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A new low-volume isosmotic polyethylene glycol solution plus bisacodyl versus split-dose 4 L polyethylene glycol for bowel cleansing prior to colonoscopy: A randomised controlled trial

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ABSTRACT

Background: 4-L polyethylene glycol preparations are effective for colon cleansing before colonoscopy. However, large volume and unpleasant taste reduce tolerability and acceptability limiting patient compliance. A new isosmotic low-volume polyethylene glycol preparation with citrates and simethicone plus bisacodyl has been developed to improve patient compliance and tolerability.
Aim: To compare the efficacy of 2 different regimens of preparation vs a split-dose of polyethylene glycol solution.
Patients and methods: In this randomised, blinded, comparative study, 153 patients were allocated to 3 arms. Arm 1 ($n = 52$) received bisacodyl and 2-L polyethylene glycol with citrates and simethicone the day before the procedure. Arm 2 ($n = 50$) received bisacodyl the day before and 2-L polyethylene glycol with citrates and simethicone on the day of colonoscopy. Control group ($n = 51$) received a split-dose of 4-L polyethylene glycol. Cleansing was evaluated according to Ottawa scale.
Results: The mean Ottawa score was not different in the 3 groups. Excellent cleansing was observed more frequently in arm 2 (70%) than in controls (49%) ($p < 0.05$). No serious adverse events were observed in the 3 regimens. The willingness to repeat the same bowel preparation was superior in arms 1 and 2 than in controls ($p < 0.001$).
Conclusions: New low-volume preparations seem to be as effective as the split 4-L polyethylene glycol regimen, showing a better tolerability and acceptability.

1. Introduction

Colorectal cancer (CRC) is the second most common cancer as well as the second leading cause of cancer-related mortality in Europe [1]. Screening and early detection of adults >50 years old have reduced the incidence and mortality over the last 15 years. Colonoscopy, the gold standard for detection of early signs of CRC, was fundamental in achieving this important success against this cancer [2]. Bowel preparation is an important quality measure for colonoscopy. Inadequate bowel cleansing may have negative consequences for the examination, including incomplete visualisation of the colon, missed detection of lesions, procedural difficulties, prolonged procedure time and reduced interval time for follow-up with significant economic impact [3]. The ideal preparation should completely and rapidly empty the colon of any material (solid, liquid, gaseous) without any effect on the gross or microscopic appearance of the colon, not cause significant shifts of fluids or electrolytes and be well tolerated and accepted by the patient [4].

Polyethylene glycol (PEG) osmotically balanced electrolyte solutions pass through the bowel without significant absorption or secretion. These preparations are therefore a safe option in patients with serum electrolyte imbalance, acute and chronic renal insufficiency and congestive heart failure [5,6] PEG is usually administered as a 4 L solution in order to achieve a satisfactory level of cleansing. However this large volume has been shown to reduce the tolerability and compliance of the bowel preparation [7]. Indeed, patient surveys have identified that the most critical step of the whole colonoscopy procedure is the large volume of liquid which needs to be ingested. This therefore creates a barrier to removing fear from patients and obtaining complete adhesion to screening campaigns. To overcome this limitation, low-volume preparations have been proposed. A new isosmotic low-volume sulphate-free PEG 2 L preparation with citrates and simethicone (PEG-CS) is now available to be used in combination with bisacodyl to improve tolerability, acceptability and compliance. The primary

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Table 1
Comparison of PEG-CS and standard PEG bowel preparations.

	PEG-CS	Standard PEG
Active ingredients	PEG, citrates, simethicone	PEG, sodium sulphate
Additional agent	Bisacodyl	–
Product description	4 sachets each containing 60.7 g of PEG 4000, 1.066 g of sodium citrate, 1.25 g of citric acid, 80 mg of simethicone	4 sachets each containing 58.32 g of PEG 4000 and 5.69 g of sodium sulphate
Mixed with	0.5 L of water	1 L of water
Total volume	2 L	4 L
Electrolytes	Sodium chloride, potassium chloride	Sodium chloride, potassium chloride, sodium bicarbonate
Osmolality (mosmol/kg)	293	285
Diet prior to colonoscopy	Clear liquid after starting solution intake	Clear liquid after starting solution intake
Bowel prep schedule[a]	Day before regimen Hour 16.00 bisacodyl 2–4 tablets Hour 20.00 PEG-CS 2 L	Split-dose The day before Hour 19.00 PEG 3 L The same day Hour 07.00 PEG 1 L
	Same day regimen Hour 22.00 bisacodyl 2–4 tablets Hour 06.00 PEG-CS 2 L	

PEG-CS, polyethylene glycol with citrates and simethicone; PEG, polyethylene glycol.
[a] Day before and same day are referred to the day of the colonoscopy.

aim of our trial was to compare 2 L PEG-CS + bisacodyl tablets given either the same day or the day before with split-dose 4 L PEG in outpatients undergoing elective colonoscopy, in terms of cleansing level.

2. Patients and methods

This is a randomised, observer-blind, parallel 3-arm, active control study including consecutive outpatients undergoing routine elective colonoscopy at the Digestive Endoscopy Unit of the Catholic University of Rome. The study protocol and informed consent form were approved by the Institutional Review Board. Outpatients aged 18–85 years undergoing routine elective colonoscopy and providing written informed consent were eligible for participation in the study. Exclusion criteria were as follows: known or suspected gastrointestinal obstruction or perforation; toxic megacolon; major colonic resection; pregnant or at risk of becoming pregnant and lactating women; known or suspected hypersensitivity to the active or other ingredients. 2 L PEG-CS (PEG 4000, sodium citrate, citric acid, simethicone and electrolytes, LOVOL-esse, Promefarm, Milano, Italy) is available as a powder for oral solution; the content of each sachet is dissolved in 500 mL of water giving a total of 2-L of isosmotic solution. In order to reduce total volume and improve patient tolerability and compliance, this new 2 L formulation is combined with the administration of 2–4 bisacodyl 5 mg coated tablets (Lovol-dyl, Promefarm, Milano, Italy). Patients received standard questions about their bowel habits. Patients with normal habits received 3 tablets, patients with higher bowel frequency or unformed-liquid stools received 2 tablets and those with infrequent, hard stools or difficult evacuation received 4 tables.

The standard 4 L PEG (polyethylene glycol 4000 with electrolyte lavage solution, SELG 1000, Promefarm) is approved worldwide for bowel preparation before colonoscopy. Detailed regimens for each arm are provided in Table 1. During a pre-endoscopic visit, patients were instructed on dietary restriction and received written instructions. Patients in each treatment group were requested to follow a low-residue diet for the last 3 days and clear liquid since the start of bowel preparation up to the procedure. All patients enrolled in this study were scheduled for colonoscopy since 11 am. Patients having a >2 h journey to reach the hospital were scheduled for afternoon colonoscopy session (2 pm–6 pm). On the day of the procedure, a second pre-endoscopic visit was performed to assess tolerability, safety, acceptability and compliance. Patients were randomly assigned to the study regimen according to a computer-generated randomisation list.

Eligible patients were sequentially numbered and received the corresponding bowel preparation pack from an investigator who did not interfere with the endoscopist who evaluated the colonic cleansing level. The study was observer blind: the endoscopists were not allowed to perform any activities associated to study preparation prior and after colonoscopy and had to avoid any discussion with the patients and the staff which could disclose the type of bowel preparation used. The examinations were performed by experienced endoscopists (>500 procedures in their medical career). A standard colonoscope (EVIS EXERA II video colonoscope CF-Q145I®, Olympus Europe Holding GmbH) was used for the examinations. For colonoscopy a conscious sedation (i.e. a combination of Petidine and Midazolam) was administered. Bowel cleansing was evaluated using the Ottawa scale [8] that is routinely used in our centre to classify the colon cleansing level. This scale requires that each section of the colon, i.e. right, mid and rectosigmoid is rated for level of cleansing according to a 5-point scale (0–4). In addition, the overall colonic fluid is rated according to a 3-point scale (0–2). As a result, the total score ranges from 0 to 14. In addition, a secondary efficacy analysis was done on the following ordered classes: total score 0–3 = excellent; 4–6 = good; 7–10 = fair; 11–14 = poor. Adequacy of the visualisation of colorectal mucosa was also assessed by using a specific 3-point scale: 1 = good (clear imaging, no or minimal amount of bubbles or foam, which could be easily removed); 2 = fair (modest amount of bubbles and foam, which could be cleared, with loss of time); 3 = poor (presence of foam and bubbles, which significantly reduced the clear visualisation of the mucosa). Completeness of the examination, total time and withdrawal time were also recorded.

Patients filled in a bowel preparation questionnaire prior to their examination and were interviewed by the study physician not involved in the endoscopic procedure. Safety was evaluated through reported adverse events, physical examination and vital signs. No laboratory evaluation was made. Tolerability was based on the occurrence and severity of the gastrointestinal symptoms associated with the bowel preparation reported on an ad hoc questionnaire. Symptoms of nausea, bloating, abdominal pain/cramps and anal irritation were scored on a 5-point scale: 0 = no distress; 1 = mild; 2 = moderate; 3 = severe; 4 = very severe.