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# Evaluation of parameters influencing the quality of colon preparation with a split-dose regimen of sulfate salts

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## Abstract

**Background** Bowel cleansing is an important factor for the quality of colonoscopy. We aimed to evaluate the efficacy of split-dose oral sulfate salts on bowel preparation and to determine parameters influencing the quality of bowel cleaning.

**Method** Consecutive adults who completed their preparation for colonoscopy with a regimen of sulfate salts were enrolled.

**Results** Of the 446 patients, 11 were excluded from the analysis. Among the 435 patients, 257 (59.1%) were female, mean age was 62.0±11.6 years and median body mass index (BMI) 26.1 kg/m$^2$ (interquartile range [IQR] 23.8-29.4). Indications for colonoscopy were screening 155 (35.6%), surveillance 102 (23.5%), or other 178 (40.9%). The median time between the end of second dose of the preparation regimen and colonoscopy initiation was 5:15 h (IQR 4:30-6:00, min: 2:20, max: 12:20). Minor adverse events were reported in 62 (14.3%) patients. BBPS=9 was observed in 279 (64.14%) patients. Segmental BBPS=3 was achieved in 387 (88.97%), 346 (79.54%) and 289 (66.44%) patients (P<0.001) in the descending, transverse and ascending colon, respectively. Multivariate analysis revealed that BMI (odds ratio [OR] 1.05, 95% confidence interval [CI] 1-1.1) and time between the end of the second laxative dose and colonoscopy initiation (OR 1.25, 95%CI 1.08-1.45) were associated with poorer bowel preparation.

**Conclusions** A split dose of oral sulfate salts is an efficacious and well tolerated regimen. Obesity and a longer time interval between the end of the second dose and colonoscopy initiation negatively influence bowel cleanliness.

**Keywords** Colonoscopy, bowel preparation, oral triphosphate

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## Introduction

Currently, colorectal cancer (CRC) is the third most common and the second most deadly cancer [1,2]. The burden of CRC may increase in coming years, considering the rising incidence of early onset colorectal cancer [3]. Primary prevention is the principal strategy to reduce CRC [4]. Currently, either colonoscopy or noninvasive methods, such as the fecal immunochemical test, are used for CRC screening.

Bowel preparation is a key performance indicator for the quality of colonoscopy [5] and is closely related to the efficacy of the examination [6]. Inadequate bowel preparation is associated with a lower adenoma detection rate [7,8], longer lasting examinations and more adverse events. Even nowadays,

inadequate bowel preparation still occurs in approximately 10-20% of cases [9].

Polyethylene glycol (PEG)-based solutions have been widely used for decades as bowel-cleansing agents, with good efficacy and without serious complications. However, the patients may encounter various difficulties during preparation intake, leading to a suboptimal result. One of the major barriers towards widely accepted colonoscopy is the large volume of conventional (PEG) preparation solutions (4 L) and their poor taste. These factors often cause patients to either postpone or avoid colonoscopy, or to be less compliant in completing their preparation, resulting in a poor outcome.

Oral sulfate salts (OSS) represent a valid alternative for colonoscopy preparation with well-documented efficacy and safety. Several randomized controlled trials have compared OSS to PEG solutions, revealing comparable efficacy. Most of the studies have been conducted in Asia (Korea [10-12], Japan [13]) and the USA [14]. Although data from Europe [15] are rather limited, the European Society of Gastrointestinal Endoscopy include OSS in the recommended preparation regimens [16].

Factors that influence bowel preparation have been studied mainly with PEG solutions, while studies that specifically examine these factors with OSS are limited. The tolerance profile of OSS solutions has been shown to be better than that of PEG-based solutions [17].

Based on our department's experience, we have been empirically administering OSS for colonoscopy preparation for the last 5 years, because we observed a better tolerance and compliance compared with the PEG solutions administered previously. The aim of our study was to evaluate the efficacy of OSS preparation and to prospectively investigate factors that may influence bowel cleaning in a split-dose regimen.

## Patients and methods

In this non-interventional single-center study we prospectively collected data from patients receiving OSS before colonoscopy for different indications in routine clinical practice. The study was registered in ClinicalTrials.gov under the identifier NCT05107505 and was approved by the hospital ethics committee.

Patients were consecutively recruited from the gastroenterology department of Alexandra General Hospital in Athens from July 1, 2021, to June 30, 2022. Written informed consent was obtained from the patient or their legally acceptable representative before their entry into the study.

### Study population

The study enrolled consecutive adult patients, capable of understanding the procedure, who had completed their colonoscopy preparation with OSS, and were willing to participate. Indications for colonoscopy included screening, post-polypectomy surveillance, and symptomatic investigation. Demographic information and medical history were documented.

Patients younger than 18 years, patients with suspected gastrointestinal occlusion, active inflammatory bowel disease, significant gastroparesis, gastric outlet obstruction or severe renal failure (end-stage renal disease requiring dialysis), as well as pregnant and lactating women, were excluded from the study. Those who had an improper laxative intake (omission of 1 of the 2 doses of the split-dose regimen) were also excluded.

### OSS/Study medication and preparation regimen

Before colonoscopy, all participants were given both verbal and written instructions on the diet and preparation intake. They were also given the option for additional clarifications via telephone or email. The participants were instructed to follow a non-fiber diet for 3 days prior to the procedure with emphasis on the last day before the procedure. According to our preparation regimen, patients were instructed to take 10 mg of bisacodyl on the evening 2 days before the examination.

We administered a commercial OSS solution (EZICLEN®), consisting of sodium sulfate, magnesium sulfate, potassium sulfate and flavoring agents in aqueous liquid form, in a split-dose regimen. OSS solution (EZICLEN®) is supplied in 2 176 mL bottles, each bottle containing 17.510 g sodium sulfate, 3.276 g magnesium sulfate and 3.130 g potassium sulfate. The content of each bottle has to be diluted with water to a solution with a final volume of 500 mL.

Proper intake requires ingestion of both bottles of OSS. Each dose of 500 mL OSS solution is followed by at least an additional 1 L of water during a 2-h period. The first dose is administered during the afternoon of the previous day and the second the day of the examination, aiming to complete the preparation 3-4 h before the start of colonoscopy. Our patients were allowed to drink water freely until 2 h before the procedure.

To evaluate the tolerability and acceptance of OSS for bowel preparation, a questionnaire was administered before the procedure. This questionnaire recorded the patient's diet prior to the examination, the exact time and duration of laxative intake, and the percentage of liquid consumed compared to the prescribed amount. Additionally, safety was evaluated through this questionnaire by assessing the adverse events.

All colonoscopies were performed by either a senior gastroenterologist or a trainee under senior supervision. Bowel cleansing adequacy was evaluated globally and by colonic segment, according to the Boston Bowel Preparation scale (BBPS) [18], with the necessary photo-documentation. Under the BBPS, a score of 9 is considered optimal whereas scores 6-8 are considered suboptimal. Global BBPS scores <6 or segmental scores <2 were excluded.

All colonoscopies were performed using high-definition endoscopes (Olympus CF-H185L, CF-HQ190L) with $CO_2$ insufflation. A water pump was also always available for use at the endoscopist's discretion. Bowel cleanliness was evaluated after its use.

Regarding sedation, all patients received a combination of midazolam and propofol, administered by trained gastroenterologists. Patients were monitored for pulse rate, oxygen saturation ($SaO_2$) levels and blood pressure throughout the procedure.

### Statistical analysis

Categorical variables were described as relative and absolute frequencies, while continuous ones were expressed as mean ± standard deviation, or median (interquartile range [IQR], minimum – maximum). The effect of covariates on the odds of having a suboptimal colon preparation was examined using univariate and multivariate logistic regression. We used McNemar's exact test to compare the optimal bowel preparation between the 3 segments of the colon. P-values <0.05 were considered statistically significant and those between 0.05 and 0.10 were considered as indicative. All analysis was performed using Stata version 15.0 software.

## Results

A total of 446 patients were initially recruited for the study. Eleven were excluded (2 patients had incomplete preparation intake of the preparation solution, 7 patients had a total BBPS<6, and 2 patients had a partial BBPS<2).

Of the 446 patients who completed the laxative intake, 435 (97.5%) achieved successful (optimal or good) preparation. Among the 435 patients included in the analysis, 257 (59.08%) were female. Mean age was 61.98±11.58 years and median body mass index (BMI) was 26.1 kg/m$^2$ (IQR 23.8-29.4 kg/m$^2$). Their indication for colonoscopy was colorectal cancer screening: 155 (35.63%), post-polypectomy surveillance: 102 (23.45%), or symptom investigation: 178 (40.92%). In addition, 172 (39.54%) patients had a history of abdominal surgery, while 115 (26.44%) had undergone digestive surgery. Patients' baseline characteristics are shown in Table 1.

The recommended diet was followed by 421 (96.78%) patients, while 379 (87.13%) patients used bisacodyl (10 mg). In our cohort, the median liquid intake was 3 L (IQR 2-3.5), with 183 (42.26%) consuming <3 L, 138 (31.87%) =3 L, and 112 (25.87%) >3 L. The median time between the end of the second laxative dose and colonoscopy initiation was 5:15 h (IQR 4:30-6:00, min 2:20, max 12:20).

Cecal intubation was achieved in 425 (97.7%) of the cases. Senior endoscopists conducted colonoscopies in 204 (46.9%) patients. Bubbles were found in 173 (39.77%) patients (Table 2).

Optimal colon preparation (BBPS=9) prior to the colonoscopy was achieved in 279 (64.14%) patients. The cleansing level was excellent (segmental BBPS=3) in 289 (66.44%) patients in the ascending colon, 346 (79.54%) in the transverse and 387 (88.97%) in the descending colon, indicating more frequent suboptimal preparation for the ascending colon compared to the transverse and the left colon (P<0.001) (Table 3). Concerning the administration of OSS preparation, we observed that optimal preparation decreases according to time, for every hour from the end of the second dose until the initiation of colonoscopy. Moreover, almost 2/3 of the patients maintained their optimal preparation until the 6$^{th}$ h after the end of the second laxative dose (Fig. 1; for details see Supplementary Table 1).

**Table 1** Descriptive characteristics of 435 patients who underwent colonoscopy. Values are mean±standard deviation or n (%)

| Variable | Value |
|---|---|
| Age (years) | 61.98±11.58 |
| Body mass index (kg/m$^2$)* | 26.1 (23.8-29.4) min-max: 17.8-43.4 |
| Sex | |
| Female | 257 (59.08) |
| Male | 178 (40.92) |
| Indication | |
| Screen | 155 (35.63) |
| Re-exam polypectomy | 102 (23.45) |
| Other | 178 (40.92) |
| Digestive surgery | |
| No | 320 (73.56) |
| Yes | 115 (26.44) |
| Abdominal surgery | |
| No | 263 (60.46) |
| Yes | 172 (39.54) |
| Constipation | |
| No | 386 (88.74) |
| Yes | 49 (11.26) |
| Diabetes | |
| No | 387 (88.97) |
| Yes | 48 (11.03) |
| Hypothyroidism | |
| No | 359 (82.53) |
| Yes | 76 (17.47) |
| Neurological drugs | |
| No | 407 (93.56) |
| Yes | 28 (6.44) |

*Median (interquartile range)

Multivariate analysis revealed that higher BMI (odds ratio [OR] 1.05, 95% confidence interval [CI] 1-1.1) and a longer time between the second laxative dose and initiation of the examination (OR 1.25, 95%CI 1.08-1.45) were associated with a higher percentage of suboptimal bowel preparation. For every extra hour between the second laxative dose and the initiation of colonoscopy, a 25% increase (95%CI 8-45%) in the odds of having suboptimal bowel preparation is expected. These results were adjusted for age (for details see Supplementary Tables 2 and 3).

The abovementioned influence of time is reflected in the delays of later appointments by the increase in the time between the end of the second laxative dose and the exam initiation for the third [5:30 hh: mm (IQR 4:45-6:30) P=0.001], the fourth [5:45 hh: mm (IQR 5:15-7:00), P<0.001], and fifth [5:30 hh: mm (IQR 4:30-6:30), P=0.003] scheduled examinations compared to the first [4:50 hh: mm (IQR 4:25-5:30)]. The second [5:00 hh: mm (IQR 4:20-5:30, P=0.38)] and paradoxically the sixth

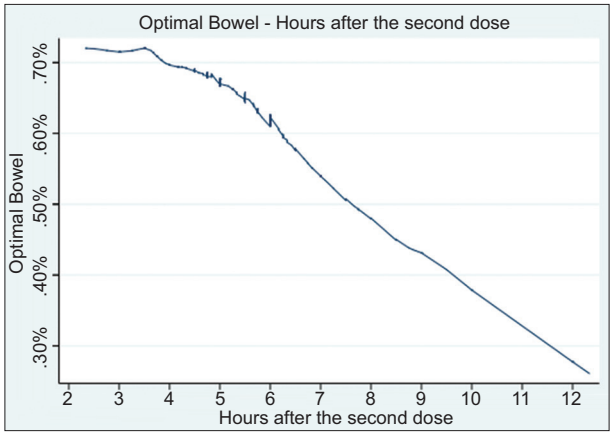


**Figure 1** Time-related effects on optimal bowel preparation in 435 patients undergoing colonoscopy: LOWESS regression

**Table 2** Clinical features of the colonic preparation and colonoscopy for 435 patients who underwent colonoscopy. Values are n (%) or median (interquartile range)

| Variable | Value |
|---|---|
| Time between second laxative dose and exam (hh: mm) | 5:15 (4:30-6:00) min-max: 2:20-12:20 |
| Liquid intake (L) | 3 (2-3.5) min-max: 1-6 |
| Adverse events | |
| No | 371 (85.29) |
| Yes | 62 (14.25) |
| Missing | 2 (0.46) |
| Diet | |
| No | 13 (2.99) |
| Yes | 421 (96.78) |
| Missing | 1 (0.23) |
| Bisacodyl | |
| No | 56 (12.87) |
| Yes | 379 (87.13) |
| Cecum catheterization | |
| No | 8 (1.84) |
| Yes | 425 (97.7) |
| Missing | 2 (0.46) |
| Endoscopist | |
| Fellow | 231 (53.1) |
| Senior | 204 (46.9) |
| Bubble | |
| No | 262 (60.23) |
| Yes | 173 (39.77) |

[5:15 hh: mm (IQR 4:30-6:00, P=0.14) appointments did not differ to the first appointment concerning the delays (Table 4).

The overall adenoma detection rate (ADR) for the entire colon was 48.74 (95%CI 43.95-53.54). The ADR for the ascending colon was 34.94 (95%CI 30.46-39.63) and for the rest of the colon it was 29.89 (95%CI 25.62-34.43). Age was the only statistically significant predictor for the total ADR and for the ADR in each segment of the colon. The level of bowel cleanliness did not affect the overall ADR, although an indication was detected for a BBPS score of 7 (OR 1.71, 95%CI 0.94-3.09, P=0.08; Table 5) (for details see Supplementary Tables 4 and 5).

A total of 61 patients (14,02%) reported minor adverse events. The most frequent adverse event was nausea, which was experienced by 8.96% (39/435) of the patients. Vomiting was reported by 3.21% (14/435) of the patients, mainly during the second dose of the OSS. Also reported were abdominal pain in 1.15% (n=5), proctalgia in 0.46% (n=2) and dizziness in 0.46% (n=2).

## Discussion

In this study, using a prospective collection of real-world data we observed that OSS is a safe and effective bowel preparation regimen for patients undergoing colonoscopy. Our findings suggest that split-dose OSS, when correctly administered, can significantly improve the quality of bowel preparation, with a successful result (total BBSP≥6 and partial BBSP≥2) in most patients (98%). However, aiming at the optimum result (BBPS=9), the efficacy of OSS was negatively influenced by the patient's BMI and the timing of the second dose intake. These results reflect in a more realistic manner the everyday practice of many participants.

According to Voiosu *et al* [15], selecting the appropriate preparation is essential for achieving the optimal level of cleansing. Medication selection may be more important than other patient-related factors. This is probably related to compliance, which depends to a great extent on the taste and the volume of the preparation regimen needed. Several studies have shown that sulfate solutions have similar efficacy to PEG-based solutions [13,14,17,19]. Factors that influence bowel preparation have been studied with PEG solutions, while equivalent studies for OSS are scarce. These studies with PEG solutions have found that patient-related factors, such as age or diabetes mellitus, can influence bowel preparation (Zad

**Table 3** Segmental and overall proportions (95%CI) of BBPS for the 435 patients who underwent colonoscopy. Optimal score was defined as grade=3 for each colon segment, and 9 for the entire colon. Suboptimal segmental score was defined as grade=2 while for the entire colon 6, 7 or 8

| BBPS | Descending colon | Transverse colon | Ascending colon | Total |
|---|---|---|---|---|
| Optimal | 88.97 (85.64-91.75) | 79.54 (75.44-83.23) | 66.44 (61.78-70.86) | 64.14 (59.43-68.65) |
| Suboptimal | 11.03 (8.25-14.36) | 20.46 (16.77-24.56) | 33.56 (29.14-38.22) | 35.86 (31.35-40.57) |

*BBPS, Boston Bowel preparation scale; CI, confidence interval*

*et al* [20]]. In another study, Cheng *et al* found that male sex and obesity were also significant factors related to inadequate preparation with PEG [21].

The benefits of a split-dose regimen for PEG preparations are well established [22,23]. Nowadays, it is considered the cornerstone of an efficient and effective bowel preparation for colonoscopy [24]. Studies examining split-dose administration of OSS come to the same conclusions, though there are far fewer data compared to PEG preparations. Palma *et al* have shown that split-dose is superior to a same-day administration of OSS preparation for achieving excellent bowel preparation cleaning (63.3% vs. 44.6%) [18]. Rex *et al* [14] demonstrated the superiority of split-dose OSS over PEG-based solutions administered the day before. With the OSS split dose, excellent preparation was achieved in 71.4%, compared to only 34.4% with PEG. Regula *et al* [15] found in 1281 patients that excellent bowel preparation with OSS was achieved in a total of 43.6%, 74.2% of whom had received a split dose. However, it should be noted that there was heterogeneity among the centers regarding the administration of split-dose preparation, with the Netherlands having the highest level of split-dose administration at 92.4%, compared to the Czech Republic at 39.8%. On the basis of the abovementioned data, we chose to use a split-dose regimen for all our patients over the last 5 years.

Bubbles in the colon lumen during colonoscopy were found in 39.77% of patients, a percentage that is comparable to the incidence of bubbles in studies using PEG solutions. Several studies have shown that simethicone can reduce the formation of bubbles and improve bowel preparation quality [25,26]. We dealt with the bubbles issue using a water pump, with or without the additional use of simethicone, and had very good results, although its use was not systematically recorded.

In a recent European study, Theunissen *et al* [27] demonstrated that the BBPS was higher for standard preparation combined with bisacodyl, whereas the use of bisacodyl was associated with higher patient discomfort. Ischemic colitis has been described as a rare complication of bisacodyl used as an adjunct in bowel preparation, both with PEG solutions and with OSS [28,29]. In our study, 87.13% of the patients used bisacodyl (10 mg) 2 days before colonoscopy without reporting any complications.

The time interval between the second dose of the preparation and colonoscopy is crucial for successful preparation. According to the European Society of Gastrointestinal Endoscopy's guidelines [16], the second dose of the preparation in a split-dose regimen should be started at least 5 h before the colonoscopy and completed at least 2 h before colonoscopy.

A meta-analysis, including 29 randomized trials involving 4040 patients with same-day evening-before preparation, and 3679 with split-dose preparation, demonstrated that the benefits of split-dose preparation were evident if the 5-h rule was observed, if the time from preparation to colonoscopy was less than 5 h, and especially when colonoscopy was performed within 3 h after the completion of the second dose [30].

In our study, higher BMI (OR 1.05, 95%CI 1-1.1) and a greater time between the second laxative dose and examination (OR 1.25, 95%CI 1.08-1.45) were correlated with a higher rate of suboptimal bowel preparation.

Five hours after the completion of the second dose of OSS, almost 70% of patients had excellent bowel preparation (Table 4). Furthermore, our study found that, even in patients with long delays exceeding 7 h, and despite the fact that many suboptimal preparations were observed, as predicted by our model, very few unacceptable preparations were recorded and excluded from the analysis. This may be attributed to the use of the water pump. It is to be noted that our study included only morning colonoscopies. We examined the indirect effect of the scheduled time of colonoscopy and found a trend of "poorer" preparation for patients who had the 3rd-5th slot in the program. This trend probably represents accumulated delays in everyday practice.

An overall ADR of 48.7% was achieved in our cohort, while segmental ADR was 34.94% in the ascending colon and 29.89% in the left colon. Bowel cleanliness, i.e., optimal vs. suboptimal bowel preparation, did not affect overall or segmental ADR,

**Table 4** Time between second laxative dose and colonoscopy initiation according to the appointment order (h: mm) for 435 patients who underwent colonoscopy

| Appointment order | Median | IQR | Min-Max | P-value |
|---|---|---|---|---|
| 1st | 4:50 | 4:25-5:30 | 2:20-12 | Reference |
| 2nd | 5:00 | 4:20-5:30 | 2:30-7:45 | 0.38 |
| 3rd | 5:30 | 4:45-6:30 | 2:30-9:00 | 0.001 |
| 4th | 5:45 | 5:15-7:00 | 3:00-12:20 | <0.001 |
| 5th | 5:30 | 4:30-6:30 | 2:45-10:00 | 0.003 |
| 6th | 5:15 | 4:30-6:00 | 3:00-12:00 | 0.14 |

*IQR, interquartile range*

**Table 5** Logistic regression for the effect of BBPS on ADR for each segment of the colon. Data are adjusted for age

| | Descending and transverse colon ADR | P-value | Ascending colon ADR | P-value | Total colon ADR | P-value |
|---|---|---|---|---|---|---|
| | OR (95%CI) | | OR (95%CI) | | OR (95%CI) | |
| BBPS | | | | | | |
| 9 | Reference | | Reference | | Reference | |
| 6 | 0.85 (0.37-1.97) | 0.7 | 1.11 (0.51-2.42) | 0.79 | 0.68 (0.32-1.45) | 0.32 |
| 7 | 1.87 (1.03-3.39) | 0.04 | 1.42 (0.78-2.58) | 0.25 | 1.71 (0.94-3.09) | 0.08 |
| 8 | 1.02 (0.56-1.86) | 0.96 | 1.44 (0.82-2.54) | 0.21 | 1.3 (0.74-2.27) | 0.36 |

*ADR, adenoma detection rate; BBPS, Boston Bowel preparation scale; OR, odds ratio; CI, confidence interval*

even though there was an indication for level 7 of BBPS (OR 1.71, 95%CI 0.94-3.09, P=0.08). In a recent meta-analysis of randomized controlled trials by Chen *et al* [31], the OSS preparation regimen had a higher ADR compared with PEG regimens (44.60% vs. 38.14%). Regarding the influence of bowel preparation on ADR, it has been reported by Calderwood *et al* [32] that good bowel preparation is better than excellent, since the ADR was higher for BBPS 6-8 than for BBPS 9.

Several adverse events have been previously reported with OSS, such as abdominal distension, abdominal pain, nausea, vomiting and headache. According to a large real-world study by Anastassopoulos *et al* [29], 299,417 patients were evaluated in European centers, for different colonoscopy preparation regimens, among which 33,465 received OSS. The study found that OSS was safer than non-OSS regimens for bowel preparation. In our study, no major complications were reported, while neither electrolyte abnormalities nor hospitalizations were observed. In the study conducted by Regula *et al* [15] in Europe, nausea was the most frequent adverse event, more frequently in women. In our study, the most frequent adverse event was nausea, which was reported in 9% of the total population (62.9% among those reporting complications).

In some studies diabetes negatively affects bowel preparation [33,34]. In our study we did not find any correlation between diabetes and suboptimal preparation. However, it should be stressed that we did not calculate the duration of diabetes mellitus, or the level of HbA1c, and we did not record the exact medications taken by the patients or whether patients were receiving insulin or not. While our study provides valuable insights into the efficacy and safety of OSS for bowel preparation before colonoscopy, there are several limitations that should be taken into consideration.

The study was conducted in a single center, which limits the generalizability of our findings. However, with our preparation, using diet and split doses of OSS, almost all patients had good acceptability, and with very few exceptions global BBPS was ≥6 and partial BBPS≥2, indicating a rather well-accepted and efficacious regimen. Although we did not use a validated score to assess patient satisfaction, especially in those with previous PEG experience, no major complaints were reported. This was a non-comparative study, meaning that we did not compare the efficacy and safety of OSS to other bowel preparation agents or non-split-dose regimens, since this was beyond the scope of our study's aims. Finally, no laboratory values were recorded in our study, which limits our ability to draw conclusions about the impact of OSS on various laboratory parameters. However, it should be noted that no major clinical side-effects were observed, which may suggest that no significant laboratory disturbances were likely to have occurred.

In conclusion, this study shows that OSS offers a safe and convenient alternative to PEG solutions for bowel preparation. BMI may influence the quality of bowel cleaning but the main parameter, which depends on the schedule of the daily endoscopic schedule and may be taken into consideration, is the time between the end of the second dose of the split regimen and colonoscopy initiation. However, it is important to notice that proper bowel preparation is crucial for the quality of colonoscopy, and factors such as BMI and preparation time should be considered when using OSS.

**Summary Box**

**What is already known:**

- Polyethylene glycol (PEG)-based solutions have been widely used for decades as bowel-cleansing agents, with good efficacy and without serious complications
- Oral sulfate salts (OSS) represent a valid alternative for colonoscopy preparation
- It has been reported, mainly in Asia and USA, that the tolerance profile of OSS solutions is better than that of polyethylene glycol (PEG)-based solutions
- Data concerning its tolerability and efficacy are scarce in Europeans populations

**What the new findings are:**

- Split dose OSS when correctly administered had excellent results on the quality of bowel preparation with a successful result in most patients
- Split dose OSS intake was completed by the vast majority of patients without major side-effects
- Optimal preparation was negatively influenced by the patient's body mass index and the timing of the second dose intake

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## Supplementary material

**Supplementary Table 1** Time between second dose of the laxative and colonoscopy for BBPS categories in 435 patients who underwent colonoscopy. Optimal preparation was defined as a sum=9. Suboptimal preparation was defined as a sum of 6, 7 or 8

| Time (h) | Optimal | Suboptimal | N |
|---|---|---|---|
| 2,3 | 11 (78.57) | 3 (21.43) | 14 (100) |
| 3,4 | 36 (69.23) | 16 (30.77) | 52 (100) |
| 4,5 | 98 (69.01) | 44 (30.99) | 142 (100) |
| 5,6 | 86 (64.18) | 48 (35.82) | 134 (100) |
| 6,7 | 35 (57.38) | 26 (42.62) | 61 (100) |
| 7,8 | 8 (44.44) | 10 (55.56) | 18 (100) |
| >8 | 5 (35.71) | 9 (64.29) | 14 (100) |
| Total | 279 (64.14) | 156 (35.86) | 435 (100) |

*BBPS, Boston Bowel preparation scale*

**Supplementary Table 2** Univariate analysis for factors associated with sub-optimal colon preparation. 435 patients underwent colonoscopy. *<0.1, **<0.05, ***<0.01

| Factors | OR | 95%CI | P-value |
|---|---|---|---|
| Age (years) | 1 | 0.98-1.02 | 0.82 |
| BMI (kg/m$^2$) | 1.05 | 1.01-1.1 | 0.03** |
| Liquid intake (lt) | 1.05 | 0.85-1.29 | 0.66 |
| Time after second laxative dose (h) | 1.26 | 1.09-1.46 | 0.002*** |
| Sex | | | |
| Female | Reference | | |
| Male | 1.46 | 0.98-2.17 | 0.06* |
| Digestive surgery | | | |
| No | Reference | | |
| Yes | 1.15 | 0.74-1.79 | 0.53 |
| Abdominal surgery | | | |
| No | Reference | | |
| Yes | 1.15 | 0.77-1.71 | 0.5 |
| Constipation | | | |
| No | Reference | | |
| Yes | 0.77 | 0.4-1.46 | 0.42 |
| Diabetes | | | |
| No | Reference | | |
| Yes | 0.79 | 0.42-1.51 | 0.48 |
| Indication | | | |
| Screen | Reference | | |
| Re-exam polypectomy | 0.89 | 0.53-1.49 | 0.65 |
| Other | 0.85 | 0.54-1.33 | 0.47 |
| Hypothyroidism | | | |
| No | Reference | | |
| Yes | 1.13 | 0.68-1.88 | 0.65 |
| Neurological drugs | | | |
| No | Reference | | |
| Yes | 1.6 | 0.74-3.46 | 0.23 |
| Diet | | | |
| No | Reference | | |
| Yes | 0.65 | 0.21-1.96 | 0.44 |
| Dulcolax | | | |
| No | Reference | | |
| Yes | 0.78 | 0.44-1.38 | 0.39 |
| Adverse events | | | |
| No | Reference | | |
| Yes | 1.34 | 0.77-2.32 | 0.3 |

*OR, odds ratio; CI, confidence interval; BMI, body mass index*

**Supplementary Table 3** Multivariate analysis for factors associated with suboptimal colon preparation in 435 patients who underwent colonoscopy. Data adjusted for age. *<0.1, **<0.05, ***<0.01

| Factors | OR | 95%CI | P-value |
|---|---|---|---|
| BMI (kg/m$^2$) | 1.05 | 1-1.1 | 0.03** |
| Time after second laxative dose (h) | 1.25 | 1.08-1.45 | 0.003*** |

*OR, odds ratio; CI, confidence interval; BMI, body mass index*

**Supplementary Table 4** PDR and ADR proportions (95% confidence interval) for each region of the colon and total for 435 patients who underwent colonoscopy

| Proportions | Ascending colon | Transverse and left colon | Total |
|---|---|---|---|
| PDR | 62.76 (58.03-67.32) | 57.47 (52.67-62.17) | 80 (75.92-83.66) |
| ADR | 34.94 (30.46-39.63) | 29.89 (25.62-34.43) | 48.74 (43.95-53.54) |

*PDR, polyp detection rate; ADR, adenoma detection rate*

**Supplementary Table 5** PDR and ADR for BBPS categories and Pearson $\chi^2$ test for 435 patients who underwent colonoscopy

| Total | PDR | | ADR | | |
|---|---|---|---|---|---|
| | No. of colonoscopies without polyps detected (%) | No. of colonoscopies with at least 1 polyp detected (%) | No. of colonoscopies without adenomas detected (%) | No. of colonoscopies with at least 1 adenoma detected (%) | |
| BBPS | P-value=0.544 | | P-value=0.075 | | |
| 6 | 10 (28.57) | 25 (71.43) | 23 (65.71) | 12 (34.29) | 35 (100) |
| 7 | 10 (17.54) | 47 (82.46) | 23 (40.35) | 34 (59.65) | 57 (100) |
| 8 | 14 (21.88) | 50 (78.13) | 29 (45.31) | 35 (54.69) | 64 (100) |
| 9 | 53 (19) | 226 (81) | 148 (53.05) | 131 (46.95) | 279 (100) |
| Total | 87 (20) | 348 (80) | 223 (51.26) | 212 (48.74) | 435 (100) |

*PDR, polyp detection rate; ADR, adenoma detection rate; BBPS, Boston bowel preparation scale*