

Oral Sulfate Solution versus Polyethylene Glycol as a Single-Day Preparation for Colonoscopy: A Randomized Control Trial

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Abstract

Background Colonoscopy is a principal diagnostic tool for most colonic disorders. Adequate bowel preparation is essential for proper visualization of the mucosa. The aim of this study was to compare the tolerability, efficacy, and safety profile of 1 L of oral sulfate solution (OSS) in comparison to 2 L of polyethylene glycol (PEG) solution.

Methods In this single-center prospective study conducted at our institute, patients were randomly assigned to receive either OSS or PEG solutions for colonoscopy preparation. Patients enrolled in either group completed a questionnaire assessing the taste of the solution used, adverse effects, and number of stools passed. Grading of the bowel cleansing quality was done as per Boston Bowel Preparation (BBP) score.

Results Total of 400 patients, with 222 patients in the PEG group and 178 patients in the OSS group, were assessed. In the PEG group, 148 (66.75%) patients were males and in the OSS group 112 (62.9%) patients were males. There was no statistical significance on comparison of the taste as “good” or “bad” in both groups. All the adverse events were mild to moderate in intensity and their frequencies were comparable for both the groups. The OSS group had better bowel preparation as per the BBP score ($p = 0.021$) and lesser cecal intubation time ($p = 0.028$).

Conclusion The present study demonstrated that 1 L of OSS is better than the well-established 2 L PEG solution, in terms of bowel preparation and shorter time to cecal intubation.

Keywords

- ▶ colonoscopy preparation
- ▶ oral sulfate solution
- ▶ polyethylene glycol

Introduction

Colonoscopy is performed as a principal diagnostic tool in most colonic disorders. Adequate bowel preparation is essential for proper visualization of the colonic mucosa. Superior cleansing minimizes the risk of missing lesions, need for repeat procedure and associated increase in cost of colonoscopy, improves cecal intubation, and decreases patient's discomfort.^{1,2}

Per oral polyethylene glycol (PEG) solution has been the most commonly used cleansing agent in recent years. This is a nondigestible, nonabsorbable, osmotically balanced laxative lavage solution, that does not alter fluid and electrolyte

balance.^{3–6} The oral sulfate solution (OSS) has been a recently developed formulation which can be administered as a same-day regimen for bowel preparation. In earlier studies, OSS has shown not to alter the serum electrolyte balance and also urine from study subjects did not commonly form a calcium precipitate.^{7,8} Unlike sodium phosphate, high doses of OSS administered to rats and dogs showed no evidence of soft tissue or kidney calcification.⁹ However, the major benefit of OSS is that only 1 L of solution has to be consumed, as compared with 2 L of PEG solution. This may increase patient's comfort. The purpose of this study was to compare the tolerability, efficacy, and safety profile of OSS in comparison to PEG solution.

Patients and Methods

This was a randomized, double-blinded, single-center study conducted at our institute from July 2018 to February 2019. Patients aged more than 18 years, from the outpatient and inpatients department, who were scheduled to undergo colonoscopy were enrolled. A written informed consent was obtained from each patient. Patients with > 50% colon resection, severe constipation (< 1 bowel movement per week), known or suspected gastroparesis, severe nausea or vomiting, bowel obstruction, cardiac and renal failure, pregnancy, and lactation were excluded. The eligible patients were randomly assigned by the envelope method to OSS and PEG groups by endoscopy room staff not involved in the colonoscopy procedure.

All study procedures were performed by trained gastroenterologists. Patients in the PEG group were asked to consume 137.15 g of commercially available PEG powder with electrolytes in 2 L of water to prepare a solution. In the OSS group, 117 mL of OSS was mixed with cold or normal water as required to make a total solution of 500 mL. Two such bottles were given to the patient, each of which had to be consumed over 10 to 20 minutes, keeping a gap of 1 hour in between the two. Preparations in both the groups were initiated 6 to 8 hours before the colonoscopy.

All the enrolled patients completed a questionnaire assessing the taste of the solution, adverse effects, and number of stools passed for either group. Adverse effects, like nausea, vomiting, abdominal pain, headache, fatigability, and others, were scored on a 5-point scale, where 1 = "none"; 2 = "mild"; 3 = "bothersome"; 4 = "distressing"; and 5 = "severely distressing." This scale has been used in earlier bowel cleansing studies.⁷ Total time taken to complete the procedure, cecal intubation and extubation time, was noted by the endoscopist performing the procedure. Grading of the preparation quality was done as per the Boston Bowel Preparation (BBP) score, which has excellent interobserver reliability, and is proven to be related to the endoscopy outcome.^{10,11} Total BBP score³ of 6 was taken as adequate preparation and score of < 6 was considered inadequate preparation.¹²⁻¹⁴

Statistical Analysis

Statistical Analysis was performed with the help of Epi Info 3.5.3. Epi Info is a trademark of the Centers for Disease Control and Prevention. Descriptive statistical analysis was performed to prepare the tables. Comparison between the groups was done with Mann-Whitney, chi-square, and *t*-test as needed. Statistical difference was considered significant when *p*-value was < 0.05.

Results

During the study period, 400 outpatients were evaluated, out of which 222 (55.5%) patients received PEG preparation and 178 (44.5%) received OSS preparation. In the PEG group 148 (66.75%) patients were males and in the OSS group 112 (62.9%) patients were males. The mean (\pm standard deviation) age of patients in the PEG group was 43.87 (\pm 13.52) years

and in the OSS group was 43.89 (\pm 13.67) years (*p* = 0.91).

► **Table 1** shows various indications for which colonoscopy was performed in both the groups. Clinically suspected irritable bowel syndrome and constipation were the most common indication in both the groups. When the taste sensation was compared on the basis of questionnaire, "good taste" was observed in 134 (60.4%) patients in the PEG group and 101 (56.7%) patients in the OSS group. The comparison between the two groups was not statistically significant (*p* = 0.57). Similarly, the rest of the patients observed "bad taste" which was also not statistically significant (*p* = 0.57) between the two groups. The colonoscopy findings were comparable in the PEG and OSS groups (► **Table 2**).

In both the groups, the most common complaint after consumption of PEG and OSS was nausea, vomiting, and abdominal bloating. The frequencies of reported adverse events, including nausea, vomiting, abdominal pain, abdominal bloating, headache, fatigue, and reeling to the head, were comparable in both the groups (► **Table 3**). All the adverse events were mild to moderate in intensity. No serious adverse events occurred in both the groups.

Complete examination of the colon was possible in 390 (97.5%) patients. Ten patients required repeat preparation. There was no difference in the two groups for the requirement of repeat preparation (2.7% vs. 2.2%, *p* = 0.88). For assessment of cleanliness, quality was assessed in 390 patients in whom complete colonoscopy could be achieved. The significant difference (*p* = 0.021) was seen favoring the OSS group in bowel cleansing as per the BBP score (► **Table 4**). The time required for cecal intubation was 5.23 \pm 3.35 minutes in the OSS group as compared with 6.05 \pm 4.1 minutes in the PEG group, which was significantly less (*p* = 0.028). We also found that as the number of stools passed after consumption of either preparation were higher than 6, BBP score also improved (*p* = 0.001).

Table 1 Indications of colonoscopy in the two groups

Indication	PEG (n = 222)	OSS (n = 178)
Irritable bowel syndrome	70 (31.5)	74 (41.5)
Inflammatory bowel disease	12 (5.4)	11 (6.2)
Pain abdomen	19 (8.5)	10 (5.6)
Gastrointestinal bleed	25 (11.3)	14 (7.1)
Constipation	61 (27.5)	47 (26.4)
Diarrhea	13 (5.9)	9 (5)
Anemia	6 (2.7)	3 (1.7)
Significant weight loss	2 (0.9)	2 (1.2)
Colorectal cancer screening	3 (1.3)	2 (1.2)
Suspected partial intestinal obstruction	1 (0.5)	0
Fissure in ano	2 (0.9)	1 (0.6)
Ileocecal ulcer	5 (2.2)	2 (1.2)
Polypectomy	2 (0.9)	0
Abdominal Koch's	1 (0.5)	3 (1.7)

Abbreviations: OSS, oral sulfate solution; PEG, polyethylene glycol. Note: The indications were comparable in both groups (*p* > 0.05).

Table 2 Colonoscopy findings in both groups, n (%)

Colonoscopy findings	PEG (n = 216)	OSS (n = 174)
Normal	127 (58.8)	108 (62.1)
Colonic polyp	17 (7.8)	12 (6.9)
Hemorrhoids	14 (6.4)	11 (6.4)
Ileal ulcer	25 (11.4)	17 (9.8)
Fissure in ano	4 (1.8)	2 (1.1)
Hemorrhoid + Fissure	1 (0.5)	2 (1.1)
Inflammatory bowel disease	5 (2.3)	3 (1.7)
Abdominal Koch's	4 (1.8)	3 (1.7)
Diverticulosis	4 (1.8)	3 (1.7)
Proctitis	5 (2.3)	7 (4)
Worm infestation	1 (0.5)	0
Colonic ulcer	3 (1.4)	2 (1.1)
Ileocolonic ulcer	4 (1.8)	2 (1.1)
Solitary rectal ulcer syndrome	1 (0.5)	0
Carcinoma colon	0	1 (0.6)
Telangiectasia	2 (0.9)	1 (0.6)

Abbreviations: OSS, oral sulfate solution; PEG, polyethylene glycol.
Note: The colonoscopy findings were comparable in both groups ($p > 0.05$).

Discussion

The diagnostic accuracy of colonoscopy depends on the quality of bowel preparation. The adenoma detection rate is low if mucosal visualization is inadequate.¹⁵ Patient compliance and tolerability to the preparation agent is of utmost importance for a successful colonoscopy. The safety of the drug used for colonoscopy preparation is also an important consideration. There is an ongoing search for the ideal cleansing preparation, aiming at better patient compliance, shorter colonic preparation time, and better cleansing effects. Consumption of PEG is often associated with poor patient tolerance. In this study, we compared new OSS with PEG solution.

There were no differences in adverse effects with either preparation. Bowel cleansing quality was better in the OSS groups than in PEG. Cecal intubation was also significantly less in the OSS group. These combined with smaller volumes of ingestion with OSS preparation suggests OSS to be the preferred agent compared with PEG.

Di Palma et al⁷ in their study showed that patients receiving the entire OSS preparation in a day reported slightly increased gastrointestinal events and higher vomiting scores compared with 4-L PEG-electrolyte lavage solution (ELS). However, this was not seen in the split-dose regimen. Rex et al¹⁶ in a multicenter study of 136 patients receiving OSS

Table 3 Incidence of adverse events, n (%)

Symptom scoring	PEG (n = 222)					OSS (n = 178)					p
	1	2	3	4	5	1	2	3	4	5	
Nausea	149 (67.1)	59 (26.6)	8 (3.6)	6 (2.7)	0	109 (61.2)	52 (29.2)	11 (6.2)	6 (3.4)	0	0.81
Vomiting	209 (94.2)	8 (3.6)	2 (0.9)	3 (1.3)	0	161 (90.5)	12 (6.7)	4 (2.2)	1 (0.6)	0	0.89
Cramps	213 (96)	9 (4)	0	0	0	170 (95.5)	3 (1.7)	3 (1.7)	2 (1.1)	0	0.88
Bloating	189 (85.1)	32 (14.4)	0	1 (0.5)	0	155 (87)	20 (11.2)	2 (1.2)	1 (0.6)	0	0.84
Headache	220 (99)	1 (0.5)	0	1 (0.5)	0	177 (99.4)	1 (0.6)	0	0	0	0.89
Fatigue	214 (96.4)	8 (3.6)	0	0	0	177 (99.4)	0	1 (0.6)	0	0	0.85
Other	221 (99.5)	0	1 ^a (0.5)	0	0	178 (100)	0	0	0	0	0.89

Abbreviations: OSS, oral sulfate solution; PEG, polyethylene glycol.
Note: 1, None; 2, Mild; 3, Bothersome; 4, Distressing; 5, Severely distressing.
^aReeling of the head.

Table 4 Preparation grade according to Boston Bowel Preparation (BBP) score, n (%)

Grade	PEG (n = 220)	OSS (n = 178)	p
Adequate (BBP \geq 6), n (%)	122 (55.5)	119 (66.9)	(0.021)
Inadequate (BBP < 6), n (%)	98 (44.5)	59 (33.1)	

Abbreviations: OSS, oral sulfate solution; PEG, polyethylene glycol.

versus 4-L of SF-PEG-ELS showed, patients who ingested the OSS had less bloating, more successful preparation, and more frequent achievement of an excellent preparation (71.4% vs. 34.3%, $p = 0.01$). Rex et al¹⁶ recently reported the results of a multicenter study that compared split-dose OSS with split-dose sodium picosulfate/magnesium citrate. Among 338 patients randomized to receive either preparation, OSS resulted in a higher rate of success (excellent or good) preparation (94.7% vs. 85.7%; $p = 0.006$) and more excellent preparations (54% vs. 26%; $p < 0.001$) compared with sodium picosulfate/magnesium citrate. Both preparations were well tolerated, and there was no difference in treatment emergent adverse events in both groups. Joshi et al¹⁷ in their cohort of 141 patients, compared PEG versus OSS preparation. Sulfate preparation resulted in better bowel cleansing ($p = 0.01$). Age, gender, and dosing schedule of preparation, including bedtime dosing of stimulant laxative, did not alter the BBP score. Nearly 15.4% of patients in their cohort reported side effects to these preparations. Our study has the limitations that we are not able to comment on “adenoma miss rate” due to study design. More study with a large number of patients may be required to validate our data.

The present study, however, demonstrated that 1 L OSS is better than well-established 2 L of PEG solution, in terms of bowel preparation and shorter time to cecal intubation with similar adverse events. More studies with a larger number of patients may be required to validate our data.

Conflict of Interest

None declared.

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