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ORIGINAL ARTICLE

A randomized controlled trial comparing polyethylene glycol + ascorbic acid with sodium picosulphate + magnesium citrate solution for bowel cleansing prior to colonoscopy

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Abstract
Introduction Adequate bowel cleansing which is acceptable to the patient is a prerequisite for safe and effective colonoscopy. A 2-L polyethylene glycol solution containing ascorbic acid and electrolytes (PEG-Asc) is an alternative to sodium picosulphate + magnesium citrate (SPS-Mg) for bowel preparation. The aim of the current study is to compare PEG-Asc to SPS-Mg in terms of tolerability and efficacy.
Methods This was a single blind, randomized controlled trial. A blinded assessment of bowel cleansing was made by the attending endoscopist. Patients completed a questionnaire on the acceptability of the preparation.
Results One hundred and thirty (130) consecutive patients attending for day case colonoscopy were randomly allocated to bowel preparation with PEG-Asc ($n = 66$) or SPS-Mg ($n = 64$). More patients found PEG-Asc to taste unpleasant (37.9 vs. 10.9 %, $P < 0.001$) and more patients found PEG-Asc to be a more distressing preparation than SPS-Mg (15.1 vs. 4.7 %, $P = 0.043$). However, there was no difference in the proportion of patients being able to complete bowel preparation (PEG-Asc vs. SPS-Mg, 92.4 vs. 93.8 %, $P = 0.520$). There was no detectable difference between PEG-Asc and SPS-Mg in the quality of cleansing with a good or very good preparation being reported by the endoscopist in 46.9 and 54.5 % of cases, respectively ($P = 0.242$).
Conclusions More patients find PEG-Asc to taste unpleasant and to be a more distressing preparation than SPS-Mg. However, there was no detectable difference between PEG-Asc and SPS-Mg in bowel cleansing prior to colonoscopy.

Keywords Bowel preparation · Colonoscopy · Polyethylene glycol · Ascorbic acid · Sodium picosulphate · Magnesium citrate

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Introduction

Adequate bowel cleansing is vital for safe and accurate colonoscopy. To be successful, the preparation must be both acceptable to the patient and effective. Patients can find many of the formulations unacceptable, in particular the taste and side effects such as headache, nausea and vomiting. The latter may result in significant non-compliance and thus a poor preparation. Inadequate preparation may result in missed lesions [1], increased procedure time, a need for repeat colonoscopy [2] as well as a reluctance to undergo repeat examinations.

There are many methods and preparations for bowel cleansing. Oral lavage with either polyethylene glycol (PEG) or sodium picosulphate (SPS)-based solutions have gained widespread acceptance. A recent meta-analysis of 6,459 patients demonstrated PEG and SPS are comparable in bowel-cleansing ability, but more patients are able to complete SPS than PEG and PEG results in more adverse events than SPS [3]. This is likely due to the salty taste and large volume of the 4-L PEG solution.

A 2-L PEG-based solution has been developed for improved patient acceptability. This contains ascorbic acid, which has a known osmotic laxative effect and a more

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pleasant taste. This 2-L preparation (PEG-Asc) or Moviprep™ when compared to standard 4-L PEG has equivalent colonic cleansing [4–6] and side effects [6] but improved taste and acceptability [4, 5]. The performance of PEG-Asc against SPS-based preparations is less well established. Until recently, only one small study [7] had evaluated both PEG-Asc and SPS-Mg, demonstrating overall superior colonic cleansing with PEG-Asc but an equivalent side effect profile with SPS-Mg. However, in a randomized study comprising of 285 patients, Manes et al. [8] reported equivalent bowel-cleansing ability between the two preparations although tolerability and palatability were better with SPS-Mg. In view of these existing differences in the literature, the aim of our study was to compare PEG-Asc with SPS-Mg in an appropriate cohort of patients scheduled to undergo elective colonoscopy. The primary endpoint of this study was patient tolerability and the secondary endpoint was efficacy of bowel preparation.

Materials and methods

Study design

This was a prospective, single centre, single blinded randomized controlled trial. Adult patients aged over 18 years referred for a colonoscopy with no known colonic malignancy or inflammatory bowel disease were eligible for inclusion. Exclusion criteria included gastrointestinal obstruction or perforation, toxic megacolon or colitis, untreated or uncontrolled arterial hypertension, known renal insufficiency (serum creatinine >100 μmol/L), symptomatic congestive heart failure or recent myocardial infarction. Patients were enrolled from the Surgical Day Ward at St. Columcille's Hospital, Loughlinstown, Dublin between March and July 2010. Written informed consent was obtained from all patients participating in the study, and the protocol was approved by the ethics committee of the hospital and was designed, conducted and monitored in accordance with the principles of the World Medical Association.

Randomization

Patients were randomized to receive either 2 L of PEG-Asc (polyethylene glycol 200 g, sodium sulphate 15 g, sodium chloride 5.4 g, potassium chloride 2 g, ascorbic acid 9.4 g and sodium ascorbate 11.8 g), Moviprep™ (Norgine Pharmaceuticals Ltd, Harefield, UK) or 300 mL of SPS-Mg (sodium picosulphate 10 mg, magnesium oxide 3.5 g, citric acid 12.0 g, potassium hydrogen carbonate 0.5 g, saccharin sodium 0.06 g and orange flavour 0.06 g), Picolax™ (Ferring Pharmaceuticals, Langley, UK). The randomization was performed according to the patients chart number. Patients with even numbers were assigned PEG-Asc and patients with odd numbers, SPS-Mg. The prescription was provided by a physician who was not involved with performing the colonoscopy and detailed instructions for the preparation of the solutions, dosing instructions and diet recommendations, to be followed prior to colonoscopy, were provided to each patient. The relevant pharmaceutical companies were not involved in the study design, did not supply any reagents and did not provide technical assistance.

Preparation instructions

PEG-Asc was presented as four sachets of powder (two A sachets and two B sachets) to be reconstituted in 2 L of water taken on the day prior to the colonoscopy. Each litre had to be drunk over a period of 1–2 h, and patients were advised to take at least 1 L of additional clear fluid after each dose. The comparator solution, SPS-Mg was presented as two sachets, to be reconstituted in 300 mL of water, which was taken on the day prior to the colonoscopy. Additionally, patients were advised to drink at least 2 L of additional clear fluid after completion. All patients were allowed a normal diet until the afternoon before the day of the colonoscopy and thereafter clear fluids only. The volume of additional fluid was not monitored, and patients were only asked if they took the specified additional clear fluid as per the directions of dosing, which was based on the respective products' summary of product characteristics. All colonoscopies were performed the morning following preparation.

Data collection

On arrival at the Surgical Day Ward, patients completed a questionnaire to record their experience of the preparation. Unfortunately, data regarding the medication history of the patients were not collected at that time. One of the four experienced colonoscopists, blinded to the type of preparation administered to the patient, performed the examination and scored the adequacy of bowel cleansing, and specifically whether it was necessary for the patient to return for another colonoscopy because of insufficient colon cleansing, using a slightly modified, but previously validated scoring system [8]. Carbon dioxide was used as the insufflating agent during all examinations.

Statistical analysis

This study was designed to demonstrate that PEG-Asc was superior in taste to SPS-Mg. Twenty to thirty-two percent (20–32 %) of patients find SPS-Mg to taste 'good' [9, 10]. To detect a clinically significant improvement from 25 %

Table 1 Patient demographics

	SPS-Mg	PEG-Asc	*P* value
Total (*n*)	64	66	–
Age, mean (SD)[a]	57.2 (15.6)	59.3 (15.6)	0.440
Sex, male (%)	27 (42.2 %)	37 (56.1 %)	0.080

SD standard deviation

[a] ANOVA, all others Fisher's exact test

of patients finding SPS-Mg to taste 'good' to 50 % of patients finding PEG-Asc to taste 'good', with a power of 80 % and an α value of 0.05, 58 patients (two-sided test) would be required per arm. In view of the potential failure of caecal intubation and the failure of patients to complete the bowel preparation prescribed, the number of subjects to be recruited was increased by 12 % from 116 to 130.

Data are presented as mean (standard deviation) or number affected (*n*, %) as appropriate. Differences between groups were compared by analysis of variance (ANOVA) for continuous variables and Fisher's exact test for categorical variables. Data analysis was carried out using SPSS version 12.0 (SPSS, Chicago, IL, USA).

Results

One hundred and thirty consecutive patients met the inclusion criteria and were randomized. There were no dropouts and follow-up data were available on all patients. Sixty-six patients received PEG-Asc and 64 patients received SPS-Mg. The two patient groups were demographically similar (Table 1).

There was no difference in the proportion of patients able to complete the respective preparation. Sixty patients in the SPS-Mg group, and 61 in the PEG-Asc group were able to complete the preparations fully (93.8 vs. 92.4 % respectively, $P = 0.520$). The remaining four (6.2 %) patients in SPS-Mg group and 5 (7.6 %) in the PEG-Asc were able to complete more than half of the prescribed solution. More patients found SPS-Mg to taste pleasant relative to PEG-Asc (31.3 vs. 13.6 %, $P = 0.013$). More patients experienced dizziness with SPS-Mg relative to PEG-Asc (25 vs. 12.1 %, $P = 0.047$). However overall, more patients found PEG-Asc to be a more distressing preparation to take than SPS-Mg (15.1 vs. 4.7 %, $P = 0.043$) (Table 2).

There was no significant difference in the endoscopists' impression of the adequacy of bowel preparation between SPS-Mg and PEG-Asc. There was no detectable difference in good/very good (46.9 vs. 54.5 %, $P = 0.242$), fair (28.1 vs. 27.3 %, $P = 0.535$) and poor (25 vs. 18.2 %, $P = 0.232$) preparations between SPS-Mg and PEG-Asc (Table 3). In 5.4 % of cases, the assessment of the caecum was judged to be suboptimal because of inadequate preparation. There was no difference between SPS-Mg and PEG-Asc (6.3 vs. 4.5 %, $P = 0.718$).

Table 2 Patient reported outcomes

	SPS-Mg	PEG-Asc	*P* value
Ability to complete	60 (93.8 %)	61 (92.4 %)	0.520
Taste			
Pleasant	20 (31.3 %)	9 (13.6 %)	**0.013**
Tolerable	37 (57.8 %)	32 (48.5 %)	0.187
Unpleasant	7 (10.9 %)	25 (37.9 %)	**<0.001**
Nausea	15 (23.4 %)	25 (37.9 %)	0.055
Vomiting	3 (4.7 %)	5 (7.8 %)	0.376
Dizziness	16 (25 %)	8 (12.1 %)	**0.047**
Abdominal cramps	29 (45.3 %)	29 (43.9 %)	0.508
Sleep disturbance	25 (39.0 %)	22 (33.3 %)	0.310
Peri-anal discomfort	28 (43.8 %)	29 (43.9 %)	0.562
Overall impression			
No problem	46 (71.9 %)	38 (57.6 %)	0.064
Bothersome	15 (23.4 %)	18 (27.3 %)	0.382
Distressing	3 (4.7 %)	10 (15.1 %)	**0.043**

Data are presented as *n* (%) and compared by Fisher's exact test

Bold values are statistically significant ($p < 0.05$)

Table 3 Endoscopic assessment of bowel preparation (modified from Saunders et al. [8])

	SPS-Mg	PEG-Asc	*P* value
Good/very good			
Small amount of fluid residue, easily suctioned allowing a complete, reliable examination	30 (46.9 %)	36 (54.5 %)	0.242
Fair			
Enough residue, fluid or solid, to prevent a completely reliable examination (i.e., small polyps <5 mm could be missed)	18 (28.1 %)	18 (27.3 %)	0.535
Poor			
Large amount of residue, endoscopic view uninterpretable: additional cleansing required	16 (25.0 %)	12 (18.2 %)	0.232

Data are presented as *n* (%) and compared by Fisher's exact test

Discussion

The current study has demonstrated that there is no difference in the proportion of patients being able to complete bowel preparation with PEG-Asc or SPS-Mg. However,

more patients found PEG-Asc to taste unpleasant and more patients found PEG-Asc to be a more distressing preparation than SPS-Mg. In addition, there was no significant difference in the quality of bowel cleansing as assessed by the attending endoscopist although it is worth noting that the study was underpowered to detect such a difference between the two preparations.

An ideal bowel preparation for colonoscopy is one that is easy to administer, has a rapid onset of action, allows close to 100 % mucosal visualization so that abnormalities are seen, is cheap, and above all is safe and acceptable to the patient. Although a number of different preparations are available, there is no single, well-tolerated agent that will achieve a completely clean bowel in all patients. Therefore, a key efficacy outcome measure for trials of bowel preparation is the quality of bowel cleansing. While the current study was not powered to compare adequacy of bowel cleansing between PEG-Asc and SPS-Mg, no significant difference was observed despite a prior study demonstrating that patients are more likely to have a higher overall quality of bowel cleansing with PEG-Asc [7]. Our findings are in line with those of Manes et al. [8] who demonstrated equivalent colonic cleansing between PEG-Asc and SPS-Mg.

Patients in this study found SPS-Mg to be a more acceptable preparation to take than PEG-Asc. More patients found PEG-Asc to taste unpleasant and to be overall, significantly more distressing. This is surprising given the proposed advantages of PEG-Asc [11] but has been observed in prior comparisons with SPS-Mg [7]. However, the adverse event of dizziness occurred more frequently in those receiving SPS-Mg. Despite these factors, the ability of patients to complete the individual preparations was not affected.

The 2-L PEG-Asc is equivalent to the standard 4-L PEG solution in the quality of bowel cleansing achieved, but has demonstrated improved compliance and palatability [4, 11]. While prior studies have shown successful bowel-cleansing rates to be higher for PEG-Asc than those observed in the current study [5, 6], these trials utilized split-dose administration techniques which significantly improve the number of satisfactory bowel preparations and increase patient compliance [12]. In patients prepared with PEG-Asc, bowel cleansing is worse when patients undergo colonoscopy in the morning, compared to afternoon procedures [6]; all our patients underwent their colonoscopy in the morning. Had the included patients undergone split-dosage PEG-Asc administration with an afternoon examination this may have affected the resultant conclusions. There was a surprisingly high poor preparation rate associated with both SPS-Mg and PEG-Asc in the current study, which is unacceptable in view of the recommendations put forward by the Joint Advisory Group (JAG) on Gastrointestinal Endoscopy (http://www.thejag.org.uk/downloads%5CUnitResources%5CBSGQualityandSafetyIndicators.pdf). Possible explanations for this include a deficiency in the information provided to the patients regarding the oral preparation solution, inadequacies in the scoring system employed or non-uniformity among endoscopists regarding assessment of colonic cleansing.

This study is limited by a number of factors. It was powered to detect an improvement in taste, a proposed advantage of PEG-Asc, when compared to SPS-Mg, based on prior comparative studies with PEG alone [9, 10]. However, Worthington et al. [7] did note patients taking SPS-Mg generally found the taste better than those taking PEG-Asc, and Manes et al. [8] in a study published after closure of the current trial also noted PEG-Asc to have an inferior taste to SPS-Mg; thus, the current study may have been underpowered. In addition to being a single centre randomized controlled trial, it was not powered for the assessment of bowel cleansing, and the adenoma detection rate or the adequacy of cleansing in each individual bowel segment was not assessed. Superior detection of both adenomas and flat sessile, serrated polyps in the right colon is a key determinant of choice of bowel preparation and the absence of data on these factors is a significant weakness. In addition, there are significant concerns that sessile, serrated polyps are particularly likely to be missed with picosulphate-based preparations. Moreover, the bowel preparation scoring system employed in the trial is significantly different from currently used scales (such as the Aronchick [13], modified Aronchick [14], Ottawa Bowel Preparation Scale [15], Harefield Cleansing Scale [16] and the Boston Bowel Preparation Scale [17]) and may be associated with significant intra- and inter-observer variability, in turn accounting for the results observed.

Despite these limitations, the current study demonstrates that there is no difference in the proportion of patients able to complete PEG-Asc and SPS-Mg for elective, diagnostic colonoscopy and there was no significant difference in the adequacy of bowel cleansing as assessed endoscopically. More patients however find PEG-Asc to taste unpleasant and be a more distressing preparation.

Conflict of interest None to declare.

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