

Comparison of Four Bowel Cleansing Agents for Colonoscopy and the Factors Affecting their Efficacy. A Prospective, Randomized Study

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ABSTRACT

Background & Aims: Adequate bowel preparation is essential for successful and effective colonoscopy. Several types of cleansing agents are currently available including low-volume solutions. The aim of this study was to compare the efficacy of four different bowel cleansing agents.

Methods: A single-center, prospective, randomized, and single-blind study was performed. Consecutive patients referred for colonoscopy were enrolled and randomized into one of the following types of laxatives: polyethyleneglycol 4L (PEG), oral sulfate solution (OSS), 2L polyethyleneglycol + ascorbate (2L-PEG/Asc), or magnesium citrate + sodium picosulfate (MCSP). The primary outcome was quality of bowel cleansing evaluated according to the Boston Bowel Preparation Scale (BBPS). Secondary outcomes were polyp detection rate (PDR) and tolerability.

Results: Final analysis was performed on 431 patients. The number of patients with adequate bowel preparation (BBPS total scores ≥ 6 and sub scores ≥ 2 in each segment) was not significantly different throughout all groups (95.4% PEG; 94.6% OSS; 96.3% 2L-PEG/Asc; 96.2% MCSP; $p=0.955$). Excellent bowel preparation (BBPS total scores ≥ 8) was associated with younger age ($p=0.007$). The groups did not have significantly different PDRs (49.5% PEG; 49.1% OSS; 38% 2L-PEG/Asc; 40.4% MCSP; $p=0.201$). The strongest predictors of pathology identification were age and male gender. The best-tolerated solution was MCSP (palatability: $p<0.001$; nausea: $p=0.024$).

Conclusion: All tested laxatives provided comparable efficacy in terms of bowel cleansing quality and PDR. The low-volume agent MCSP was the best tolerated.

Key words: bowel preparation – cleansing agents – colonoscopy – quality of colonoscopy – screening – polyp detection rate.

Abbreviations: ADR: adenoma detection rate; Asc: ascorbate; BBPS: Boston Bowel Preparation Scale; CIR: cecal intubation rate; CRC: colorectal cancer; ESGE: European Society of Gastrointestinal Endoscopy; FOBT: fecal occult blood test; HGD: high grade dysplasia; HP: hyperplastic polyp; LGD: low grade dysplasia; MCSP: magnesium citrate + sodium picosulfate (MCSP); OSS: oral sulfate solution; PDR: polyp detection rate; PEG: polyethyleneglycol; SSP/A: sessile serrated polyp/adenoma; TSA: traditional serrated adenoma.

INTRODUCTION

Colorectal cancer (CRC) is the third most common malignant disease worldwide with 1.8 million new cases and 860,000 deaths globally in 2018 [1]. The Czech Republic has one of the highest incidences of CRC, but since the organized screening program launched in 2000, both incidence and mortality have been gradually decreasing [2-4].

A successful screening program requires high-quality and effective colonoscopy, which is crucial for detecting premalignant lesions or early stages of CRC. Adequate bowel preparation is essential for safety, diagnostic accuracy, and technical feasibility of the examination, both for the screening program and colonoscopy in general. It also serves as a quality indicator for low gastrointestinal endoscopy. Moreover, two other performance measures for colonoscopy, cecal intubation rate (CIR) and the adenoma detection rate (ADR), depend on the quality of bowel preparation [5]. Using an appropriate conversion factor, polyp detection rates (PDRs) can replace ADRs for colonoscopy quality assessments [6]. Based on quality indicators, the European Society of Gastrointestinal

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Endoscopy (ESGE) recommends that the rate of adequate bowel preparation should be at least 90% [5]. Nevertheless, inadequate bowel preparation is observed in approximately 25% of colonoscopies, so it still requires improvement. Poor bowel preparation is associated with an increased risk of complications, lower ADRs and CIRs, necessary repeated or reduced intervals between procedures, resulting in increased healthcare costs [7]. Lower ADRs and CIRs increase the risk of interval CRC [8, 9]. Likewise, a 1% increase in ADR predicts a 3% decrease in the risk of interval CRC [10]. Because of these results, different endoscopic approaches improving ADR exist and are still developing. According to meta-analysis from 2019 comparing the efficacy of these different methods (add-on devices, enhanced imaging techniques, new scopes and low-cost optimizing existing methods) there is an association with a moderate increase in ADR compare to high-definition colonoscopy, but no technology is superior to each other [11].

Predictive factors of inadequate bowel preparation include advanced age, male gender, decreased colon transit, comorbidities (e.g. diabetes, stroke, dementia), polypharmacy, and inpatients with prolonged immobility and low compliance due to underlying disease [12]. Aside from risk factors, different mechanisms of a laxative's action should be considered for each patient depending on their conditions, comorbidities, and preferences. Polyethyleneglycol (PEG) 4L has been considered as a gold standard in bowel preparation for a long time. However, the large volume of solution is not well tolerated and leads to poor compliance and decreased quality of colon cleansing. To improve patient tolerability, low-volume agents have been designed. Currently, many laxatives with different mechanism of action and volume are available. According to the ESGE's updated bowel preparation guideline from 2019, the use of high volume or low volume PEG-based or non-PEG based agents is recommended for routine bowel preparation. Split-dose administration is clearly recommended for elective colonoscopy and same-day bowel preparation can be used for afternoon colonoscopy [13]. While many previous studies have compared different agents, the aim of this study was to compare the effectiveness of four bowel cleansing agents that are most commonly used in the Czech Republic.

METHODS

The present study was prospective, randomized, single-blind, and unicentric. The study was approved by the Ethics Committee of Military University Hospital Prague and was registered on ClinicalTrials.gov. (NCT03242369). All patients signed an informed consent with a study inclusion.

From September 2017 to April 2019, outpatients over 18 years of age undergoing colonoscopy from all indications (e.g., screening, fecal occult blood test positive (FOBT+), and diagnostic colonoscopies) were offered the opportunity to participate in the study. Exclusion criteria were scheduled therapeutic procedures, having a previous colonoscopy less than five years ago, and inpatients. Sample size was designed to achieve at least 90% power to detect a Chi square test effect size of 0.2 with a significance level of 0.05. Required study sample was at least 400 patients. Patients were randomized to a specific type of laxative using predetermined generated

randomization scheme. Randomization was stratified by age and gender (i.e., men ≥ 60 years, women ≥ 60 years, men ≤ 60 years, women ≤ 60 years).

All individuals were educated both verbally and in written form about the bowel cleansing process and regimen before colonoscopy. Patients answered a questionnaire where they evaluated the tolerability of their respective cleansing process (e.g., palatability, ease of laxative preparation, individual symptoms).

Patients consumed low residue diets for 3-5 days before colonoscopy and clear liquid diets the day before colonoscopy was recommended.

Split-dose preparation was explicitly recommended (i.e., first half of dose was taken the evening before colonoscopy, second half of dose was finished 4-6 hours before procedure).

Cleansing agents used were: 1) PEG 4L (Fortrans; Ipsen Pharma, France) is a high molecular weight nonabsorbable polymer (3350 or 4000) [12]; 2) Oral sulfate solution (OSS) (Eziclen; Ipsen Pharma, France) consists of concentrated sulfate solutions (Na_2SO_4 , MgSO_4 , K_2SO_4) that works as an osmotic laxative [12]; 3) PEG (2L) + ascorbate (2L-PEG/Asc) (Moviprep; Norgine Ltd, Great Britain) consists of high molecular weight nonabsorbable polymer (3350) and ascorbic acid, for which the level exceeds absorption capacity in the small intestine and results in osmotic effect [12]; 4) magnesium citrate + sodium picosulfate (MCSP) (Picoprep; Ferring Pharmaceuticals, Czech Republic) have hyperosmolar and stimulant laxative properties [12]. Magnesium citrate stimulates cholecystokinin production which causes higher intestinal motility [12].

Colonoscopies were routinely performed with conscious sedation (i.e., opioids and benzodiazepines) by six experienced endoscopists. All medical staff were blinded to the type of laxative being used. Complete colonoscopy with cecal intubation and visualization of the whole cecum and its landmarks were standardly performed. Cecum intubation was documented both in written report and photo documentation. Withdrawal time was noted in the examination report.

Quality of bowel cleansing was evaluated according to the Boston Bowel Preparation Scale (BBPS). This 4-point scoring system evaluates quality of preparation in each colon segment: right colon, transverse colon, and left colon. The total score ranges from 0-9 points and it is the sum of three sub-scores from each segment (0-3). Adequate bowel preparation is indicated by a BBPS total score ≥ 6 points and at least ≥ 2 points in each colon segment. Excellent bowel preparation is indicated by a BBPS score ≥ 8 points and at least ≥ 2 points in each colon segment [14] (Fig. 1). The total score and sub-scores were standardly noted in the examination report.

All detected polyps were removed and sent for histological examination. Pathology reports were reviewed and recorded. The number of detected polyps, their sizes, and histological characteristics were monitored. Histological characteristics were assessed according to the Vienna classification system (i.e., adenoma with low grade/high grade dysplasia or carcinoma; type: tubular, villous or tubulovillous). The fourth edition of the WHO classification of digestive tumors was used for classification of serrated lesions (i.e., hyperplastic polyp (HP), sessile serrated polyp/adenoma (SSP/A), or traditional

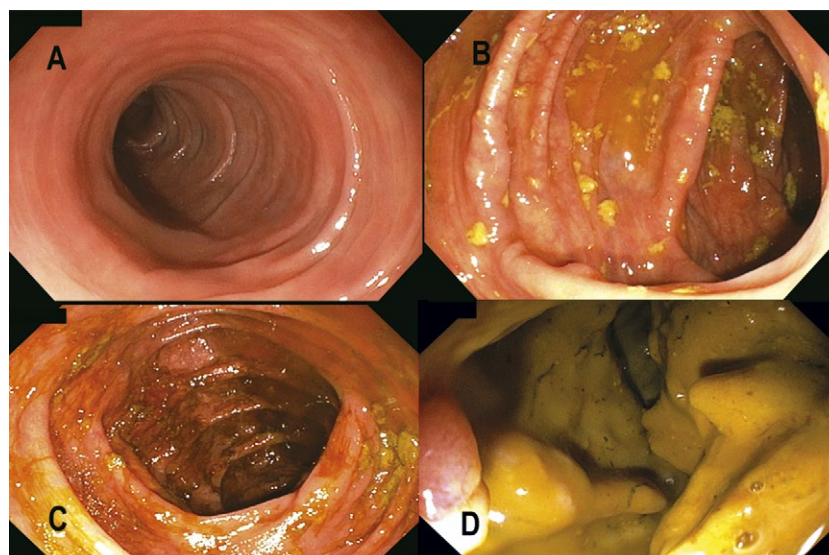


Fig. 1. A: Bowel scoring 3 points according to the BBPS; B: Bowel scoring 2 BBPS points; C: Bowel scoring 1 BBPS point; D: Bowel scoring 0 BBPS points; BBPS = Boston Bowel Preparation Scale.

serrated adenoma (TSA) [15, 16]. Advanced neoplasia was defined as lesion ≥ 10 mm in diameter or histologic finding of villous structure and/or adenomas with high grade dysplasia (HGD) or cancer. Assessment of pathology identification was evaluated according to PDR (i.e., proportion of total colonoscopy procedures for which at least one polyp was removed) [5].

Patients completed questionnaires regarding their subjective evaluation. All observed parameters were evaluated in detail: palatability as excellent, pleasant, tolerable or intolerable; ease of the laxative preparation as easy, acceptable, difficult or impracticable; individual symptoms as the occurrence of nausea, vomiting, abdominal pain, dehydration, others, or no symptoms. Patients also indicated chosen administration of laxative (split-dose/non-split dose).

All data were collected and recorded into a single form and were validated and analyzed by the Institute of Biostatistics and Analyses of Masaryk University in Brno. Data were initially analyzed using descriptive statistics. Quantitative variables were expressed using mean and standard deviation. Qualitative variables were expressed as absolute numbers and their percentage for the observed variable. Statistical comparisons of main parameters (i.e., quality of bowel preparation and pathology identification) among all tested target groups were performed using Fisher's exact test. Adequate and excellent bowel preparation was also evaluated according to the split or non-split regimen. Statistical comparisons of tolerability (i.e., ease of the laxative preparation and individual symptoms) were performed using Fisher's exact test and Pearson chi square test (i.e., palatability). Multivariate analysis (logistic regression) was also used to evaluate predictors affecting adequate and excellent bowel preparation (parameters: age, gender, solution administration, cleansing agents), pathology identification and detection of advanced colorectal neoplasia (parameters: age, gender, solution administration, colonoscopy indication, cleansing agents). P values of less than 0.05 were considered

statistically significant. Statistical analysis was performed using Stata/IC 15 software.

The primary outcome was the comparison of the quality of bowel preparation. The secondary outcomes were comparison of pathology identification and tolerability.

RESULTS

In total, 449 individuals met the inclusion criteria and final analysis was performed on 431 patients. All analyzed individuals underwent a total colonoscopy procedure except for one patient because of poor bowel preparation (scoring 0 points in all segments was considered). In eight analyzed patients, the type of laxative was known prior to colonoscopy by mistake. Fig. 2 shows distribution of the patients participating in the study. There was no statistical difference in demographic data between patients in each randomized group. Table I presents baseline characteristics of all groups.

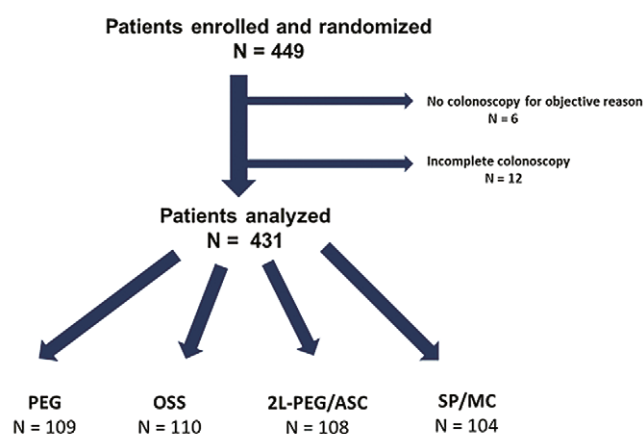


Fig. 2. Patients' distributions. PEG: polyethylenglycol; OSS: oral sulfate solution; ASC: ascorbate; SP/MC: sodium picosulfate/magnesium citrate.

Table I. Baseline characteristics of the patients

	PEG (N=109)	OSS (N=110)	2L-PEG/Asc (N=108)	MCSP (N=104)
Men N, (%)	55 (50.5 %)	54 (49.1 %)	55 (50.9 %)	54 (51.9 %)
Women N, (%)	54 (49.5 %)	56 (50.9 %)	53 (49.1 %)	50 (48.1 %)
Average age (SD)	58.8 (9.7 %)	57.4 (11.9 %)	57.6 (12.7 %)	58.4 (13.0 %)
Indication N, (%)				
CRC symptoms	36 (33.0)	46 (41.8)	43 (39.8)	33 (31.7)
FOBT positive colonoscopy	21 (19.3)	19 (17.3)	23 (21.3)	16 (15.4)
Screening colonoscopy	39 (35.8)	34 (30.9)	30 (27.8)	39 (37.5)
Others	13 (11.9)	11 (10.0)	12 (11.1)	16 (15.4)

PEG: polyethylenglycol; OSS: oral sulfate solution; 2L-PEG/Asc: 2L polyethylenglycol + ascorbate; MCSP: magnesium citrate + sodium picosulfate; CRC: colorectal cancer; FOBT: fecal occult blood test; SD: standard deviation.

Based on the results, all the solutions were successful in bowel cleansing. All patients completed the process of bowel preparation and split-dose administration was preferred by 82%. There were no significant differences in adequate bowel preparation rates among the four tested agents ($p=0.955$) (Table II). Also, total BBPS scores were very similar in each group with similar sub-scores for each colonic segment (Table II). Excellent bowel preparation was detected slightly more often in the PEG and OSS groups but was not statistically significant different from the other groups ($p=0.37$). Within each respective group, patients that adhered to the split-dose regimen did not have better quality of preparation than those who did not (Table II). Based on logistic regression analysis, no parameter was determined to affect adequate bowel preparation (Table III). However, patients < 50 years old had statistically significantly excellent bowel preparation more often ($p=0.007$) (Table III).

Although there was a slight trend in favor of PEG and OSS, no statistically significant differences in PDRs ($p=0.201$) or detection of advanced colorectal neoplasia ($p=0.778$) were found among all tested groups (Table IV). Logistic regression analysis showed age > 50 years (age 50-65 years: $p=0.004$; age >65 years: $p<0.001$) and male gender ($p<0.001$) were significant predictors of higher PDR. Only the male gender

was a significant predictive factor for detection of advanced colorectal neoplasia ($p=0.01$) (Table V).

The majority of the patients assessed the process of bowel preparation as “easy” regardless of the laxative administered ($p=0.128$). Palatability was significantly higher in the MCSP group ($p<0.001$). Among all evaluated symptoms, only nausea was observed significantly less common in the MCSP group compared to the other agents ($p=0.024$). Detailed data of tolerability is shown in Table VI.

DISCUSSION

Many studies comparing quality of bowel preparation have already been published. There is a high degree of heterogeneity among the studies because of the different study designs, including different types of compared agents, administration, and evaluation scales [17-26]. The present study was a prospective, randomized, unicentric, and investigator-blinded study. To our knowledge, this is the first published study comparing efficiency of bowel preparation among four cleansing agents.

Our results demonstrate no superiority in quality of bowel cleansing and PDRs among the tested solutions. The present cleansing quality results confirmed the conclusions of many

Table II. Quality of bowel preparation

	PEG (N=109)	OSS (N=110)	2L-PEG/Asc (N=108)	MCSP (N=104)	p
Adequate bowel preparation (BBPS ≥ 6), N (%)	104 (95.4 %)	104 (94.6 %)	104 (96.3 %)	100 (96.2 %)	0.955
Excellent bowel preparation (BBPS ≥ 8), N (%)	94 (86.2 %)	92 (83.6 %)	84 (77.8 %)	83 (79.8 %)	0.370
Average BBPS score (SD)					
Total	8.4 (1.1)	8.4 (1.3)	8.3 (1.3)	8.3 (1.0)	
Right colon	2.6 (0.6)	2.7 (0.6)	2.6 (0.6)	2.6 (0.6)	
Transverse colon	2.9 (0.4)	2.8 (0.5)	2.8 (0.5)	2.8 (0.4)	
Left colon	2.9 (0.4)	2.9 (0.4)	2.9 (0.4)	2.9 (0.3)	
Split-dose regimen:					
Number of patients	86	89	99	80	
Adequate bowel preparation (BBPS ≥ 6), N (%)	83 (96.5 %)	84 (94.4 %)	95 (96.0 %)	78 (97.5 %)	0.799
Non-split regimen:					
Number of patients	23	21	9	24	
Adequate bowel preparation (BBPS ≥ 6), N (%)	21 (91.3 %)	20 (95.2 %]	9 (100.0 %)	22 (91.7 %)	1.000

BBPS: Boston Bowel Preparation Scale. For abbreviations see Table I.

Table III. Predictors of adequate and excellent bowel preparation

Adequate:		OR (95%CI)*	p
Age	< 50	7.299 (0.900-59.179)	0.063
Reference: > 65	50-65	2.088 (0.784-5.563)	0.141
Gender	Men	1.419 (0.552-3.652)	0.468
Reference: Women			
Bowel preparation regimen	Split regimen	1.645 (0.556-4.868)	0.368
Reference: Non-split regimen			
Preparation	OSS	0.752 (0.220-2.576)	0.650
Reference: PEG	2L-PEG/ASC	1.184 (0.302-4.646)	0.809
	MCSP	1.288 (0.326-5.096)	0.718
Excellent:		OR (95%CI)*	p
Age	<50	3.181 (1.370-7.388)	0.007
Reference: > 65	50-65	1.304 (0.754-2.255)	0.343
Gender	Men	1.216 (0.737-2.005)	0.444
Reference: Women			
Bowel preparation regimen	Split regimen	0.903 (0.460-1.773)	0.768
Reference: Non-split regimen			
Preparation	OSS	0.768 (0.363-1.626)	0.491
Reference: PEG	2L-PEG/ASC	0.541 (0.263-1.113)	0.095
	MCSP	0.603 (0.287-1.264)	0.180

For abbreviations see Table I.

previous studies [17-21]. In contrast, Rex et al. [36] observed higher rates of successful bowel preparation in the OSS group as compared to the PEG group (for adequate bowel preparation $p=0.04$; for excellent bowel preparation $p<0.001$). However, different types of laxative administration were used for each group; OSS was administered via split-dose preparation and PEG was administered the evening before colonoscopy). In our study, 82% of patients accepted the split-dose regimen, which, according to previous studies, significantly improves the quality of bowel cleansing [23]. A recent study performed by Rostom et al. [25] found that PEG was superior to MCSP via a split dose regimen ($p=0.007$) [24] while Kwon et al. [25] demonstrated better efficiency of OSS than 2-L PEG/

Asc in an Asian population ($p=0.06$). Yoo et al. [19] reported more frequent excellent preparation (BBPS > 8) in patients administered MCSP as compared to patients given 2-L PEG/Asc ($p=0.003$). This discrepancy among results is probably due to the heterogeneous designs of the studies. Similar to our study, two previous studies that focused on bowel preparation quality and analyzed ADRs or PDRs did not find any significant differences among cleansing solutions [20, 26].

The split-dose regimen was accepted most often in the 2L-PEG/Asc group (92%). Since 2L-PEG/Asc led to a higher occurrence of nausea and abdominal pain during the cleansing process compared to the other laxatives, the patients may have decided to split the laxative into two doses.

Table IV. Identified pathology

	PEG (N=109)	OSS (N=110)	2L-PEG/Asc (N=108)	MCSP (N=104)	p
At least 1 detected polyp, N (%)	54 (49.5 %)	54 (49.1 %)	41 (38.0 %)	42 (40.4 %)	0.201
Polyp size, N (%)					
< 10 mm	51 (46.8 %)	52 (47.3 %)	39 (36.1 %)	40 (38.5 %)	
≥ 10 mm	10 (9.2 %)	9 (8.2 %)	10 (9.3 %)	12 (11.5 %)	
Total number of polyps	116	125	106	91	
Average no of polyp for 1 patient (SD)	2.1 (1.8)	2.3 (2.2)	2.6 (2.7)	2.2 (1.3)	
Average polyp size, mm, (SD)	5.2 (3.4)	5.2 (3.2)	5.8 (3.8)	5.7 (5.5)	
Advanced neoplasia, N (%)	12 (11.0 %)	11 (10.0 %)	12 (11.1 %)	15 (14.4 %)	0.778
Histological type, N (%)					
Hyperplastic polyp	17 (15.6 %)	24 (21.8 %)	17 (15.7 %)	20 (19.2 %)	0.586
SSP/SSA, TSA	5 (4.6 %)	2 (1.8 %)	3 (2.8 %)	3 (2.9 %)	0.691
LGD adenoma	43 (39.5 %)	40 (36.4 %)	32 (29.6 %)	32 (30.8 %)	0.379
HGD adenoma or cancer	2 (1.8 %)	3 (2.7 %)	2 (1.9 %)	4 (3.9 %)	0.754

SSP/A: sessile serrated polyp/adenoma; TSA: traditional serrated adenoma; LGD: low grade dysplasia; HGD: high grade dysplasia; For abbreviations see Table I.

Table V. Predictors of pathology identification

All identified pathologies		OR (95%CI)*	p
Age	50-65	2.474 (1.344-4.555)	0.004
Reference: < 50	> 65	3.742 (1.941-7.212)	< 0.001
Gender	Men	3.457 (2.267-5.270)	< 0.001
Reference: Women			
Indication	Symptoms of colorectal neoplasia	1.031 (0.511-2.080)	0.933
Reference: Others	Primary screening colonoscopy	1.991 (0.981-4.045)	0.057
	FOBT + colonoscopy	1.701 (0.794-3.644)	0.172
Bowel preparation regimen	Split regimen	1.134 (0.659-1.949)	0.650
Reference: Non-split regimen			
Preparation	SPS	1.120 (0.627-2.001)	0.701
Reference: PEG	2L-PEG/ASC	0.615 (0.341-1.111)	0.107
	PS/MC	0.674 (0.372-1.222)	0.194
Advanced neoplasia		OR (95%CI)*	p
Age	50-65	2.474 (1.344-4.555)	0.004
Reference: < 50	> 65	3.742 (1.941-7.212)	< 0.001
Gender	Men	3.457 (2.267-5.270)	< 0.001
Reference: Women			
Indication	Symptoms of colorectal neoplasia	1.031 (0.511-2.080)	0.933
Reference: Others	Primary screening colonoscopy	1.991 (0.981-4.045)	0.057
	FOBT + colonoscopy	1.701 (0.794-3.644)	0.172
Bowel preparation regimen	Split regimen	1.134 (0.659-1.949)	0.650
Reference: Non-split regimen			
Preparation	SPS	1.120 (0.627-2.001)	0.701
Reference: PEG	2L-PEG/ASC	0.615 (0.341-1.111)	0.107
	PS/MC	0.674 (0.372-1.222)	0.194

For abbreviations see Table I

Some studies have determined that age and gender are risk factors for poor bowel preparation [27, 28]. In contrast,

our study did not corroborate these findings and determined that age was the only predictive factor for excellent bowel

Table VI. Tolerability of bowel cleansing agents

	PEG (N=109)	OSS (N=110)	2L-PEG/Asc (N=108)	MCSP (N=104)	p
Ease of the laxative preparation					
Easy	83 (76.2 %)	92 (83.6 %)	90 (83.3 %)	93 (89.4 %)	0.128
Acceptable	25 (22.9 %)	15 (13.6 %)	17 (15.7 %)	10 (9.6 %)	
Difficult	1 (0.9 %)	3 (2.7 %)	1 (0.9 %)	1 (1.0 %)	
Impracticable	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	
Palatability					
Excellent	2 (1.8 %)	2 (1.8 %)	3 (2.8 %)	19 (18.3 %)	< 0.001
Pleasant	31 (28.4 %)	14 (12.7 %)	23 (21.3 %)	64 (61.5 %)	
Tolerable	65 (59.6 %)	70 (63.6 %)	67 (62.0 %)	21 (20.2 %)	
Intolerable	11 (10.1 %)	24 (21.8 %)	15 (13.9 %)	0 (0.0 %)	
Symptoms					
Nausea	13 (11.9 %)	18 (16.4 %)	22 (20.4 %)	7 (6.7 %)	0.024
Vomiting	5 (4.6 %)	5 (4.6 %)	4 (3.7 %)	0 (0.0 %)	0.107
Abdominal pain	10 (9.2 %)	17 (15.5 %)	18 (16.7 %)	7 (6.7 %)	0.070
Dehydration	6 (5.5 %)	5 (4.6 %)	1 (0.9 %)	3 (2.9 %)	0.227
Others	8 (7.3 %)	11 (10.0 %)	11 (10.2 %)	11 (10.6 %)	0.848
No adverse events	79 (72.5 %)	69 (62.7 %)	71 (65.7 %)	79 (76.0 %)	0.137

For abbreviations see Table I.

preparation (BBPS ≥ 8). Patients <50 years old have up to three times the chance to achieve excellent bowel preparation compared to patients over 65 years of age. The higher chance of achieving excellent bowel preparation in younger patients might be due to lower comorbidities, incidence, and polypharmacy and better compliance with bowel preparation.

Adequate bowel preparation and complete colonoscopy are basic conditions of valid colonoscopy. Both PDR and ADR are indicators of pathology identification providing information about visualization of colonic mucosa [5]. In addition to quality of bowel preparation, PDR is also affected by patient factors such as personal and family history of CRC [29], metabolic risk factors [30], gender, and age [31, 32]. In accordance with the previous studies, the present study determined that male gender and age are independent predictive factors that affect colorectal neoplasia detection. Contrary to our initial assumptions and previous literature [33], there were no significant differences in PDRs between screening, FOBT+, and diagnostic colonoscopies. Endoscopists themselves play a crucial role in PDRs, partly due to individual variations in mucosa inspection techniques, including withdrawal time [34]. All physicians participating in the study were experienced certified endoscopists meeting the requirements for PDR values according to the ESGE guidelines [5]. Polyp detection rate values for the individual endoscopists ranged between 45–72 %.

In the present study, the best-tolerated agent was low-volume MCSP with significantly better palatability and lower incidence of nausea as compared to the other agents. Even though abdominal pain was observed slightly more often in the OSS and 2-L PEG/Asc groups, there were no statistically significant differences in occurrence of individual symptoms among the groups except for nausea. Similar to our study, a recent European multicentric study found that patient compliance with OSS administration was excellent regardless of administration (i.e., same-day or split-dose) and that the most frequent adverse symptoms for OSS were nausea and abdominal pain [35]. In another study, the same symptoms were significantly more frequent in the OSS group compared to the 2-L PEG/Asc group [25]. In contrast, Kim et al. [21] described no differences in adverse events among patients receiving OSS or 2L-PEG/Asc. Consistent with our study, Yoo et al. [19] observed better tolerability of MCSP compared to 2-L PEG/Asc and a meta-analysis by Jin et al. [20] found better tolerability of MCSP compared to PEG. Furthermore, Rex, Di Palma et al. [36] did not observe any differences in adverse events among patients receiving OSS or MCSP. Due to the discrepancy in results among these studies, further studies are needed.

Our study had several strengths. First, it compared four different (high or low-volume) agents. Second, clinical outcomes were collected in one tertiary endoscopy center with highly standardized examination processes and quality monitoring. Third, the final analysis was performed on a high number of patients. Fourth, evaluation of bowel cleansing quality was carried out according to a validated BBPS, which provided reliable and accurate comparisons between solutions in three colonic segments and in the colon overall.

There were some limitations of this study. No laboratory tests were performed; therefore, any electrolyte changes and

the safety of each solution could not be compared. Presence of bubbles was not monitored and evaluated. Since screening or FOBT positive colonoscopies were not the only indications, there were various indications for colonoscopy that could have affected the colorectal neoplasia detection rates. Tolerability was assessed by questionnaire only.

CONCLUSIONS

Our study demonstrated that no single cleansing agent was superior among all tested agents. Polyethylenglycol, oral sulfate solution, 2L-polyethylenglycol + ascorbate, and magnesium citrate + sodium picosulfate were equally effective in bowel preparation and pathology identification. However, magnesium citrate + sodium picosulfate had significantly better tolerability than the others, which could improve better compliance with bowel preparation.

Conflicts of interest: None to declare.

Authors' contributions: S.S., P.U. and M.Z. designed the study. K.K., T.G., G.V. performed the research. K.K. collected the data. O.N., O.M. analyzed the data. K.K. drafted the manuscript. S.S. supervised the study and revised the manuscript. All authors approved the final version of the article.

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