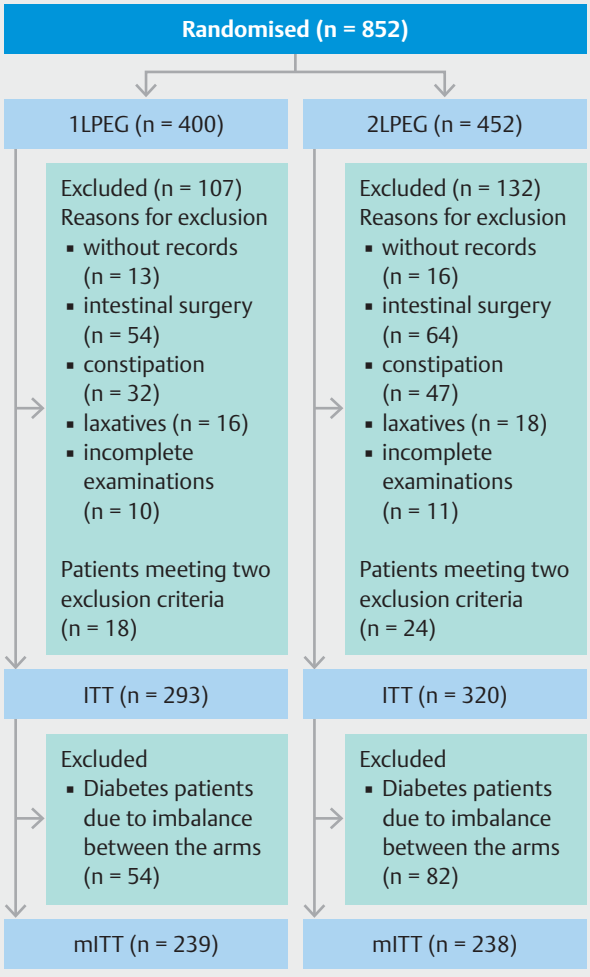
The primary outcome measure of the study was comparative cleansing efficacy between 1-L PEG and 2-L PEG, as assessed on the BBPS [29]. During the colonoscopy, the colonoscopist assessed each of the three colon segments on the BBPS (right colon, including the cecum; transverse colon, including hepatic and splenic flexures; and left colon, including the descending/sigmoid colon and rectum) and assigned each a score of 0 to 3 (0, segment was unclean with non-visualized mucosa due to stools, which cannot be removed; 3, a segment of mucosa easily seen without residues). Successful overall bowel preparation is defined as a BBPS score of >6 with no individual segment scoring <2.

Secondary outcome measures included comparing the quality of bowel preparation in patients who had a morning or afternoon colonoscopy and those who received written, oral and additional telephone re-education on the day before the colonoscopy versus written and oral information only. The level of patient satisfaction with the two bowel preparation regimens was also assessed through a comparative analysis of the patient satisfaction questionnaire (full survey included in the protocol within the supplementary materials).

Statistical methods

Assuming overall cleansing success rates of 90 % for the two groups, and with a noninferiority margin of 5 %, a sample size of 213 patients per group provided at least 90 % power to demonstrate noninferiority of each bowel preparation.

A descriptive analysis was calculated for all variables of interest. Mean values and standard deviations were calculated for all continuous variables where the distribution was normal; median values and percentiles were used otherwise. Comparative analysis between interventions was calculated using the Chi-square test. Statistical analysis was performed using SPSS software, version 23 (IBM, Armonk, New York, United States).



▶ **Fig. 1** Patient disposition.

Results

Patients

Between January and July 2019, 852 patients agreed to participate in the study and were randomized to 1-L PEG (n = 400) or 2-L PEG (n = 452) and subsequently screened for eligibility. After exclusion criteria were applied and those who had their procedure cancelled were removed, there remained 293 and 320 patients available for the analyses in the 1-L PEG and 2-L PEG arms, respectively (the intention-to-treat [ITT] group) (▶ **Fig. 1**).

Baseline characteristics of the patients in the 1-L PEG and 2-L PEG groups are provided in ▶ **Table 1**. Median age (quartiles) was 61 (18–86) years, and 53.5 % of patients were male. Baseline characteristics were balanced between the two treatment groups, with the exception of the proportion of patients with diabetes mellitus, which was lower in the 1-L PEG group than

▶ **Table 1** Baseline characteristics.

	1-L PEG (n = 293)	2-L PEG (n = 320)	*P* value
Median age (quartiles), years	61 (18–86)	61 (18–86)	ns[1]
Male, n (%)	158 (53.9)	170 (53.1)	0.843
Median height (quartiles), m	1.65 (1.46–1.87)	1.64 (1.42–1.97)	ns[1]
Median weight (quartiles), kg	72 (44–115)	71 (38–108)	ns[1]
Median BMI (quartiles), kg/m^2	26.2 (17.9–44.6)	26.3 (11.7–40.0)	ns[1]
Diabetes mellitus, n (%)	54 (18.4)	82 (25.6)	0.032[2]
Oral antidiabetic medications, n (%)	52 (17.7)	80 (25.0)	0.029[2]
Anticoagulants, n (%)	15 (5.1)	20 (6.3)	0.547[2]
Antiplatelets, n (%)	41 (14.0)	46 (14.4)	0.892[2]
Antidepressives, n (%)	43 (14.7)	38 (11.9)	0.306[2]
Reason for colonoscopy, n (%)			
▪ Screening	35 (12.1)	33 (10.5)	0.554[2]
▪ Surveillance	124 (42.8)	155 (49.5)	0.096[2]
▪ Diagnostic	65 (22.4)	66 (21.1)	0.693[2]
▪ Therapeutic	66 (22.8)	58 (18.5)	0.199[2]
Period of colonoscopy, n (%)			
▪ Morning	184 (62.8)	200 (62.5)	0.939[2]
▪ Evening	109 (37.2)	120 (37.5)	0.939[2]

PEG, polyethylene glycol; BMI, body mass index; ns, not significant.
[1] Mann-Whitney U test.
[2] X^2 test.

in the 2-L PEG group (18.4 % vs. 25.6 %, *P* = 0.032). Consequently, the use of oral antidiabetic medications was also lower in the 1-L PEG group (17.7 % vs. 25.0 %, *P* = 0.029). To account for this imbalance between the two treatment groups, it was decided to also conduct all efficacy and safety analyses in a group that excluded all the patients with diabetes from both treatment arms. This group was called the modified-ITT group (mITT).

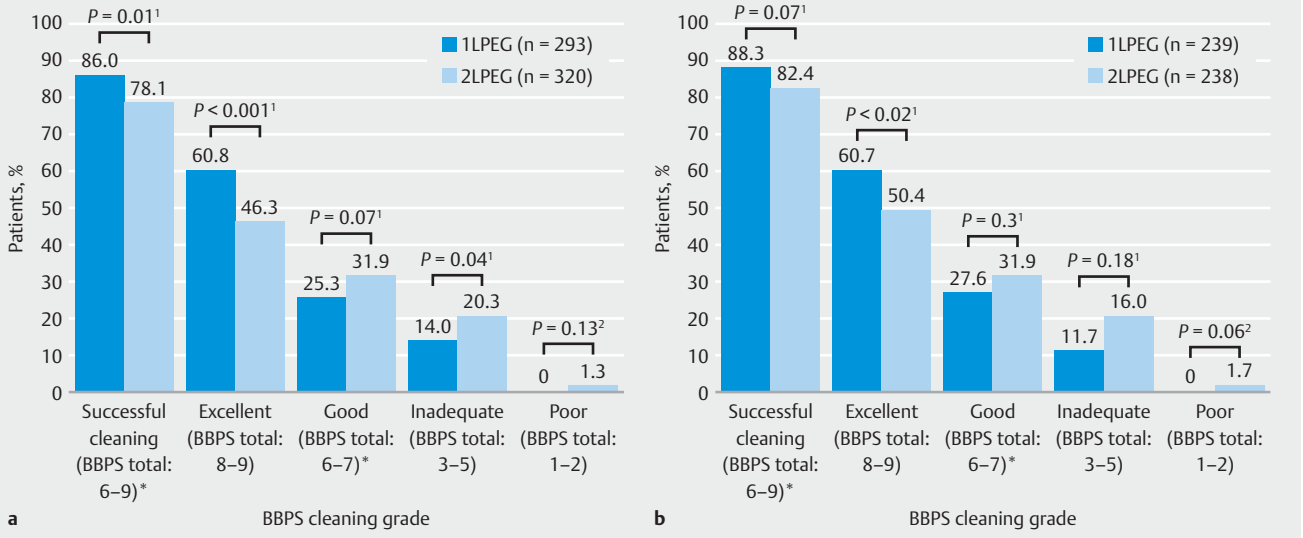
Cleansing efficacy

A comparison of BBPS cleansing grades between 1-L PEG and 2-L PEG is presented in ▶ **Fig. 2**. Overall in the ITT population, 1-L PEG was associated with a significantly higher rate of overall successful bowel cleansing (BBPS score 6–9, 86.0 % vs. 78.1 %; *P* = 0.011) and a significantly improved rate of excellent overall bowel cleansing (BBPS score 8 or 9, 60.8 % vs. 46.3 %; *P* < 0.001) (▶ **Fig. 2a**). After diabetic patients were excluded from the analysis in the mITT population, there was no significant difference in overall successful cleansing rates on the BBPS between 1-L PEG and 2-L PEG (88.3 % vs. 82.4 %; *P* = 0.067) (▶ **Fig. 2b**). However, the overall rate of excellent cleansing remained significantly improved with 1-L PEG vs. 2-L PEG (60.7 % vs. 50.4 %; *P* < 0.024).

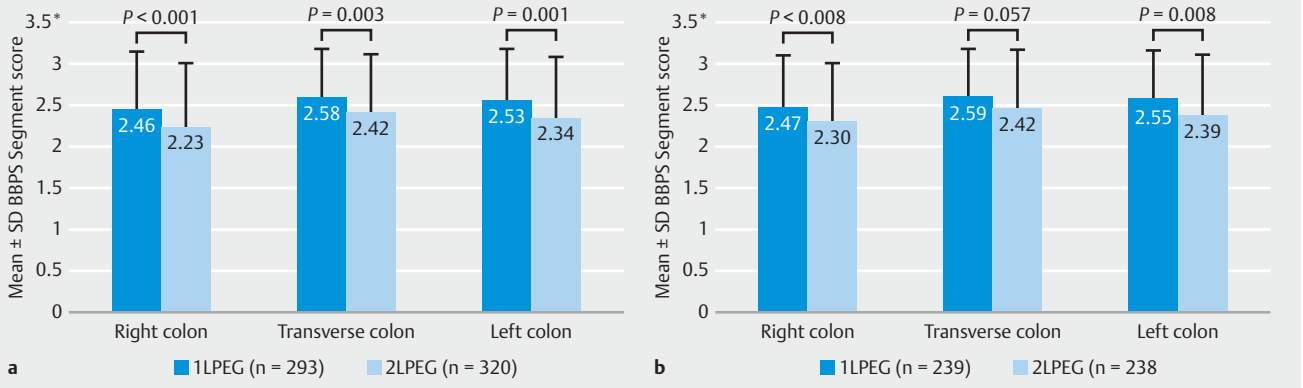
A comparison of mean BBPS segmental cleansing scores between 1-L PEG and 2-L PEG is presented in ▶ **Fig. 3**. In the ITT population, 1-L PEG was associated with a significantly higher mean ± SD cleansing score in the right (2.46 ± 0.67 vs. 2.23 ± 0.76; *P* < 0.001), left (2.53 ± 0.64 vs. 2.34 ± 0.72; *P* < 0.001), and transverse (2.58 ± 0.61 vs. 2.42 ± 0.69; *P* = 0.003) colon compared with 2-L PEG (▶ **Fig. 3a**). After diabetic patients were excluded from the analysis in the mITT population, the mean scores in the right and left colon remained significantly improved with 1-L PEG versus 2-L PEG (▶ **Fig. 3b**).

The timing of the colonoscopy significantly affected the overall success of bowel preparation. Procedures occurring in the morning, after a day-before dosing regimen, had a significantly higher rate of inadequate preparation than procedures occurring in the afternoon, when the colonoscopy dosing regimen was performed in the morning (25.3 % vs. 6.1 %; *P* < 0.001). There were no significant differences between the type of bowel preparation (1-L PEG vs. 2-L PEG) administered and the timing of colonoscopy (*P* = 0.939).

In the ITT population, a total of 205 patients received a telephone re-education call, in addition to oral and written instructions (1-L PEG n = 104; 2-L PEG n = 101). Patients who received a telephone call were significantly older (age: 63 (18–84) years vs. 60 (18–86) years; *P* = 0.031) and also more frequently had their colonoscopy scheduled for the morning (78.0 % vs. 55.2 %; *P* < 0.001). Overall, there was no significant improvement in the rate of the successful bowel preparation as measured by the BBPS when patients received additional telephone



▶ **Fig. 2** Bowel cleansing efficacy assessed by BBPS grade with 1-L PEG and 2-L PEG in the **a** ITT population and **b** mITT population. Statistical tests: [1]X^2 test; [2]Fisher exact test. *No individual segment scored < 2.



▶ **Fig. 3** Mean ± SD BBPS segmental cleansing scores with 1-L PEG and 2-L PEG in the **a** ITT population and **b** mITT population. Statistical tests: Student's t-test. *Individual BBPS segment maximum score = 3.

re-education compared with those who only received oral and written information on bowel preparation (82.4% vs. 81.4%; $P = 0.762$).

Safety

Adverse events experienced by patients in each treatment group are presented in ▶ **Table 2**. All AEs were mild to moderate in intensity, and none resulted in patients discontinuing the bowel preparations. Overall, there were significantly more incidences of nausea (43.0% vs. 28.8%; $P < 0.001$) and vomiting (19.1% vs. 9.4%; $P = 0.001$) in patients receiving 1-L PEG compared with 2-L PEG. Successful bowel cleansing was achieved in all patients experiencing nausea and vomiting. Incidence of nausea was significantly higher in patients receiving their colonoscopy in the morning than in those having an afternoon procedure (38.8% [149/384] vs. 30.1% [69/229], $P = 0.03$). The incidence of vomiting was also higher but was not significantly different (15.4% [59/384] vs. 11.8% [27/229], $P = 0.21$). Incidences of AEs in the mITT population are presented in **Supplementary Table 1**.

Patient satisfaction survey

The results of the patient satisfaction survey in the ITT population are presented in ▶ **Table 3**. The majority of patients in both arms rated the overall experience of taking the bowel preparation as reasonable or better. If another colonoscopy was required, significantly more patients in the 2-L PEG arm would have the same bowel preparation again compared with the 1-L PEG arm (64.1% vs. 48.1%; $P < 0.001$). The vast majority in both arms would not have refused to repeat the preparation although refusal was higher with 1-L PEG (18.4% vs. 11.3%; $P =$

▶ **Table 2** Adverse events (ITT population).

Adverse effects, n (%)	1-L PEG	2-L PEG	*P* value
All patients, n	293	320	
▪ Headache, n (%)	25 (8.5)	31 (9.7)	0.62
▪ Abdominal distension, n (%)	43 (14.7)	45 (14.1)	0.841
▪ Nausea, n (%)	126 (43.0)	92 (28.8)	<0.001
▪ Vomiting, n (%)	56 (19.1)	30 (9.4)	0.001
Nausea and vomiting by procedure time			
▪ Morning procedure, n	184	200	
▪ Nausea, n (%)	84 (45.7)	65 (32.5)	0.008
▪ Vomiting, n (%)	36 (19.6)	23 (11.5)	0.029
▪ Afternoon procedure, n	109	120	
▪ Nausea, n (%)	42 (38.5)	27 (22.5)	0.008
▪ Vomiting, n (%)	20 (18.3)	7 (5.8)	0.003

Statistical comparison: X^2 test.
ITT, intention to treat; PEG, polyethylene glycol.

0.012). Patient satisfaction survey results for the mITT are published in **Supplementary Table 2**.

Discussion

In this large, prospective, comparative, single-center, randomized, colonoscopist-blinded trial, the cleansing efficacy and safety of, and patient satisfaction with, two PEG-based bowel preparations were compared in a real-world group of patients undergoing routine colonoscopy in a clinical gastroenterology department. In this setting, 1-L PEG was associated with a higher rate of overall successful bowel cleansing and excellent-level bowel cleansing on the BBPS, as well as significantly improved mean segmental cleansing scores in the right and left colon compared with 2-L PEG.

The imbalance of patients with diabetes between the two arms required correction after randomization as diabetes is a known risk factor for inadequate bowel preparation. Once the imbalance was removed, 1-L PEG appeared to deliver a higher, but not significantly so, level of overall successful bowel cleansing compared with 2-L PEG. 1-L PEG did show additional performance at the excellent cleansing level in the right and left colon.

These results appeared to broadly reflect the efficacy results of the Phase III MORA study, a large, randomized, multicenter, active-controlled, comparative clinical trial that compared 1-L PEG with 2-L PEG [28]. In the MORA study, 1-L PEG was associated with noninferior levels of overall bowel cleansing success on the BBPS (and also the Harefield Cleansing Scale [HCS]) [30], but was also associated with superior right colon cleansing on both the BBPS and HCS. Post hoc analysis of the MORA trial also showed that 1-L PEG was associated with a significantly increased number of segments with excellent cleansing on the HCS [31].

The advantages of higher-than-adequate cleansing at the whole colon level remain inconsistently reported [18, 32–34]. However, studies have shown that excellent levels of cleansing in the right colon support greater detection of flat or sessile serrated adenomas and that these types of adenomas are favorably distributed in the right colon versus the left [18, 21, 22]. Interval cancers, caused by missed lesions, are also significantly more likely to occur in the right colon as compared with the left [20]. Therefore, there does appear to be an additional clinical need for considering the right colon cleansing performance when selecting a bowel preparation for colonoscopy.

Our study also found that there was no additional benefit from telephone re-education to the success of bowel preparation. The extent to which this result was influenced by the significantly greater proportion of patients who received a telephone call also having their colonoscopy scheduled for the morning is not clear, as the study also showed morning colonoscopy was associated with significantly greater levels of inadequate preparation. However, good oral clarification of the importance of bowel preparation during appointments and well-written patient information seem to be sufficient to reinforce the importance of preparation to the success of colonoscopy and in delivering adequate levels of cleansing.

Overall, all AEs reported by patients were mild to moderate and did not result in discontinuation or cleansing failures. Nausea and vomiting were more frequently observed with 1-L PEG than 2-L PEG. The majority of patients receiving both treatments rated the preparation experience as reasonable or better (good or excellent), although there was a small increase in the proportion of patients rating the experience negatively who received 1-L PEG.

▶ **Table 3** Patient satisfaction survey results from patients receiving either 1-L PEG or 2-L PEG (ITT population).

Variables, n (%)	1-L PEG (n = 293)	2-L PEG (n = 320)	*P* value
Global experience			
▪ Excellent	4 (1.4)	3 (0.9)	0.619
▪ Good	66 (22.5)	78 (24.4)	0.590
▪ Reasonable	143 (48.8)	183 (57.2)	0.046
▪ Weak	61 (20.8)	48 (15.0)	0.060
▪ Bad	19 (6.5)	8 (2.5)	0.016
Consume the entire preparation as instructed	293 (100)	320 (100)	–
How you classify the ease of preparation			
▪ Very easy	2 (0.7)	2 (0.6)	0.930
▪ Easy	70 (23.9)	76 (23.8)	0.967
▪ Tolerable	137 (46.8)	172 (53.8)	0.084
▪ Difficult	66 (22.5)	64 (20.0)	0.445
▪ Very difficult	18 (6.1)	6 (1.9)	0.006
Flavor of preparation			
▪ Excellent	0 (0)	1 (0.3)	0.552
▪ Good	32 (10.9)	55 (17.2)	0.026
▪ Tolerable	124 (42.3)	160 (50.0)	0.047
▪ Weak	102 (34.8)	83 (25.9)	0.013
▪ Bad	35 (11.9)	21 (6.6)	0.021
Would you like to repeat the preparation			
▪ No	152 (51.9)	115 (35.9)	<0.001
▪ Yes	141 (48.1)	205 (64.1)	<0.001
Would you refuse to repeat?			
▪ No	239 (81.6)	284 (88.8)	0.012
▪ Yes	54 (18.4)	36 (11.3)	0.012
Patient had a previous colonoscopy	254 (86.7)	275 (85.9)	0.787
Patient had a different bowel preparation for this procedure	248 (97.6)	196 (71.5)	<0.001
Preparation this time was			
▪ More pleasant	108 (44.4)	78 (40.6)	0.475
▪ Less pleasant	111 (45.7)	86 (44.8)	0.854
▪ Equal	24 (9.9)	28 (14.6)	0.133

Statistical tests: X^2 test.
L-PEG, polyethylene glycol; ITT, intention to treat.

There were also higher rates of nausea and vomiting observed in this study compared with the MORA trial for both treatments. 2-L PEG, which was administered as an overnight split-dosing regimen in the MORA trial, was associated with nausea and vomiting rates of 3.4% and 1.1% of patients compared with rates of 28.8% and 9.4% in this study with same-day dosing. As MORA contained both an overnight split-dosing and morning-only dosing arm for 1-L PEG, it is possible to compare against the morning-only regimen (for afternoon procedures) used in this study. In MORA, nausea and vomiting were reported by 4.8% and 6.3% of patients, compared with 38.5% and 18.3% in this study. One reason for this difference might be the differences in AE reporting between a randomized clinical trial and our real-world study (physician assessed vs. patient

reported). In MORA, overnight split-dosing of 1-L PEG was associated with a lower rate of vomiting (3.8 %) compared with morning-only dosing (6.3 %), suggesting this regimen might result in reduced incidence of vomiting. However, due to cultural and social reasons, overnight split-dosing of bowel preparations is associated with low adherence in the population served by our gastroenterology department. Therefore, the standard protocol for colonoscopies is to use the same-day dosing regimens used in this study, which are adjusted to the procedure time. It is also possible that the particular flavor or sweetness of 1-L PEG was less palatable for the population examined in our study than in other populations, such as in the United States. In the NOCT study, which was conducted in multiple sites in the United States, overnight split-dose 1-L PEG appeared to have greater acceptability of taste (66.7 % of patients rating it as very acceptable or acceptable) than in our study, although different patient questionnaires were used, so the results were not directly comparable [35].

The limitations of this study include the use of a different dosing regimen to that recommended in clinical guidelines, the initial imbalances of baseline characteristics between the groups, the real-world nature of the study, the low educational level in the population (assessed at enrollment), and that patients were instructed to report particular adverse events during the bowel preparation procedure. The initial imbalances in diabetes patients were corrected after randomization. As patients were asked to report specific AEs of interest and those that are the most common AEs associated with bowel preparation, it is possible that this resulted in over-reporting, particularly for more subjective AEs, such as nausea.

Conclusions

In conclusion, in this real-world randomized study, 1-L PEG was associated with higher levels of excellent bowel cleansing and greater mean scores in individual bowel segments on the BBPS than 2-L PEG. Both preparations were well tolerated, with most AEs being mild-to-moderate. Incidence of nausea and vomiting appeared higher in patients treated with 1-L PEG than 2-L PEG, but had no impact on bowel preparation completion.

Acknowlegements

These data were submitted and accepted for presentation at the European Society of Gastrointestinal Endoscopy (ESGE) Days 2020 meeting prior to the cancellation of the meeting. The authors would like to thank all the patients for their participation in the study. Medical writing assistance was provided by Rory Elsome, BSc (TVF Communications, London, UK) and funded by Norgine Ltd. The study was sponsored by the Gastroenterology Department of the Hospital of Senhora da Oliveira – Guimarães.

Competing interests

Dr. Rosa has a consulting services agreement with Medtronic.

References

[1] Nishihara R, Wu K, Lochhead P et al. Long-term colorectal-cancer incidence and mortality after lower endoscopy. N Engl J Med 2013; 369: 1095–1105

[2] Brenner H, Chang-Claude J, Jansen L et al. Reduced risk of colorectal cancer up to 10 years after screening, surveillance, or diagnostic colonoscopy. Gastroenterology 2014; 146: 709–717

[3] Kaminski MF, Wieszczy P, Rupinski M et al. Increased rate of adenoma detection associates with reduced risk of colorectal cancer and death. Gastroenterology 2017; 153: 98–105

[4] Rex DK, Imperiale TF, Latinovich DR et al. Impact of bowel preparation on efficiency and cost of colonoscopy. Am J Gastroenterol 2002; 97: 1696–1700

[5] Clark BT, Rustagi T, Laine L. What level of bowel prep quality requires early repeat colonoscopy: systematic review and meta-analysis of the impact of preparation quality on adenoma detection rate. Am J Gastroenterol 2014; 109: 1714–1724

[6] Anderson JC, Butterly LF, Robinson CM et al. Impact of fair bowel preparation quality on adenoma and serrated polyp detection: data from the New Hampshire colonoscopy registry by using a standardized preparation-quality rating. Gastrointest Endosc 2014; 80: 463–470

[7] Hassan C, Bretthauer M, Kaminski MF et al. Bowel preparation for colonoscopy: European Society of Gastrointestinal Endoscopy (ESGE) guideline. Endoscopy 2013; 45: 142–150

[8] Kaminski MF, Thomas-Gibson S, Bugajski M et al. Performance measures for lower gastrointestinal endoscopy: a European Society of Gastrointestinal Endoscopy (ESGE) Quality Improvement Initiative. Endoscopy 2017; 49: 378–397

[9] Johnson DA, Barkun AN, Cohen LB et al. Optimizing adequacy of bowel cleansing for colonoscopy: recommendations from the U.S. multi-society task force on colorectal cancer. Gastrointest Endosc 2014; 80: 543–562

[10] Spada C, Cannizzaro R, Bianco MA et al. Preparation for colonoscopy: Recommendations by an expert panel in Italy. Dig Liver Dis 2018; 50: 1124–1132

[11] 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

[12] Tariq H, Kamal MU, Sapkota B et al. Evaluation of the combined effect of factors influencing bowel preparation and adenoma detection rates in patients undergoing colonoscopy. BMJ Open Gastroenterol 2019; 6: e000254

[13] 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

[14] Lee YJ, Kim ES, Choi JH et al. Impact of reinforced education by telephone and short message service on the quality of bowel preparation: a randomized controlled study. Endoscopy 2015; 47: 1018–1027

[15] Gálvez M, Zarate AM, Espino H et al. A short telephone-call reminder improves bowel preparation, quality indicators and patient satisfaction with first colonoscopy. Endosc Int Open 2017; 5: E1172–E1178

[16] Lieberman DA, Rex DK, Winawer SJ et al. Guidelines for colonoscopy surveillance after screening and polypectomy: a consensus update by the US Multi-Society Task Force on Colorectal Cancer. Gastroenterology 2012; 143: 844–857

[17] 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 quiz e14-15

[18] Clark BT, Laine L. High-quality Bowel preparation is required for detection of sessile serrated polyps. Clin Gastroenterol Hepatol 2016; 14: 1155–1162

[19] Fischbach W, Elsome R, Amlani B. Characteristics of right-sided colonic neoplasia and colonoscopy barriers limiting their early detection and prognosis: a review of the literature. Expert Rev Gastroenterol Hepatol 2018; 12: 585–596

[20] 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

[21] 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

[22] 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

[23] Kim SH, Kim JH, Keum B et al. A randomized, endoscopist-blinded, prospective trial to compare the efficacy and patient tolerability between bowel preparation protocols using sodium picosulfate magnesium citrate and polyethylene-glycol (1 L and 2 L) for Colonoscopy. Gastroenterol Res Pract 2020; 2020: 9548171

[24] Munsterman ID, Cleeren E, van der Ploeg T et al. Pico-Bello-Klean study: effectiveness and patient tolerability of bowel preparation agents sodium picosulphate-magnesium citrate and polyethylene glycol before colonoscopy. A single-blinded randomized trial. Eur J Gastroenterol Hepatol 2015; 27: 29–38

[25] Bitoun A, Ponchon T, Barthet M et al. Results of a prospective randomised multicentre controlled trial comparing a new 2-L ascorbic acid plus polyethylene glycol and electrolyte solution vs. sodium phosphate solution in patients undergoing elective colonoscopy. Aliment Pharmacol Ther 2006; 24: 1631–1642

[26] Ell C, Fischbach W, Layer P et al. Randomized, controlled trial of 2 L polyethylene glycol plus ascorbate components versus sodium phosphate for bowel cleansing prior to colonoscopy for cancer screening. Curr Med Res Opin 2014; 30: 2493–2503

[27] Plenvu powder for oral solution – Summary of Product Characteristics (SmPC) – (eMC). https://www.medicines.org.uk/emc/product/8578

[28] Bisschops R, Manning J, Clayton LB et al. Colon cleansing efficacy and safety with 1 L NER1006 versus 2 L polyethylene glycol + ascorbate: a randomized phase 3 trial. Endoscopy 2019; 51: 60–72

[29] 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

[30] Halphen M, Heresbach D, Gruss H-J et al. Validation of the Harefield Cleansing Scale: a tool for the evaluation of bowel cleansing quality in both research and clinical practice. Gastrointest Endosc 2013; 78: 121–131

[31] Repici A, Coron E, Sharma P et al. Improved high-quality colon cleansing with 1L NER1006 versus 2L polyethylene glycol + ascorbate or oral sulfate solution. Dig Liver Dis 2019; 51: 1671–1677

[32] Calderwood AH, Thompson KD, Schroy PC et al. Good is better than excellent: bowel preparation quality and adenoma detection rates. Gastrointest Endosc 2015; 81: 691–699.e1

[33] Pontone S, Hassan C, Maselli R et al. Multiple, zonal and multi-zone adenoma detection rates according to quality of cleansing during colonoscopy. United European Gastroenterol J 2016; 4: 778–783

[34] Adike A, Buras MR, Gurudu SR et al. Is the level of cleanliness using segmental Boston bowel preparation scale associated with a higher adenoma detection rate? Ann Gastroenterol 2018; 31: 217–223

[35] DeMicco MP, Clayton LB, Pilot J et al. Novel 1 L polyethylene glycol-based bowel preparation NER1006 for overall and right-sided colon cleansing: a randomized controlled phase 3 trial versus trisulfate. Gastrointest Endosc 2018; 87: 677–687.e3