Same-day Versus Split-dose Bowel Preparation Before Colonoscopy

A Meta-Analysis

Yuan-Lung Cheng, MD,† Kuang-Wei Huang, MD,‡ Wei-Chih Liao, MD,*† Jiing-Chyuan Luo, MD,†§ Keng-Hsin Lan, MD, PhD,†§‖ Chien-Wei Su, MD, PhD,†§ Yuan-Jen Wang, MD,§¶ and Ming-Chih Hou, MD†§*

Background: Split-dose regimens (SpDs) were recommended as a first choice for bowel preparation, whereas same-day regimens (SaDs) were recommended as an alternative; however, randomized trials compared them with mixed results. The meta-analysis was aimed at clarifying efficacy level between the 2 regimens.

Materials and Methods: We used MEDLINE/PubMed, EMBASE, Scopus, CINAHL, Cochrane Library, and Web of Science to identify randomized trials published from 1990 to 2016, comparing SaDs to SpDs in adults. The pooled odds ratios (ORs) were calculated for preparation quality, cecal intubation rate (CIR), adenoma detection rate (ADR), and any other adverse effects.

Results: Fourteen trials were included. The proportion of individuals receiving SaDs and SpDs with adequate preparation in the pooled analysis were 79.4% and 81.7%, respectively, with no significant difference [OR = 0.92; 95% confidence interval (CI), 0.62-1.36] in 11 trials. Subgroup analysis revealed that the odds of adequate preparation for SaDs with bisacodyl were 2.45 times that for SpDs without bisacodyl (95% CI, 1.45-4.51, in favor of SaDs with bisacodyl). Subjects received SaDs experienced better sleep.

Conclusions: SaDs were comparable with SpDs in terms of bowel cleanliness, CIR, and ADR, and could also outperform SpDs in preparation quality with bisacodyl. SaDs also offered better sleep the previous night than SpDs did, which suggests that SaDs might serve as a superior alternative to SpDs. The heterogenous regimens and measurements likely account for the low rates of optimal bowl preparations in both arms. Further studies are needed to validate these results and determine the optimal purgatives and dosages.

Key Words: bowel preparation, same-day regimen, split-dose regimen

(*J Clin Gastroenterol* 2017;00:000–000)

Optimal bowel preparation is crucial for increased effectiveness of colonoscopy in both clinical and screening settings. However, the requirement of restricted diets for several days, and an unpalatable (large) volume of purgatives, made patient tolerance and compliance the main barriers to adequate bowel preparation. Split-dose regimens (SpDs) for bowel preparation were shown to improve colonic cleanliness and adenoma detection, and are thus recommended as a routine bowel preparation in guidelines.[1,2] The guidelines also recommend that same-day regimens (SaDs) can be offered to patients as an alternative for bowel preparation. Both guidelines base their views of the alternative on a prospective study from Longcroft-Wheaton and Bhandari,[3] which revealed that SaDs were more effective than SpDs, with fewer adverse effects and less sleep disturbances. Several randomized trials evaluated their effects, and revealed mixed results to SpDs; thus, we performed a meta-analysis to clarify the efficacy and tolerability of the 2 regimens.

MATERIALS AND METHODS

Search Strategy and Trial Selection

Systemic searches were performed in October 2016 using MEDLINE/PubMed, EMBASE, Scopus, CINAHL, Cochrane Library, and Web of Science for randomized controlled trials. Search terms were: (1) colonoscopy, (2) bowel preparation, and (3) randomized. Only fully published randomized trials with one arm using purgatives on the day of colonoscopy, with the other arm using purgatives on the previous day and the day of colonoscopy, were included. Trials including pediatric patients were excluded. References from the reviewed articles were searched (in terms of any articles that may have been missed).

Choice of Outcomes

The primary outcome measure was bowel cleanliness, defined as adequate or satisfactory preparation—with use of both unvalidated and validated preparation scales (Ottawa, Boston, and Aronchick scales). If no adequate dichotomous result was reported, an excellent or successful

Received for publication December 13, 2016; accepted April 18, 2017.
From the *Taipei Municipal Gan-Dau Hospital; †School of Medicine, Faculty of Medicine; ‖Department and Institute of Pharmacology, National Yang-Ming University; ‡Department of Internal Medicine, Division of Gastroenterology, Taipei Beitou Health Management Hospital; §Department of Medicine, Division of Gastroenterology; and ¶Healthcare Center, Taipei Veterans General Hospital, Taipei, Taiwan.
supported by grants from Taipei Veterans General Hospital (V105-C-024), National Yang-Ming University, and the Ministry of Science and Technology, Taiwan (MOST 104-2314-B-010-013-MY2).
Y.L.C. and W.C.L.: study concept and design, analysis and interpretation of data, drafting of manuscript; K.W.H.: study concept and design, analysis and interpretation of data;; J.C.L., K.H.L., and C.W.S.: study concept and design, discussion and support; M.C.H. and Y.J.W.: overall study concept and design, analysis and interpretation of data, critical revision of the manuscript for intellectual content and final drafting.
The authors declare that they have nothing to disclose.
Address correspondence to: Ming-Chih Hou, MD, Department of Medicine, Division of Gastroenterology, Taipei Veterans General Hospital, 201, Section 2, Shih-Pai Road, Taipei, Taiwan (e-mail: mchou@vghtpe.gov.tw).
Address correspondence to: Yuan-Jen Wang, MD, Healthcare Center, Taipei Veterans General Hospital, 201, Section 2, Shih-Pai Road, Taipei, Taiwan (e-mail: yjwang@vghtpe.gov.tw).

DOI: 10.1097/MCG.0000000000000860

preparation was used for analysis. If no information on colon preparation quality was offered, then right side colon cleanliness was used for the sensitivity analysis. SpDs were defined as the administration of primary purgatives on the day before colonoscopy, as well as the day of the procedure. SaDs were defined as having no primary purgative the day before the colonoscopy, but adjuvants were allowed.

Secondary outcomes included cecal intubation rate (CIR), adenoma detection rate (ADR), patient willingness to repeat the preparation, sleep disturbance, and side effects including nausea, vomiting, and abdominal pain/cramps.

Validity Assessment

Two investigators (Y.L.C. and K.W.H.) assessed citation eligibility, with any discrepancies resolved by an independent reviewer (M.C.H.). The quality of the trials was graded using the Cochrane risk bias tool. Then 2 authors independently validated data extraction and other entries.

Statistical Analysis

Preplanned sensitivity analyses assessing bowel cleanliness examined SpDs for varying volume versus that in SaDs. Values for intention-to-treat were preferred to per-protocol when both were presented. We included non-compliant patients or withdrawals in the intention-to-treat analysis to minimize bias, whereas missing values were assumed to have a poor outcome. No attempt at determining values from graphics or figures was performed to avoid possible subjectivity.

Statistical analysis was conducted with Review Manager (Version 5.3; Cochrane Collaboration, Oxford, GB). Outcomes of dichotomous variables were presented as odds ratios (ORs) and 95% confidence intervals (CIs). Statistical heterogeneity was assessed using the Higgins I^2 test. The DerSimonian and Laird random effects model was used for the pooled analysis. Subgroup analysis was performed to characterize heterogeneity, with results including >3 trials were reported in sensitivity analyses.

RESULTS

Study Selection and Characteristics

Overall, 484 citations were retrieved, 259 articles were rejected on the basis of titles and abstracts, 225 articles were reviewed, and 14 articles were included (Fig. 1).[4–17] A fully published article with an abstract, which clearly mentioned SaD versus SpD preparation, was excluded because of an unavailable full text.[18]

Table 1 summarizes the characteristics of 14 trials, comparing SaD and SpD bowel preparations. The quality of bowel cleanliness was evaluated with Aronchick, Ottawa, and Boston scales in 11 trials, whereas 3 trials used unvalidated scales.[11,12,16] Clean colon preparation was reported but not defined in 1 trial.[16] Scores <5 in the Ottawa scale were considered adequate in 2 studies,[7,13] and Cesaro et al[4] revealed only excellent preparation as a score ≤ 3, whereas Zhang et al[17] counted a score <7 as a successful preparation. Three trials did not document dichotomous outcomes of bowel cleanliness.[6,9,14]

Three trials also used bisacodyl 10 to 20 mg in the arm of SaD preparation,[4,10,16] and 2 trials used bisacodyl in both arms the previous evening[5,12]; the other 9 trials did not use adjuvants in either arm. Two trials had different diet restriction in the 2 arms,[13,16] and 1 trial did not describe the preparation diet at all.[15] Other trials had the same diet restriction during preparation in both arms.

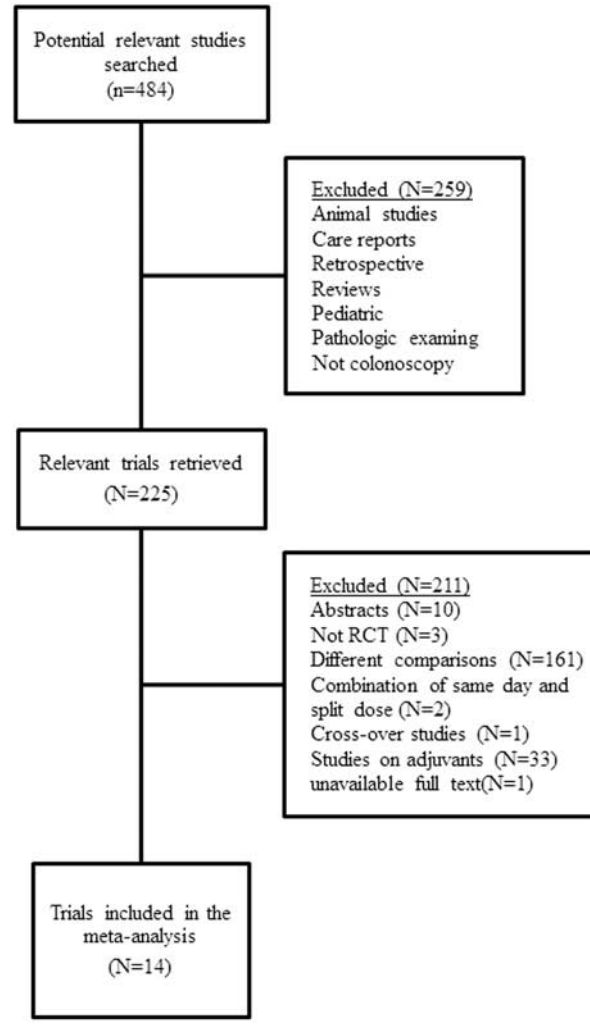

FIGURE 1. Flowchart for the inclusion of studies.

According to the American Society for Gastrointestinal Endoscopy (ASGE) guidelines, the second dose of SpDs should be administered 3 to 8 hours before the start of colonoscopy.[19] Colonoscopy was performed in the time window in 7 trials,[5–8,11,13,17] whereas another 4 trials might have included patients who did not have a colonoscopy within the optimal interval[4,12,14,15]; whether colonoscopy timing was optimal could not be distinguished in the other 3 trials.[9,10,16]

No significant publication bias was detected for the primary outcome of quality of bowel preparation by visual evaluation of the funnel plot (Fig. 2). The Cochrane risk bias tool mapped the authors' judgments about each risk of item bias, as seen in Figure 3. One study used a poor method in the sequence generation process.[5]

Quality of Bowel Preparation

Kotwal et al[9] concluded that there was no significant difference between groups with decent preparation for any segment of the colon, but did not reveal information about the rate of adequate or satisfactory bowel cleanliness.

TABLE 1. Summaries and Jadad Score of Studies Included in the Meta-Analysis

References	Study Type/ Location	No. Patients (Same Day/ Split)	Definition of Adequate or Satisfactory	Diet During Preparation	Bowel Preparation Type	Colonoscopy Timing	Jadad Score
Cesaro et al[4]	RCT Italy	50/51	Ottawa scale. Excellent score ≤ 3	Low-residue diet for 3 days and clear liquid since the start of bowel preparation	Same day: bisacodyl 10-20 mg at 10 PM the day prior; PEG-CS 2 L 6 AM of the day Split: 3 L PEG 7 PM the day prior; 1 L PEG 7 AM of the day	11:00-18:00	2
Chan et al[5]	RCT Malaysia	152/143	BBPS. Satisfactory as good or intermediate	Low-residue diet the day prior, clear liquid after 6 PM the day prior	Same day: 2 L PEG 5-6 am Split: 1 L PEG 8-8:30 PM, 1 L PEG 5:30-6:00 AM Both: bisacodyl 5 mg 2 tablets for 2 evenings	Morning	1
Chen et al[6]	RCT China	51/49	Aronchick scale. No dichotomous outcome	Fasting after 6 PM the day prior	Same day: 3 L PEG 8 AM of the day Split: NaP 8 PM the day prior and 8 AM of the day	Afternoon (13:00-16:00)	2
Kang et al[7]	RCT Korea	98/99	Ottawa scale. Adequate score < 5	Low-residue diet for 3 d	Same day: SP 6 AM and 10 AM of the day Split: 2 L PEG at 6 PM the day prior, 2 L PEG 5 h before colonoscopy	Afternoon	3
Kim et al[8]	RCT Korea	50/150	Aronchick scale Excellent and good as adequate Ottawa scale scores were reported	Low fiber diet for 3 d	Same day: 4 L PEG 6 h before colonoscopy split: 1. 2 L PEG 6 PM the day prior, 2 L PEG 4-6 h before colonoscopy 2. SPMC 1 sachet 6 PM the day prior; 1 sachet 4-6 h before colonoscopy 3. SPMC 1 sachet 6 PM, 1 sachet 9 PM the day prior; 1 sachet 4-6 h before colonoscopy	Not described	1
Kotwal et al[9]	RCT USA	60/60	Ottawa scale. No dichotomous outcome	Clear liquid the day prior	Same day: 4 L PEG 5-9 AM of the day Split: 2 L PEG 7-9 PM the day prior; 2 L PEG 7-9 AM of the day	After 11am	3
Kwon et al[10]	RCT Korea	92/97	BBPS. Score ≥ 6 adequate	Low fiber diet for 3 d, soft meal the day prior	Same day: bisacodyl 20 mg 8 PM the day prior; 1 L PEG/Asc 6 AM of the day Split: 1 L PEG/Asc 8 PM the day prior and 1 L PEG/Asc 6 AM of the day	Not described	3
Matro et al[11]	RCT USA	65/60	Unvalidated 4-point scale. Adequate as excellent and good	Low-residue breakfast before 10 AM the day prior, clear liquid up to 2.5 hours before	Same day: 1 L PEG 7 h before, 1 L PEG 4 h before Split: 1 L PEG 6 PM the day prior, 1 L PEG 4 h before colonoscopy	Afternoon	3
Parra-Blanco et al[12]	RCT Spain	43/45	Unvalidated 5-point scale. Good and excellent score > 4	Low fiber diet the day prior, clear liquid after completing bowel preparation	Same day: 3 L PEG 6 AM of the day Split: NaP 8 PM the day prior; NaP 6 AM of the day Both: bisacodyl 15 mg the day prior	09:00-15:00	2
Seo et al[13]	RCT Korea	103/102	Ottawa scale. Adequate score < 5	Low-residue diet for 3 d	Same day: 2 L PEG 5 h before colonoscopy Split: 2 L PEG at 6 PM the day prior; 2 L PEG 5 h before	09:00-17:00	3

TABLE 1. (*continued*)

References	Study Type/ Location	No. Patients (Same Day/ Split)	Definition of Adequate or Satisfactory	Diet During Preparation	Bowel Preparation Type	Colonoscopy Timing	Jadad Score
Shah et al[14]	RCT India	103/97	Ottawa scale. No dichotomous outcome	Liquid diet the day prior, clear liquid after midnight	Same day: 2 L PEG 5-7 AM of the day Split: 1 L PEG 6-7 PM the day prior, 1 L PEG 6-7 AM of the day	11:00-16:00	3
Tellez-Avila et al[15]	RCT Mexico	61/67	BBPS. Satisfactory score 2 or 3	Not described	Same day: 2 L PEG 6-8 AM of the day Split: 2 L PEG 5-7 PM the day prior; 2 L PEG 6-8 AM of the day	Not described	3
van Vugt van Pinxteren et al[16]	RCT Netherlands	53/63	Unvalidated 4-point scale. Clean colon rate reported but not defined	Same day: lightly digestible products for 2 d, fluid on the day prior Split: light breakfast and lunch day prior	Same day: 4 L PEG unspecified time of day; $MgSO_4$ 15 g and bisacodyl 10 mg the day prior Split: NaP evening the day prior; NaP 3 h before colonoscopy	Afternoon	2
Zhang et al[17]	RCT China	159/159	Ottawa scale. Successful score < 7	Low-residue food the day prior	Same day: 2 L PEG 4-6 h before colonoscopy Split: 1 L PEG at 9 PM the day prior; 2- PEG 4-6 h before colonoscopy	Not described	3

Asc indicates ascorbic acid; BBPS, Boston Bowel Preparation Scale; CS, citrates and simethicone; NaP, sodium phosphate; PEG, polyethylene glycol; RCT, randomized controlled trial; SPMC, sodium picosulfate with magnesium citrate.

Shah et al[14] provided information only about average Ottawa scores, and did not disclose adequate bowel preparation in either group. Chen et al[6] showed SpD was better than SaD, but the trial did not offer dichotomous information. In the analysis of the remaining 11 studies, 79.4% (735/926) of patients using SaDs had adequate bowel cleanliness, whereas the proportion of patients with the same level of bowel cleanliness was 81.7% (846/1036) with SpDs (Fig. 4). The pooled analysis revealed comparable bowel cleanliness in the 2 arms (OR = 0.92; 95% CI, 0.62-1.36) with substantial heterogeneity ($I^2 = 60$), so subgroup analysis evaluated the influence of bisacodyl on bowel cleanliness. Comparing SaDs with bisacodyl to SpDs without it the previous evening showed the results favored SaDs in bowel cleanliness (OR, 2.45; 95% CI, 1.45-4.15; $I^2 = 0\%$). If both arms eliminated adjuvants, the analysis revealed that SpDs had better bowel cleanliness with no heterogeneity (OR, 0.66; 95% CI, 0.49-0.88) (Table 2).

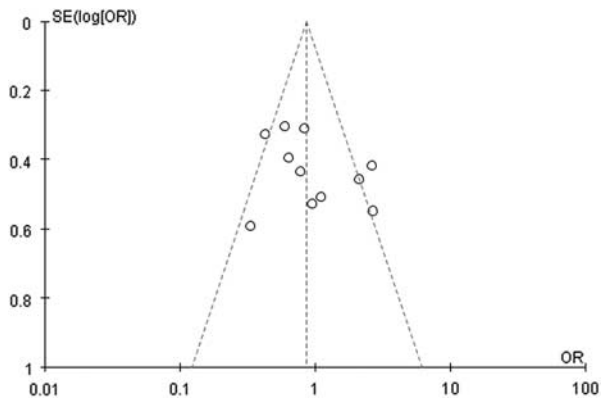

FIGURE 2. Funnel plot. No significant publication bias noted in primary outcome. OR indicates odds ratio.

CIR and ADR

CIRs were reported in 6 studies, whereas 94.1% and 94.6% of patients using SaDs and SpDs achieved cecal intubation, respectively.[4,5,7,9,13,15] The OR ratio was 0.87 (95% CI, 0.49-1.54) with no heterogeneity existing between the 2 arms with $I^2 = 0\%$. ADRs were found in 7 studies and the results were 26.7% and 29.4% in SaDs and SpDs, respectively.[4,5,7,11,13,15,17] The OR was 0.87 (95% CI, 0.67-1.13) with low heterogeneity ($I^2 = 12\%$) (Figs. 5, 6).

Patient Tolerance

Willingness to repeat, plus completion of bowel preparation fluid, was reported in 8 and 11 trials, respectively. There was no significant difference between the 2 arms (Table 3). Side effects including nausea, vomiting, and abdominal pain/cramps also revealed no significant difference in the meta-analysis. The 95% CIs were 0.86-1.85, 0.58-1.91, and 0.75-1.72, respectively, with substantial heterogeneity. Eight trials provided information about sleep disturbances, with analysis showing that patients using SaDs had better sleep quality (OR, 0.44; 95% CI, 0.24-0.82).[7,8,11,13–17]

DISCUSSION

The quality of bowel preparation is essential for screening colonoscopy to identify precancerous or cancerous lesions. Patient compliance with diet restriction and large-volume purgative consumption was important to

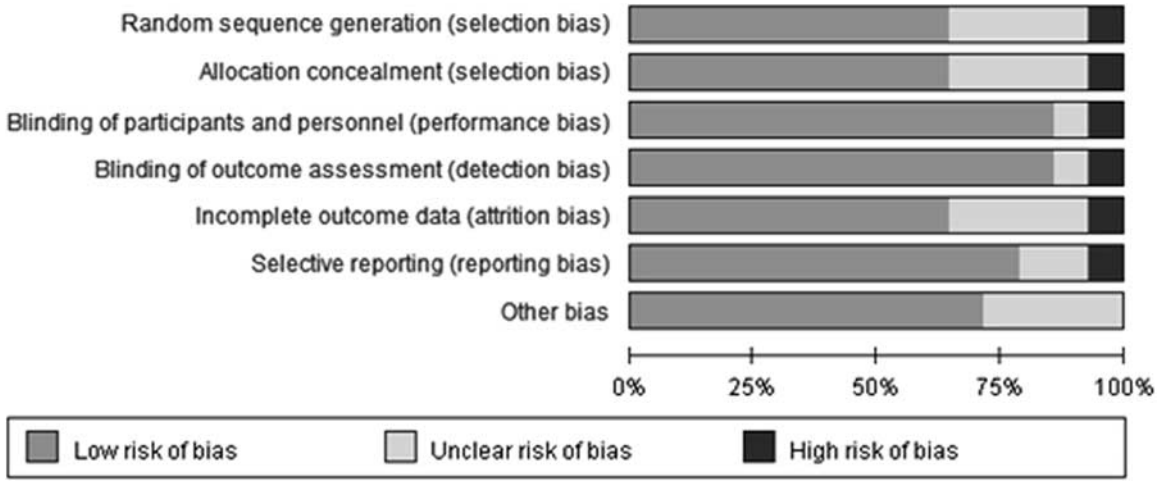

FIGURE 3. Cochrane risk bias tool.

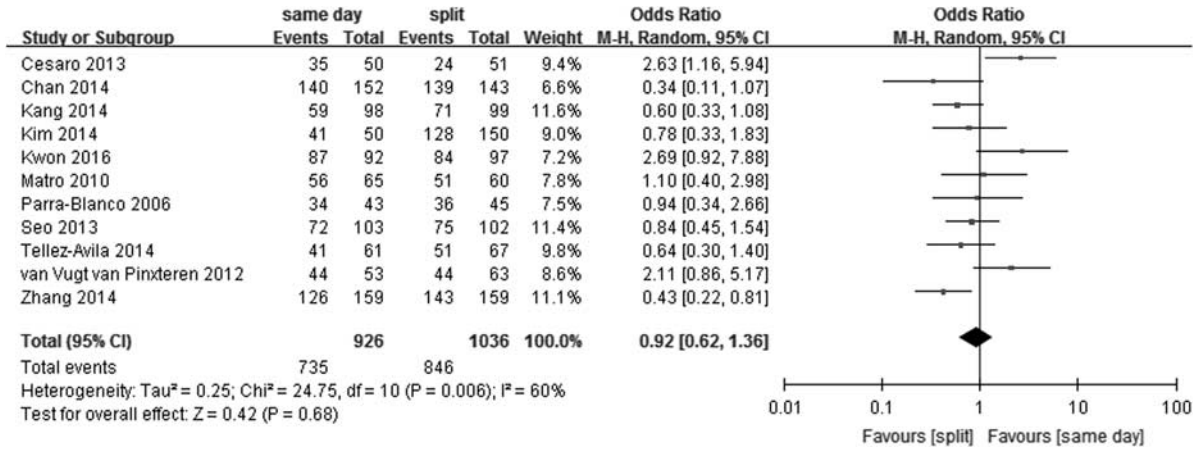

FIGURE 4. Forest plot comparing bowel cleanliness for SaDs versus SpDs. CI indicates confidence interval. M-H indicates Mantel-Haenszel.

TABLE 2. Primary Outcome: Adequate Bowel Cleanliness

Outcomes	No. Trials	No. All Patients	OR (95% CI)	Ratio in Arms [Same Day/Split (%)]	Heterogeneity (*P*)	I^2 (%)
Same day with bisacodyl vs. split without bisacodyl	3	406	2.45 (1.45-4.15) Favors same-day dosing	85.1/72.0	0.92	0
Same day without bisacodyl vs. split without bisacodyl	6	1173	0.66 (0.49-0.88) Favors split-dosing	73.7/81.5	0.61	0
Same day with bisacodyl vs. split with bisacodyl	2	383	0.58 (0.21-1.60)	89.2/93.1	—	—

CI indicates confidence interval; OR, odds ratio.

achieve better quality of bowel preparation. In this meta-analysis, we found SaDs to be comparable with SpDs in terms of bowel cleanliness, CIR, and ADR, as they outperformed SpDs in bowel cleanliness, with the addition of bisacodyl. Patients receiving SaDs also experienced better sleep the previous night.

The standard bowel preparation for colonoscopy was adapted from methods to prepare patients for abdominal

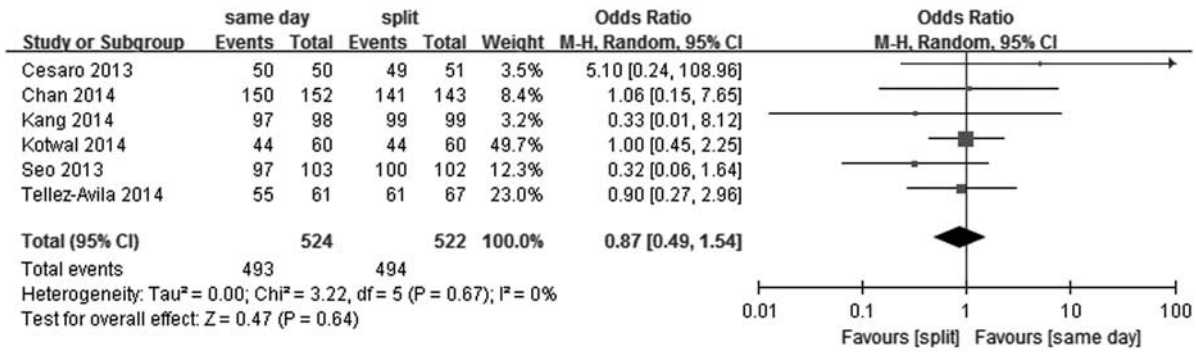

FIGURE 5. Forest plot for SaDs versus SpDs on cecal intubation rate. CI indicates confidence interval. M-H indicates Mantel-Haenszel.

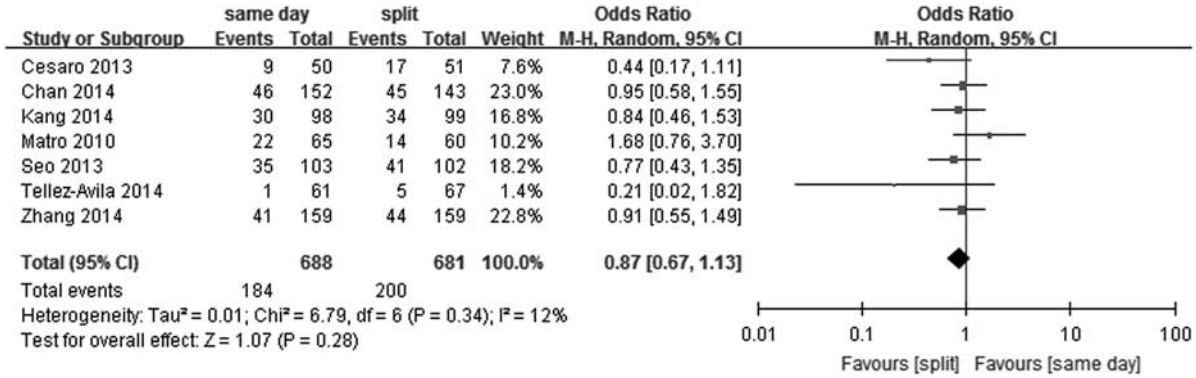

FIGURE 6. Forest plot for SaDs versus SpDs on adenoma detection rate. CI indicates confidence interval. M-H indicates Mantel-Haenszel.

TABLE 3. Secondary Outcomes: Patient Tolerance

Outcomes	No. Trials	No. All Patients	OR (95% CI)	Ratio in Arms [Same Day/Split (%)]	Heterogeneity (*P*)	I^2 (%)
Willingness to repeat	8	1251	1.08 (0.45-2.61)	75.1/72.3	< 0.001	89
Completion of bowel preparation	11	1966	0.89 (0.45-1.78)	90.2/90.5	< 0.001	70
Side effects						
Any side effects	6	936	0.86 (0.53-1.39)	39.4/41.3	0.04	57
Nausea	11	2038	1.26 (0.86-1.85)	29.6/25.7	< 0.001	70
Vomiting	10	1937	1.05 (0.58-1.91)	11.1/9.4	< 0.001	70
Abdominal pain/cramps	11	2038	1.14 (0.75-1.72)	13.3/12.5	0.02	51
Sleep disturbance	8	1489	0.44 (0.24-0.82)	22.3/37.4	< 0.001	83
			Favors same-day dosing			

CI indicates confidence interval; OR, odds ratio.

surgery; purgatives were taken and finished the evening before colonoscopy.[20] In the 1990s, investigators started to challenge the traditional preparation methods: Frommer[21] concluded that SpD with sodium phosphate (NaP) was better than NaP or polyethylene glycol (PEG) the day before (in terms of efficacy with bowel cleansing). Church also suggested that the timing of PEG administration was the major quality determinant of bowel preparation, and speculated an optimal time window for bowel cleansing after gut lavage; this was because of the influx of small-bowel contents into the colon after the optimal time window.[22,23] A meta-analysis reviewed 38 further trials comparing the efficacy of bowel cleansing between SpDs and day before regimens; it was concluded that SpDs were better in terms of the quality of bowel preparation.[24] SpDs were recommended by ASGE as a routine bowel preparation in the guidelines as well, with an interval of 3 to 8 hours between the second dose of SpDs and the time of colonoscopy for optimal cleansing.[19]

However, SpDs can interrupt sleep, cause nocturnal incontinence, and influence the function of patients during the preparation period. Therefore, several studies were

performed to establish the hypothesis that gut lavage on the day of colonoscopy would provide equal efficacy in bowel cleanliness, along with reduced preparation time and less adverse effects. Longcroft-Wheaton and Bhandari[3] prospectively assigned patients to SpD or SaD with sodium picosulphate (SP) before colonoscopy, with the results revealing that SaD offered better quality of bowel cleanliness, and less impairment in daily activities and adverse effects. This meta-analysis reviewed 14 randomized trials comparing SaDs to SpDs, such that the pooled analysis disclosed that SaDs offered equal quality of bowel preparation and less sleep disturbance. Accordingly, SaDs could be a better alternative to SpDs because of increased tolerance, along with equal bowel preparation quality.

Heterogeneity was noted among studies, which suggested disagreements in findings, and several factors could be responsible for the heterogeneity (Table 1). First, regimens used in SaD and SpD arms varied. PEG is associated with less electrolyte imbalance and used in both arms of most trials.[2] Four trials used the same volume of PEG in both arms: 1 trial found that SpD had a better quality score without reporting adequate preparation rate,[14] and the other 3 trials revealed no significant difference between SaDs and SpDs.[5,8,11] Five studies used different volumes of PEG in 2 arms: Kwon et al[10] (1 L SaD vs. 2 L SpD), Seo et al[13] (2 L SaD vs. 4 L SpD), and Tellez-Avila et al[15] (2 L SaD vs. 4 L SpD) showed no significant difference between the 2 arms. However, the study by Zhang et al[17] compared 2 L PEG SaD to 3 L PEG SpD, with the result showing that SpD was significantly better than SaD (79.2% vs. 89.9% in SaD and SpD, respectively, $P = 0.008$). On the contrary, Cesaro et al[4] found significantly more adequate preparations for 2 L PEG SaD plus bisacodyl compared with 4 L PEG SpD (70% vs. 49%, $P = 0.033$). Although most trials administered PEG solution in both arms, 5 trials used different purgatives in 2 arms. Chen et al[6] showed a better score in the cleansing effect of NaP SpD than 3 L PEG SaD, the other 4 trials found no difference between SaDs and SpDs (Kang et al[7] compared SP SaD to 4 L PEG SpD, Kim et al[8] compared 4 L PEG SaD to SP SpD, Parra-Blanco et al[12] compared 3 L PEG SaD to NaP SpD, and van Pinxteren et al[16] compared 4 L PEG SaD to NaP SpD). Second, colonoscopy was performed in 3 to 8 hours after the administration of the last dose of purgatives (the optimal window) in 7 trials.[19] Five trials found no difference between 2 arms in bowel cleansing effect,[5,7,8,11,13] whereas the other 2 trials showed SpDs had a significantly higher rate of adequate preparation than SaDs.[6,17] As for the 4 trials including patients not having a colonoscopy within the optimal interval, 1 trial found that SpD was better in bowel cleansing,[14] whereas another trial showed that SaD had a better performance than SpD.[4] There was no significant difference of preparation quality in the other 2 trials.[12,15] Third, the definition of adequate bowel preparation varied between studies. Although Ottawa scale was used most frequently among studies, Boston and Aronchick scales were also used in 5 studies,[5,6,8,10,15] and 3 studies evaluated bowel preparation quality by unvalidated scales.[11,12,16] Fourth, a wide range of diet plans during preparation among studies could be another factor responsible for the heterogeneity. Provided with the heterogenous designs between studies, further large-scale homogeneous studies are needed to validate our result that SaDs could be a better alternative to SpDs.

Patient compliance is a crucial factor regarding the quality of bowel preparations. Large liquid volumes (4 L) were used to achieve an optimal cathartic effect. However, high-volume purgatives can cause nausea, vomiting, abdominal fullness, and cramping.[19] Therefore, several adjuvants were studied to reduce the required volume of purgatives and to increase the quality of bowel preparation, showing that bisacodyl was the most promising agent among them. By 1994, Adams et al[25] designed a randomized trial to demonstrate that bisacodyl could improve colon preparation, including a reduced volume of PEG, along with better tolerance among patients. Later, Ker[26] and Parente et al[27] came to the same conclusion, that is, that the addition of bisacodyl in either regimen could achieve an equal bowel cleaning result with a lower volume of purgatives. Other than NaP and PEG, bisacodyl also enhanced the strength of SP in terms of its effectiveness of bowel preparations.[28] In our review, 5 studies took advantage of bisacodyl,[4,5,10,12,16] and 3 of them administered bisacodyl only in the SaD arm.[4,10,16] The subgroup analysis showed that bisacodyl could assist SaDs towards achieving better quality of bowel preparation than SpDs, without the addition of bisacodyl (Table 2). Accordingly, bisacodyl taken the previous evening was essential for optimizing SaDs. However, the broad 95% CI between 1.45 and 4.51 indicates that the result needs further studies to validate.

ASGE releases quality indicators for improvement, and recommends that CIR should be $>90\%$ in all examinations, and 95% in screening colonoscopy.[29] CIR showed no difference between SaDs and SpDs in our study; however, although CIR was over 90% in all other trials reporting the quality indicator, Kotwal et al[9] found CIR at 86.3% and 84.6% in SaDs and SpDs arms, respectively. The inclusion of hospitalized patients with different indications could explain the low CIR.

ADR is identified as another primary indicator by ASGE: a minimum target for it in a population over 50 years old should be $\geq 25\%$ (for men $\geq 30\%$, for women $\geq 20\%$). In the meta-analysis, no difference in ADR was noted between the 2 arms. However, ADR was $>25\%$ in both arms among ADR-reported trials, except those of Tellez-Avila et al[15], Cesaro et al,[4] and Matro et al[11] The ADR in the SpD arm of Matro and colleagues was 24.1% and that in the SaD arm of Cesaro and colleagues was 18% while Tellez-Avila and colleagues reported unacceptably low ADR in both arms, with an average age of patients about 55 years (1.7% and 8.2% in SaDs and SpDs, respectively). Furthermore, ADR in the SaD arm of the trial from Cesaro and colleagues was lower than in the SpD arm (18% vs. 34%), even though SaD achieved greater cleanliness than SpD. The inconsistency between bowel preparation quality and ADR was also noted in previous studies.[30,31] Jover et al[31] reported ADR being associated with excellent colon cleanliness was lower than those with good to fair cleanliness. Calderwood and colleagues evaluated bowel preparation quality and ADR, with the Boston Bowel Preparation Scale (BBPS), and found ADR associated with total BBPS scores of 6, 7, and 8 was higher than those with a score of 9. (BBPS 6: 40.4%, BBPS 7: 40.6%, BBPS 8: 38.8% vs. BBPS 9: 34.4%). Distraction or a false sense of confidence in an excellent preparation should be avoided in the inspection phase.[30] Other variables should be searched and analyzed in future studies.

This meta-analysis demonstrated that over 90% of patients could finish the preparation fluid in both arms, and that nausea/vomiting/abdominal pain happened in both arms as well, but without a significant difference. However, sleep disturbance occurred less often with SaDs. Patients in 2 trials, who needed to wake up early to finish bowel preparation for morning colonoscopy, still had better sleep quality.[13,14] The result suggested that SaDs could serve as a viable alternative to SpDs, with the additional benefit of increased patient compliance.

The strength of this study is that it used only randomized controlled trials performed in China, Korea, Malaysia, India, Italy, Spain, Netherlands, Mexico, and the United States, so the results could be applied to all populations. However, there are several limitations. First, the heterogenous measurement of preparation quality by a mix of validated and unvalidated scores was the likely reason that the pooled rate of adequate preparation in these 2 groups (79.4% and 81.7%) was lower than what was typically reported (most studies looking at SpD preparation showed rates of adequate preparation >90%). Second, the diet during preparation varied among studies and the length of time for diet restriction also differed, so the influence on bowel cleanliness could not be further analyzed. Third, studies used different purgatives with various dosages in SaDs and SpDs, so the superiority among them could not be determined. Fourth, adverse effects and sleep disturbance were analyzed in a dichotomous manner, so that bias might exist in these subjective variables. Fifth, most studies excluded patients with surgical bowel resection, major psychiatric illness, severe cardiac, hepatic, or renal failure, such that conclusions from this meta-analysis could not be widely applied.

In conclusion, SaDs were comparable with SpDs in bowel cleanliness, CIR, and ADR, and could outperform SpDs in bowel cleanliness with the addition of bisacodyl. SaDs also offered better sleep the previous night than SpDs. This suggests that SaDs with bisacodyl could serve as a superior alternative to SpDs. Further studies are needed to validate the results and determine optimal purgatives and dosages.

REFERENCES

1. Hassan C, Bretthauer M, Kaminski MF, et al. Bowel preparation for colonoscopy: European Society of Gastrointestinal Endoscopy (ESGE) guideline. *Endoscopy*. 2013;45:142–150.
2. Johnson DA, Barkun AN, Cohen LB, et al. Optimizing adequacy of bowel cleansing for colonoscopy: recommendations from the US multi-society task force on colorectal cancer. *Gastroenterology*. 2014;147:903–924.
3. Longcroft-Wheaton G, Bhandari P. Same-day bowel cleansing regimen is superior to a split-dose regimen over 2 days for afternoon colonoscopy: results from a large prospective series. *J Clin Gastroenterol*. 2012;46:57–61.
4. Cesaro P, Hassan C, Spada C, et al. A new low-volume isosmotic polyethylene glycol solution plus bisacodyl versus split-dose 4 L polyethylene glycol for bowel cleansing prior to colonoscopy: a randomised controlled trial. *Dig Liver Dis*. 2013;45:23–27.
5. Chan WK, Azmi N, Mahadeva S, et al. Split-dose vs same-day reduced-volume polyethylene glycol electrolyte lavage solution for morning colonoscopy. *World J Gastroenterol*. 2014;20:14488–14494.
6. Chen H, Li X, Ge Z. Comparative study on two colonic bowel preparations for patients with chronic constipation. *Scand J Gastroenterol*. 2009;44:375–379.
7. Kang MS, Kim TO, Seo EH, et al. Comparison of the efficacy and tolerability between same-day picosulfate and split-dose polyethylene glycol bowel preparation for afternoon colonoscopy: a prospective, randomized, investigator-blinded trial. *Intest Res*. 2014;12:53–59.
8. Kim ES, Lee WJ, Jeen YT, et al. A randomized, endoscopist-blinded, prospective trial to compare the preference and efficacy of four bowel-cleansing regimens for colonoscopy. *Scand J Gastroenterol*. 2014;49:871–877.
9. Kotwal VS, Attar BM, Carballo MD, et al. Morning-only polyethylene glycol is noninferior but less preferred by hospitalized patients as compared with split-dose bowel preparation. *J Clin Gastroenterol*. 2014;48:414–418.
10. Kwon JE, Lee JW, Im JP, et al. Comparable efficacy of a 1-L PEG and ascorbic acid solution administered with bisacodyl versus a 2-L PEG and ascorbic acid solution for colonoscopy preparation: a prospective, randomized and investigator-blinded trial. *PLoS One*. 2016;11:e0162051.
11. Matro R, Shnitser A, Spodik M, et al. Efficacy of morning-only compared with split-dose polyethylene glycol electrolyte solution for afternoon colonoscopy: a randomized controlled single-blind study. *Am J Gastroenterol*. 2010;105:1954–1961.
12. Parra-Blanco A, Nicolas-Perez D, Gimeno-Garcia A, et al. The timing of bowel preparation before colonoscopy determines the quality of cleansing, and is a significant factor contributing to the detection of flat lesions: a randomized study. *World J Gastroenterol*. 2006;12:6161–6166.
13. Seo EH, Kim TO, Park MJ, et al. Low-volume morning-only polyethylene glycol with specially designed test meals versus standard-volume split-dose polyethylene glycol with standard diet for colonoscopy: a prospective, randomized trial. *Digestion*. 2013;88:110–118.
14. Shah H, Desai D, Samant H, et al. Comparison of split-dosing vs non-split (morning) dosing regimen for assessment of quality of bowel preparation for colonoscopy. *World J Gastrointest Endosc*. 2014;6:606–611.
15. Tellez-Avila FI, Murcio-Perez E, Saul A, et al. Efficacy and tolerability of low-volume (2 L) versus single- (4 L) versus split-dose (2 L + 2 L) polyethylene glycol bowel preparation for colonoscopy: randomized clinical trial. *Dig Endosc*. 2014;26:731–736.
16. van Vugt van Pinxteren MW, van Kouwen MC, van Oijen MG, et al. A prospective study of bowel preparation for colonoscopy with polyethylene glycol-electrolyte solution versus sodium phosphate in Lynch syndrome: a randomized trial. *Fam Cancer*. 2012;11:337–341.
17. Zhang S, Li M, Zhao Y, et al. 3-L split-dose is superior to 2-L polyethylene glycol in bowel cleansing in Chinese population: a multicenter randomized, controlled trial. *Medicine (Baltimore)*. 2015;94:e472.
18. Labenz J, Peitz U, Leverkus F, et al. Bowel cleansing prior to colonoscopy—golytely lavage versus a combination regime. *Eur J Gastroenterol & Hepat*. 1991;3:781–784.
19. Saltzman JR, Cash BD, Pasha SF, et al. Bowel preparation before colonoscopy. *Gastrointest Endosc*. 2015;81:781–794.
20. Mussetto A, Frazzoni L, Paggi S, et al. Split dosing with a low-volume preparation is not inferior to split dosing with a high-volume preparation for bowel cleansing in patients with a history of colorectal resection: a randomized trial. *Endoscopy*. 2015;47:917–924.
21. Frommer D. Cleansing ability and tolerance of three bowel preparations for colonoscopy. *Dis Colon Rectum*. 1997;40:100–104.
22. Cohen LB. Split dosing of bowel preparations for colonoscopy: an analysis of its efficacy, safety, and tolerability. *Gastrointest Endosc*. 2010;72:406–412.
23. Church JM. Effectiveness of polyethylene glycol antegrade gut lavage bowel preparation for colonoscopy—timing is the key!. *Dis Colon Rectum*. 1998;41:1223–1225.
24. Martel M, Barkun AN, Menard C, et al. Split-dose preparations are superior to day-before bowel cleansing regimens: a meta-analysis. *Gastroenterology*. 2015;149:79–88.

25. Adams WJ, Meagher AP, Lubowski DZ, et al. Bisacodyl reduces the volume of polyetylene-glycol solution required for bowel preparation. *Dis Colon Rectum*. 1994;37:229–233.
26. Ker TS. Comparison of reduced volume versus four-liter electrolyte lavage solutions for colon cleansing. *Am Surgeon*. 2006;72:909–911.
27. Parente F, Vailati C, Bargiggia S, et al. 2-Litre polyethylene glycol-citrate-simethicone plus bisacodyl versus 4-litre polyethylene glycol as preparation for colonoscopy in chronic constipatione. *Dig Liver Dis*. 2015;47:857–863.
28. Hookey LC, Vanner SJ. Pico-salax plus two-day bisacodyl is superior to pico-salax alone or oral sodium phosphate for colon cleansing before colonoscopy. *Am J Gastroenterol*. 2009;104:703–709.
29. Rex DK, Schoenfeld PS, Cohen J, et al. Quality indicators for colonoscopy. *Gastrointest Endosc*. 2015;81:31–53.
30. Calderwood AH, Thompson KD, Schroy PC III, et al. Good is better than excellent: bowel preparation quality and adenoma detection rates. *Gastrointest Endosc*. 2015;81:691.e1–699.e1.
31. Jover R, Zapater P, Polania E, et al. Modifiable endoscopic factors that influence the adenoma detection rate in colorectal cancer screening colonoscopies. *Gastrointest Endosc*. 2013;77:381.e1–389.e1.