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The Efficacy of Simethicone With Polyethylene Glycol for Bowel Preparation

A Systematic Review and Meta-Analysis

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Background: Simethicone (SIM) is a commonly used antifoaming agent in the clinic. However, it has not been clarified whether SIM can improve the quality of intestinal preparation and the detection rates of adenomas (ADR) and polyps (PDR). This systematic review and meta-analysis were carried out to mainly evaluate the effect of SIM in bowel preparation for colonoscopy.

Materials and Methods: An electronic and a manual search of the literature for studies was conducted in PubMed, EMBASE, and Web of Science in all published data before February 1, 2020. The primary outcomes were the quality of bowel preparation and the ADR and PDR. All the data were calculated using a pooled estimate of risk ratio with 95% confidence intervals, and a random-effect model was used for the calculation.

Results: Eighteen randomized controlled trials with 7187 patients were included in this meta-analysis. Polyethylene glycol (PEG) with SIM improved colon cleansing ($P < 0.00001$), PDR ($P = 0.006$) and the detection rate of lesions in the right colon ($P < 0.00001$) when compared with PEG alone. There was no difference in the ADR ($P = 0.68$), withdrawal time ($P = 0.06$), cecal intubation rate ($P = 0.98$), and cecal intubation time ($P = 0.65$) between 2 groups. The rate of abdominal bloating rate was higher in the PEG group, but there was no significant difference in vomiting ($P = 0.65$), and abdominal pain ($P = 0.25$).

Conclusions: SIM improves the quality of bowel cleanliness and PDR but not ADR. Besides, SIM improves the detection rate of lesions in the right colon and decreased abdominal bloating, but do not affect vomiting and abdominal pain or cramping.

Key Words: simethicone, colonoscopy, intestinal preparation, adenoma detection rate, polyp detection rate

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The authors declare that they have nothing to disclose.

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Colorectal cancer (CRC) is the most frequent malignant neoplasm in most countries. In the United States, CRC is the second leading cause of death from cancer.[1] Colonoscopy can decrease the incidence and mortality of CRC significantly through the detection and removal of adenomatous polyps and other precancerous lesions.

Efficacy of bowel cleansing is an important determinant of outcomes of colonoscopy.[2] Inadequate bowel preparation leaves a residual fecal residue or even fecal mass in the intestinal cavity and bubbles over colonic mucosa, thus result in longer procedure time and the need for early repetition of colonoscopy.[3] To improve efficacy and patient compliance, antifoaming drugs have been used as adjuvant to the standard colonic preparation products.[4]

Simethicone (SIM) is a commonly used antifoaming agent in the clinic.[5] By reducing the surface tension of bubbles in the lumen of the digestive tract, it can remove the bubble and improve the clarity of examination. Furthermore, it can reduce abdominal distention, thus resulting in a significant reduction of the number of patients with gastrointestinal discomfort symptoms.

There is no consensus on the routine use of silicone oil in intestinal preparation. One meta-analysis showed that oral SIM improved bowel cleanness and mucosal visibility but not overall adenoma detection rate (ADR) or polyp detection rate (PDR).[6] However, another meta-analysis showed that polyethylene glycol (PEG) with SIM improved colon cleansing and ADR when compared with PEG alone.[7] Thus, to date, whether it had a beneficial role for ADR or PDR had yet to be confirmed. This study, aiming to include all relevant randomized controlled trails (RCTs), is the first to evaluate the role of SIM in intestinal preparation in terms of its effects on intestinal cleanliness and the ADR and PDR when combined with laxative.

The objective of our systematic review was to identify, assess, and meta-analyze data from RCTs evaluating the effects of SIM on bowel preparation quality and the ADR and PDR for colonoscopy. In addition, we compared adverse events withdrawal time, cecal intubation time, and rates in the SIM treatment arm and the non-SIM arm.

MATERIALS AND METHODS

All analyses were based on previous published studies, thus no ethical approval and patient consent are required.

Search Strategy

Online databases (PubMed, EMBAS, and Web of Science) were searched for eligible studies published from January 1988 to January 2020. Citation selection utilized a highly sensitive search strategy to identify randomized trials with MeSH headings related to (1) colonoscopy; (2) cathartics; and (3) SIM. The

Medline search strategy was: Search ((((((((((Cathartics) OR Bowel Evacuants) OR Evacuants, Bowel) OR Purgatives) OR Bowel Preparation Solutions) OR Preparation Solutions, Bowel) OR Solutions, Bowel Preparation))) OR ((((((((((((Colonoscopy) OR Colonoscopies) OR Colonoscopic Surgical Procedures) OR Colonoscopic Surgical Procedure) OR Procedure, Colonoscopic Surgical) OR Procedures, Colonoscopic Surgical) OR Surgical Procedure, Colonoscopic) OR Surgery, Colonoscopic) OR Surgical Procedures, Colonoscopic) OR Colonoscopic Surgery) OR Colonoscopic Surgeries) OR Surgeries, Colonoscopic))) AND simethicone [Title/Abstract]. After excluding duplicated articles, the reference lists of relevant studies were searched further for potentially missed articles.

Selection Criteria

Studies that met all the following inclusion criteria were considered eligible:

(a) RCTs;
(b) adult patients (age 18 y and above) receiving colonoscopy;
(c) articles in English;
(d) studies comparing a bowel preparation with SIM to a bowel preparation without SIM;
(e) studies using outcome measures to evaluate the effectiveness of the bowel preparation were included.

Exclusion criteria were:

(a) trials comprising only animals, pediatric or inflammatory bowel disease patient populations;
(b) non-English articles;
(c) computed tomography colonography or small bowel enteroscopy or capsule endoscopy;
(d) studies only published as abstracts were excluded.

Finally, 18 kinds of qualified literature were included in this systemic review and meta-analysis (Fig. 1).

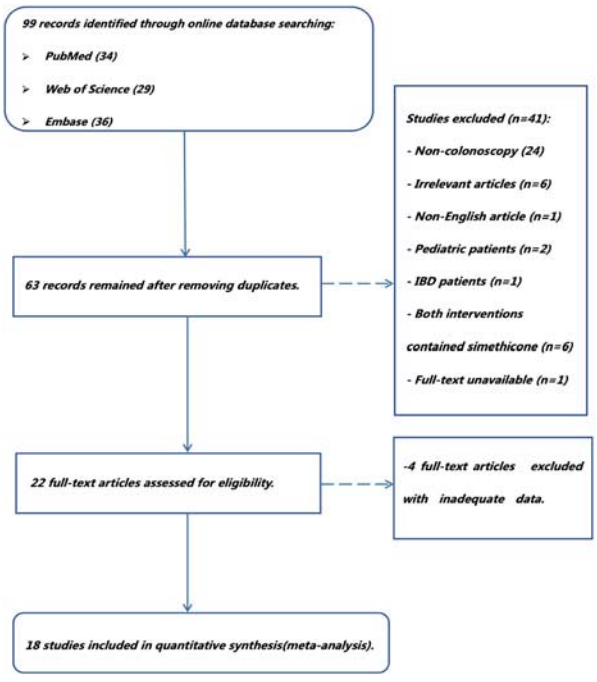

FIGURE 1. Flow chart of the selection process for the meta-analysis. IBD indicates inflammatory bowel disease.

Data Collection

Two reviewers (M.Y. and Z.L.) extracted data using a standardized form independently. The following data were extracted from each article: name of the first author, year of publication, country of study origin, patient characteristics (sample size; mean age; sex), use of cathartics and dosage of oral SIM, scale used to evaluate colon cleansing, degree of colon cleansing, mucosal bubble score, withdrawal time of colonoscopy, cecal intubation rate and cecal intubation time, the preparations to colonoscopy intervals, and overall ADR or PDR. In addition, the location and number of adenomas or polyps per patient were obtained as data presented. Data were extracted as originally stated or following appropriate calculations as necessary. If data were missing or unavailable from a study, the authors were contacted to provide the missing data, if possible.

Outcome Assessment

The primary outcomes of these studies were:

(a) bowel preparation quality in the whole colon;
(b) ADR and PDR in the whole colon and right colon.

The secondary outcomes included cecal intubation rate and cecal intubation time, withdrawal time of colonoscopy and side effects such as abdominal bloating, vomiting, and abdominal pain or cramping. The studies scored the quality of bowel preparations using validated scales either the Boston Bowel Preparation Scale[8] (BBPS), the Ottawa Bowel Preparation Quality Scale[9] (OBPS), Aronchick Scale,[10] or their nonvalidated scales.

Definitions for successful and unsuccessful bowel preparations were established a priori using existing validated scales or author's definitions of successful bowel preparations where validated scales were not used. In the included studies, the authors defined high quality bowel preparation as a BBPS score of ≥ 6,[11–17] an OBPS of <5,[17–20] and an Aronchick Scale score between 1 and 3.[15,17,21–23] For studies not using a validated scale, their scale's determination of adequate and inadequate was used.

Quality Assessment

Trail quality was graded using the Cochrane risk of bias tool for RCTs.[24] Two reviewers assessed quality measurements for included studies, and discrepancies were adjudicated by collegial discussion. It comprised of 7 items: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other bias. For each item, the risk of bias was assessed as "low risk," "unclear risk," or "high risk" (Fig. 2). All data abstraction and entries were validated independently by 2 authors.

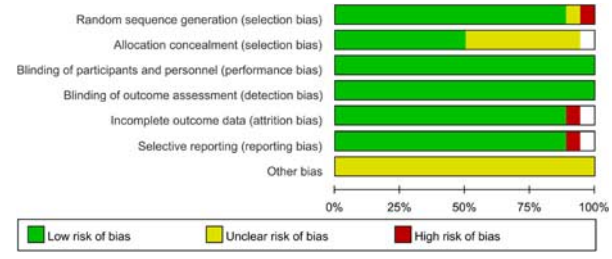

FIGURE 2. Cochrane collaboration's risk of bias assessment of included studies.

Statistical Analysis

All statistical analyses were performed by Review Manager software (RevMan, version 5.3.5, Copenhagen). Weighted mean differences with 95% confidence interval (95% CI) as the effect estimate and the risk ratio (RR) with 95% CI were used to analyze continuous data and dichotomous data, respectively. The difference was statistically significant in the case of CIs at a level of 95% or $P < 0.05$. A forest plot was conducted to test the heterogeneity between RCTs. $I^2 < 25$ was regarded as low heterogeneity, I^2 between 25% and 75% was regarded as medium heterogeneity, and $I^2 \geq 75\%$ was regarded as high heterogeneity.[25] A fixed-effect model or a random-effect model was chosen based on the forest plot and the degree of heterogeneity. Sensitivity analysis was performed by excluding the included studies one by one. Publication bias was assessed with funnel plots.

RESULTS

Study Selection

As shown in Figure 1, a total of 99 records were initially identified including 34 records from PubMed, 36 records from Embase, and 29 records from Web of Science. After duplicates were excluded, 63 records were identified through online database searching. After reviewing the titles and the abstracts, 22 articles were retrieved as full texts. Four articles with insufficient data were further exclude. Finally, 18 articles[11–23,26–30] fulfilled the inclusion criteria and were included in the meta-analysis.

Risk of Bias Assessment and Sensitivity Analysis

Of the 18 trials, 13 trials were single-blinded, 4 trials were double-blinded, and 1 trial did not describe a method to ensure that the endoscopist remained blinded to the intervention. The blind method was not considered an impairment because the outcomes were objective and assessed by blinded observers. Whether other biases existed was unclear. Publication bias testing could not be completed because of the low number of included trials in the analysis.

We performed sensitivity analysis on the results with significant statistical heterogeneity to assess the stability of our results. Whether a single study substantially altered the heterogeneity of the summary estimate was assessed by excluding a single study. Sensitivity analysis was performed by repeating the meta-analysis with the exclusion of 1 study at a time to assess the overall effect of the exclusion on the pooled RRs.

Study Characteristics

Eighteen RCTs with 7187 patients conducted between 1988 and 2019 were included in the final meta-analysis. The main characteristics of the 18 studies are shown in Table 1. Of these, 7 were multicenter studies. The indications for colonoscopy were similar between studies with most patients receiving colonoscopy for CRC screening. Among these studies, 9 were from Europe, 5 from Asia, and 4 from the United States. The sample size ranged from 90 to 2802. All studies had at least 1 treatment arm adding SIM into oral bowel preparation regimen, and at least 1 treatment arm without SIM, allowing for the effect of SIM on bowel cleanliness to be assessed. The amount of SIM added varied in the included articles. Except 2 studies using sodium phosphate for bowel cleansing, the rest of these studies used 2 or 4 L of PEG.

Quality of Bowel Cleansing

Seven RCTs used BBPS to evaluate the quality of bowel cleansing, 4 used OBPS and 4 used ABPS. The RCT conducted by Valiante and colleagues reported the Harefield cleansing scale of colonoscopy,[31] and the RCT conducted by Matro and colleagues used their nonvalidated scales.

Compared with the non-SIM group, the quality of bowel cleansing in SIM group was statistically significantly higher across studies (95% CI, 1.04-1.08; $I^2 = 68\%$; $P < 0.00001$; Fig. 3), demonstrating that the quality of bowel preparation for colonoscopy in SIM group was higher than that of the non-SIM group. Heterogeneity was high, and a random-effect model was used to summarize effect size.

A subgroup analysis of bowel preparations comparing the use of SIM in single-dosing and split-dosing regimens was performed. In the single-dosing analysis, the PEG+SIM arm had a 1.15 greater odds of having a successful bowel preparation than the PEG arm (4 trials; 95% CI, 1.09-1.21; $I^2 = 23\%$; $P < 0.00001$; Fig. 4). Heterogeneity was moderate and statistically significant across studies. However, in the split-dosing subgroup, the PEG+SIM arm only had a 1.03 greater odds of having a successful bowel preparation than the PEG arm (9 trials; 95% CI, 1.01-1.05; $I^2 = 57\%$; $P < 0.0009$; Fig. 4), indicating the effect of mixing SIM with split-dosing regimen was not obvious.

Overall ADR and PDR

ADRs were available in 9 studies, and PDRs were recorded in 11 studies. The pooled RR using a random-effect model for PDR (RR = 1.13; 95% CI, 1.04-1.23; $I^2 = 28\%$; $P = 0.006$; Fig. 5) was statistically significant in the SIM or control group. However, the pooled RR using a random-effect model for ADR (RR = 1.02; 95% CI, 0.93-1.11; $P = 0.68$; $I^2 = 41\%$; Fig. 6) was not statistically significant in the SIM or control group. Sensitivity analysis and bias analysis of the results revealed an important factor affecting the heterogeneity and stability of the results in 1 study, where the control group was given either a divided dose or a single dose. When a postsensitivity analysis was performed without this study, we found that the heterogeneity was lower than before and the results tended to be stable.

ADR and PDR in the Right Colon

Five studies reported the detection rates of lesions in the right colon, which showed statistically significant difference (RR = 1.57; 95% CI, 1.33-1.86; $P < 0.00001$; $I^2 = 74\%$; Fig. 7). After sensitivity analysis, we found that after removing Bai et al,[11] the statistical results are still significant. However, after removing Bai et al,[11] I^2 dropped from 75 to 44, which was the main factor affecting heterogeneity. It is probably because the withdrawal time of this study was shorter than other studies. But there has been no bias.

Cecal Intubation Rate and Cecal Intubation Time

Ten studies in the analysis reported the cecal intubation rate and 6 studies reported cecal intubation time, showing no statistically significant difference between the SIM group and the control group (Fig. 8A: RR = 1.00; 95% CI, 0.99-1.01; $P = 0.98$; $I^2 = 0\%$, Fig. 8B: RR = 0.08; 95% CI, −0.28 to 0.44; $P = 0.65$; $I^2 = 75\%$).

Adverse Events

No statistically significant differences were observed in abdominal pain rates (RR = 0.94; 95% CI, 0.84-1.04; $P = 0.25$; $I^2 = 64\%$; Fig. 9) and vomiting rates (RR = 1.07; 95% CI, 0.80-1.43; $P = 0.65$; $I^2 = 0\%$; Fig. 10) between the 2 groups.

TABLE 1. Basic Characteristics of the Studies Included in the Meta-Analysis

References	Country	Intervention	SIM-Dose	Sample Size (n)	Mean Age (y)	Sex (Female%)	ADR (%)	PDR (%)	Bowel Cleansing Scale
Bai et al[11]	China	2LPEG	30 mL	289	50.73	47.0	14.3	38.0	BBPS
		2LPEG+SIM		294	50.13	46.0	21.0	30.0	
Cesaro et al[18]	Italy	4LPEG	80 mg	51	56.00	49.0	34.0	—	OBPS
		2LPEG-CSB		102	59.00	57.8	25.0	—	
de Leone et al[19]	Italy	4LPEG	80 mg	79	60.90	65.8	46.7	—	OBPS
		2LPEG-CBS		78	61.80	61.5	43.6	—	
Gentile et al[21]	Italy	2LPEG-Asc	160 mg	60	55.00	43.4	—	—	ABPS
		4LPEG+SIM		60	53.00	51.7	—	—	
Jansen et al[26]	The Netherlands	4LPEG	20 mL	91	59.30	54.9	—	29.7	NA
		4LPEG+SIM		91	57.50	53.8	—	25.3	
		2LPEG		102	56.60	59.8	—	13.7	
		2LPEG+SIM		86	58.70	64.0	—	26.7	
		NAP		91	56.50	51.6	—	26.4	
Matro et al[27]	USA	PEG	40 mg	61	—	—	—	—	NA
		PEG+SIM		62	—	48.0	—	—	
Moraveji et al[12]	USA	2LPEG	40 mg	139	56.96	66.2	38.8	33.3	BBPS
		2LPEG+SIM		129	56.30	62.8	33.3	38.8	
Parente et al[30]	Italy	4LPEG	80 mg	181	59.00	60.0	—	49.2	OBPS
		2LPEG-CSB		189	60.00	54.0	—	48.1	
Pontone et al[20]	Italy	2LPEG-ASC	160 mg	72	60.10	45.0	13.0	—	ABPS
		2LPEG+SIM		72	57.60	50.0	19.7	—	
Repici et al[22]	Italy	2LPEG-Asc	80 mg	204	59.40	48.5	—	—	BBPS
		2LPEG-CSB		204	59.10	52.0	—	—	
Rishi et al[13]	USA	2LPEG+CS	200 mg	84	59.60	59.5	—	—	BBPS
		2LPEG+CSB		84	54.00	53.6	—	—	
Shaver et al[14]	USA	PEG	75 mL	59	63.10	—	—	55.9	NA
		PEG+SIM		56	62.30	—	—	57.1	
Tongprasert et al[28]	Thailand	NAP	240 mg	60	56.50	61.7	—	46.7	NA
		NAP+SIM		62	57.50	56.5	—	50.0	
Valiante et al[29]	Italy	4LPEG	80 mg	126	61.30	35.7	—	56.3	Harefield Cleansing Scale
		2LPEG-CSB		138	63.60	40.6	—	76.1	
Yeo et al[15]	Korean	2LPEG-ASC	400 mg	30	47.53	33.3	—	40.0	BBPS
		2LPEG-ASC+SIM		30	50.43	36.7	—	40.0	ABPS
		2LPEG-ASC+water		30	46.00	43.4	—	30.0	
Yoo et al[16]	Korean	2LPEG-ASC	400 mg	130	53.27	65.0	46.0	—	BBPS
		2LPEG-ASC+SIM		130	56.97	59.0	50.0	—	
Zhang et al[17]	China	2LPEG	30 mL	290	45.50	40.0	15.5	32.1	BBPS
		2LPEG+SIM		289	44.70	43.3	22.1	33.9	OBPS ABPS
Zorzi et al[23]	Italy	4LPEG	80 mg	938	59.90	42.8	34.8	—	ABPS
		2LPEG-ASC		924	59.80	44.6	37.4	—	
		2LPEG-CSB		940	59.80	45.2	34.3	—	

ADR indicates adenoma detection rate; BBPS, Boston Bowel Preparation Scale; NA, not available; NAP, sodium phosphate; OBPS, Ottawa Bowel Preparation Quality Scale; PEG, Polyethylene glycol.

Compared with the control group, the abdominal bloating rates in the SIM group were statistically significantly different across studies (RR = 0.73; 95% CI, 0.66-0.80; $P < 0.00001$; $I^2 = 93\%$; Fig. 11). High heterogeneity might be the result of unquantified evaluation criteria of abdominal distension, which was artificially evaluated by patients according to their perception.

Withdrawal Time

Five studies reported withdrawal time, showing no statistically significant difference between the SIM group and the control group (RR = −0.28; 95% CI, −0.57 to 0.01; $P = 0.06$; $I^2 = 81\%$; Fig. 12).

DISCUSSION

Compared with the traditional examination methods, colonoscopy has clear advantages in the diagnosis and treatment of intestinal diseases. Clear inspection field of vision is the prerequisite for accurate diagnosis of lesions. At the same time, poor intestinal preparation leads to bubbles, mucus, and fecal contamination in the intestinal cavity, which will reduce the clarity of

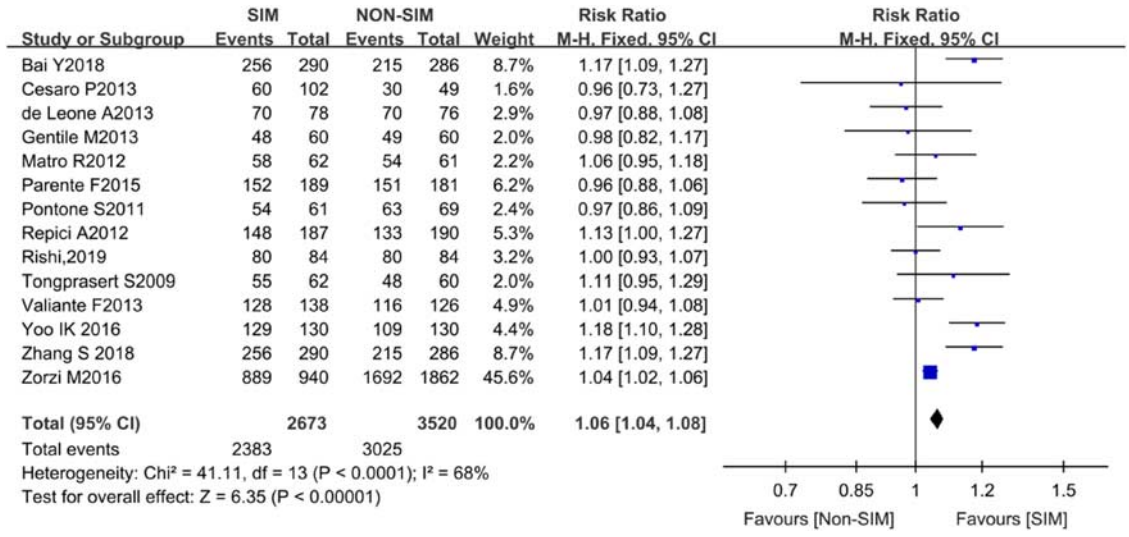

FIGURE 3. Comparison of successful bowel preparation rates between PEG only treatment and PEG+SIM treatment. CI indicates confidence interval; PEG, polyethylene glycol; SIM, simethicone.

vision field of colonoscopy, impair the diagnosis of minor gastrointestinal lesions, prolong the duration of colonoscopy, and aggravate the procedure-induced pain experienced by patients.[3] Previous studies have shown that SIM combined with laxatives could effectively reduce intestinal bubbles and improve the clarity of endoscopic vision during colonoscopy.[32] However, whether this method can improve the quality of bowel preparation and the diagnosis of intestinal microlesions still requires more proof. This study was the first to address these questions.

This systematic review and meta-analysis including 18 RCTs was carried out to review the literature on SIM for colonoscopy. The primary outcomes were bowel preparation quality, and ADR and PDR. The secondary outcomes were cecal intubation rate and time, withdrawal time,

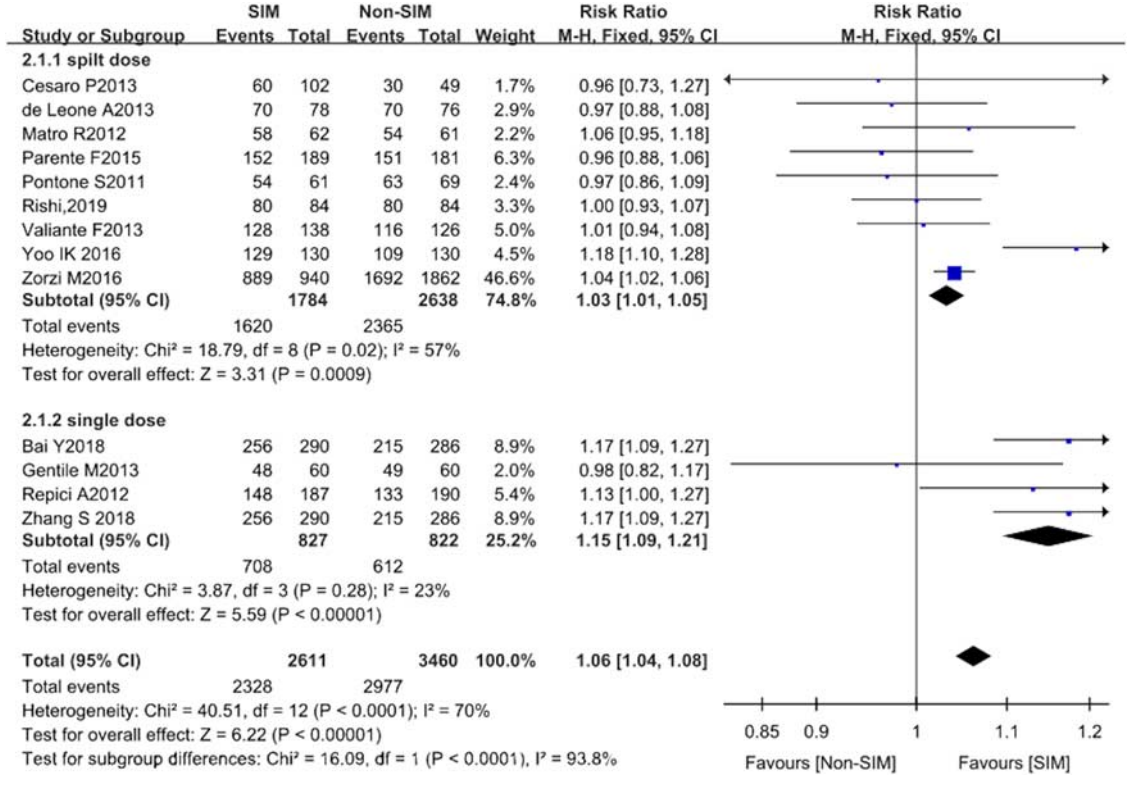

FIGURE 4. Subgroup analysis for the comparison of successful bowel preparation rates between the use of SIM in single-dosing and split-dosing regimens. CI indicates confidence interval; SIM, simethicone.

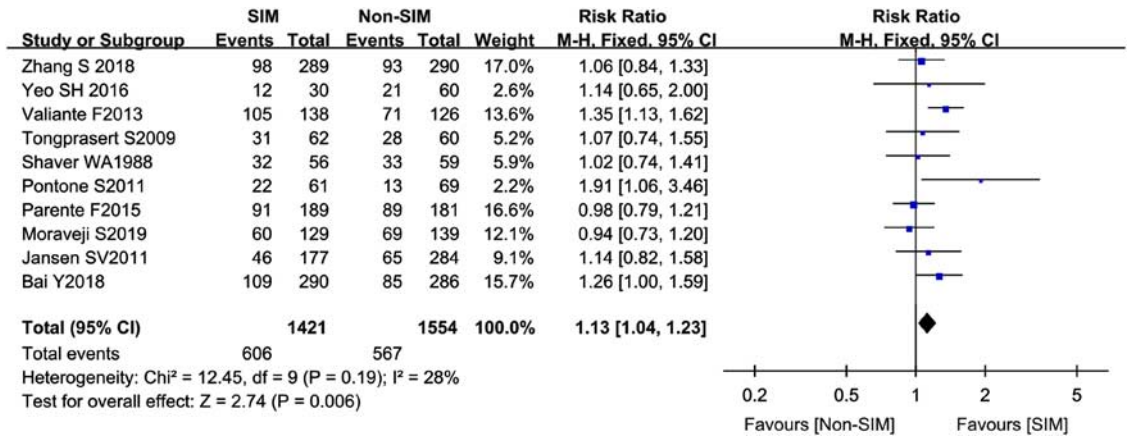

FIGURE 5. Comparison of polyp detection rates between PEG only treatment and PEG+SIM treatment. CI indicates confidence interval; PEG, polyethylene glycol; SIM, simethicone.

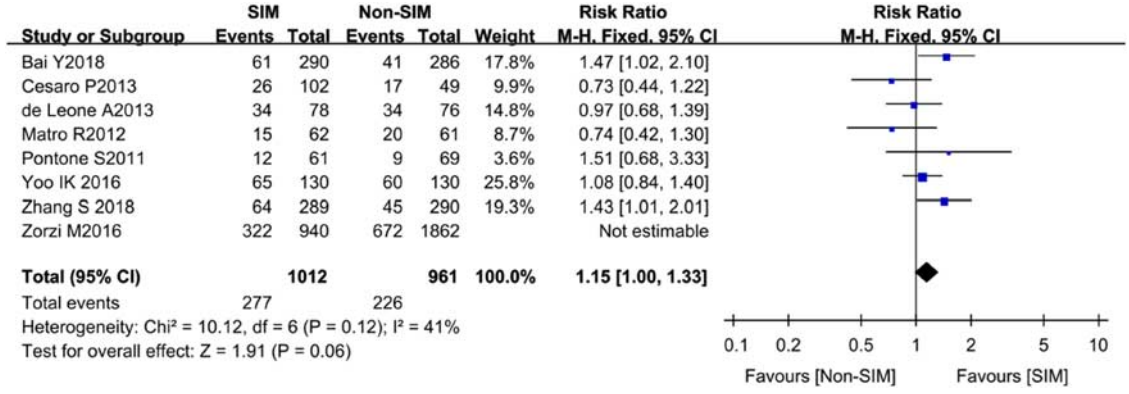

FIGURE 6. Comparison of adenoma detection rates between PEG only treatment and PEG+SIM treatment. CI indicates confidence interval; PEG, polyethylene glycol; SIM, simethicone.

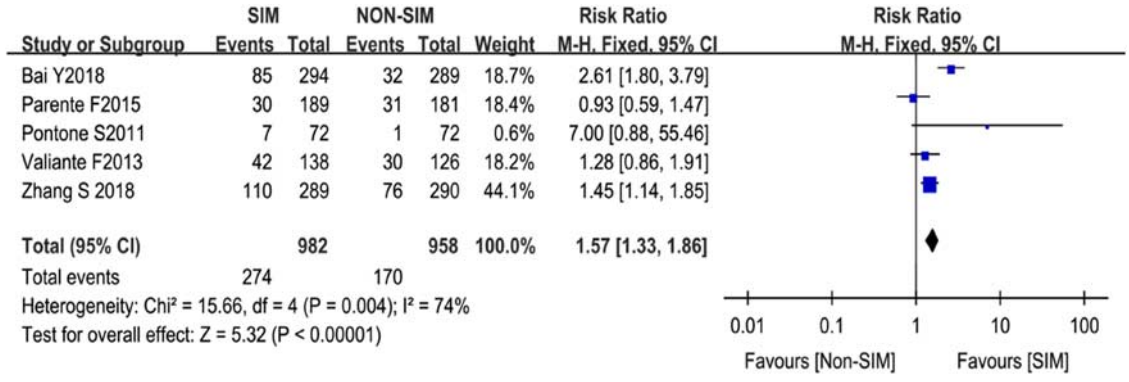

FIGURE 7. Comparison of adenoma and polyp detection rates in the right colon between PEG only treatment and PEG+SIM treatment. CI indicates confidence interval; PEG, polyethylene glycol; SIM, simethicone.

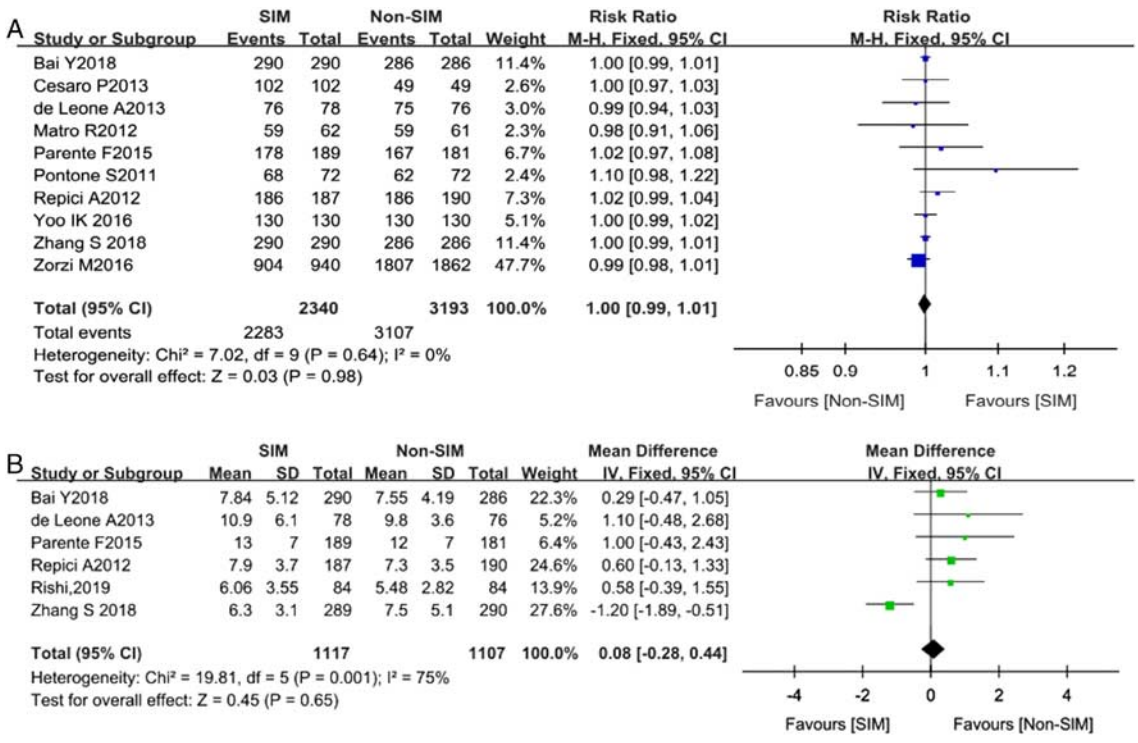

FIGURE 8. Comparison of cecal intubation rates (A) and cecal intubation time (B) between PEG only treatment and PEG+SIM treatment. CI indicates confidence interval; PEG, polyethylene glycol; SIM, simethicone.

adverse events such as abdominal bloating, vomiting, and abdominal pain or cramping.

As our results showed, adding SIM to the bowel preparation regimen improved the quality of bowel cleanliness and polyp detection rate but not ADR. The withdrawal time, cecal intubation time, and cecal intubation rate were not statistically significant in the SIM or control group. Besides, we found that SIM could decrease abdominal bloating but had no effect on vomiting and abdominal pain or cramping.

The underlying mechanism of SIM in improving bowel cleansing is still unknown. Apart from reducing the surface tension of the intestinal contents, SIM may potentially decrease the resistance from bubbles, thereby promoting intestinal peristalsis.[17] In our study, compared with the non-SIM group, the quality of bowel cleansing in SIM group was statistically significantly higher across studies. Furthermore, the subgroup analysis revealed that the effect of adding SIM as single-dosing regimen was more obvious than that as split-dosing regimen. This was likely because a single dose

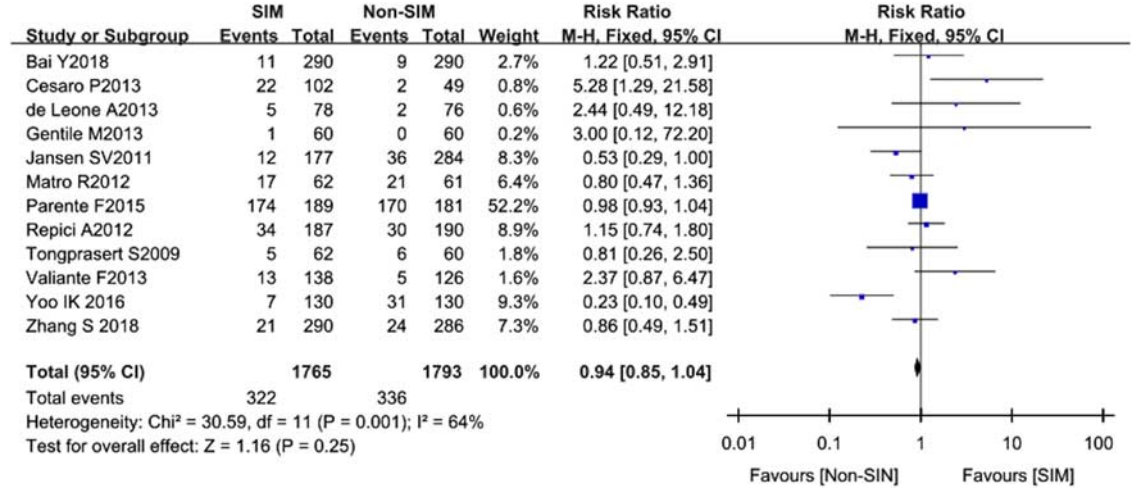

FIGURE 9. Comparison of abdominal pain/cramping rates between PEG only treatment and PEG+SIM treatment. CI indicates confidence interval; PEG, polyethylene glycol; SIM, simethicone.

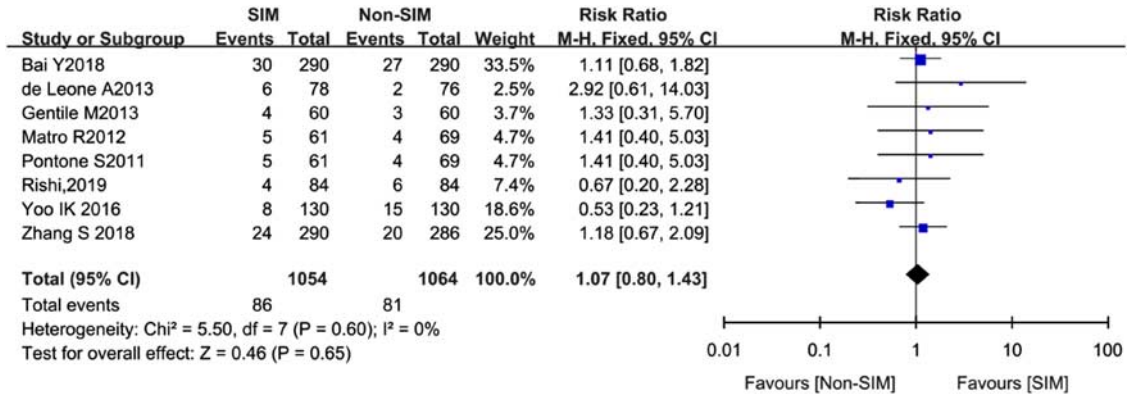

FIGURE 10. Comparison of vomiting rates between PEG only treatment and PEG+SIM treatment. CI indicates confidence interval; PEG, polyethylene glycol; SIM, simethicone.

intestinal preparation plan often fails to achieve satisfactory results so that SIM can provide more obvious improvement on intestinal preparation. Colonoscopy interval was significantly associated with bowel cleansing in the current study. Three articles compared the preparations to colonoscopy interval and have shown that the optimal interval required to achieve adequate bowel cleansing was between 2 and 7 hours, whereas the risk of inadequate cleansing significantly increased if the colonoscopy was carried out after 7 hours. We hope that more future studies will incorporate this indicator for analysis.

Although SIM did not improve the overall ADR, it did improve the detection rate of lesions in the right colon. We performed a sensitivity analysis of the results, showing that the result of Zorzi et al[23] was an important factor affecting heterogeneity and stability of results. The variations in clinical protocols (such as different reagents and their volumes, use of adjuvants) as well as varying definitions for both split doses could explain this observation. Besides, the detection rates of ≤ 10 mm adenomas and polyps have been reported in several RCTs. Bai et al[11] reported that 122 adenomas (size ≤ 10 mm) in the SIM group versus 60 in the non-SIM group were detected. Pontone et al[20] reported significant evidence of a greater number of microadenomas diagnosed in the PEG +SIM group than PEG only group. Zhang et al[17] reported 45 adenomas (size ≤ 10 mm) in the SIM group versus 27 in the control group. Despite the small sample sizes, these results suggested that better bowel preparation may make it easier to detect small adenomas. And additional larger clinical trials are required to answer this question definitively.

Colonoscopy is the most direct way to diagnose and treat colorectal diseases, but it has a certain rate of missed diagnosis of lesions, especially in the right colon.[33] Because of the deep fold of the right colon, the lesions are often flat, resulting in a higher rate of missed diagnosis. Therefore, it is of great clinical significance to reduce the missed diagnosis of polypoid lesions in the right colon. In this study, compared with the non-SIM group, the detection rate of lesions in the right colon in SIM group was statistically significantly higher. Zhang et al[17] reported that ADR in the right colon was significantly higher for the SIM group than the conventional group. As demonstrated in our meta-analysis, SIM could reduce mucus or bubbles, produce a clearer field of vision, and increase the detection rate of right colonic polyps, which would likely lead to an increase in the effectiveness of colonoscopy.

Regarding adverse events, we found that SIM could significantly decrease the odds of abdominal bloating. Better tolerance of patients can improve the quality and

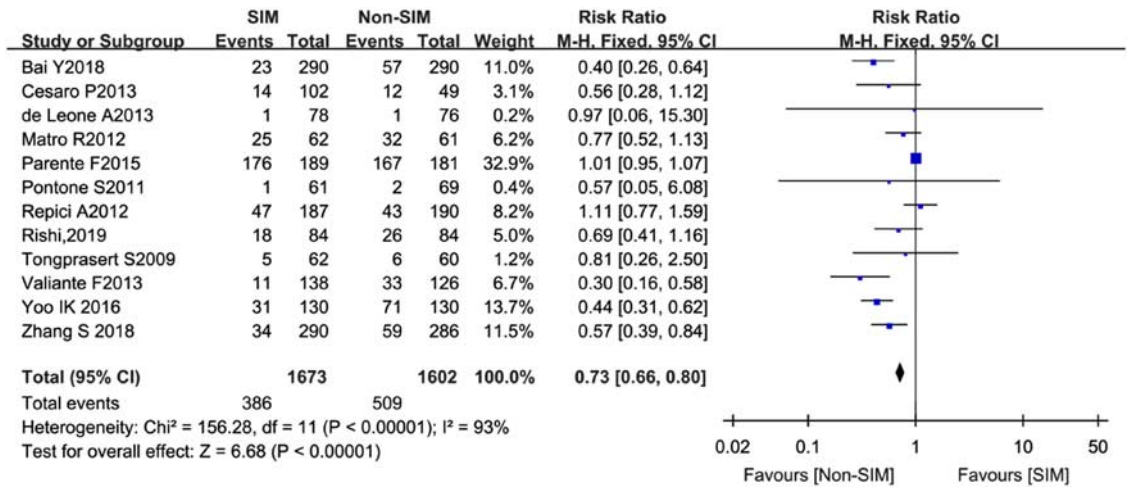

FIGURE 11. Comparison of abdominal bloating rates between PEG only treatment and PEG+SIM treatment. CI indicates confidence interval; PEG, polyethylene glycol; SIM, simethicone.

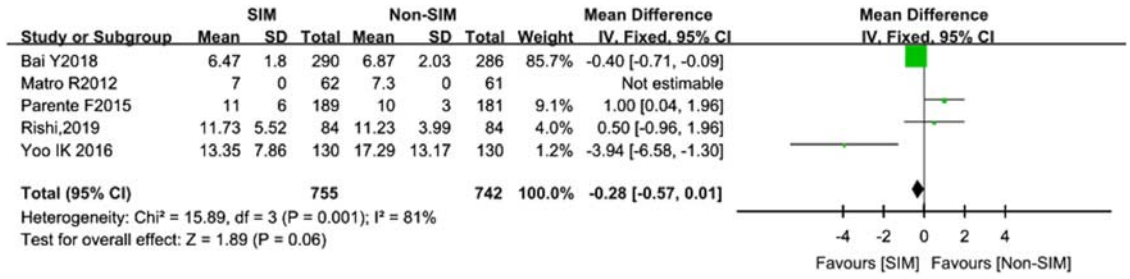

FIGURE 12. Comparison of withdrawal time between PEG only treatment and PEG+SIM treatment. CI indicates confidence interval; PEG, polyethylene glycol; SIM, simethicone.

compliance of intestinal preparation and reduce the fear of endoscopic examination.

Recently, the study by Ofstead et al[34] pointed out that SIM solutions usually contain sugars and thickeners, which may be left in the enteroscopy channel during endoscopic use, promote the formation of biofilms and contribute to microbial growth and biofilm development. However, the available data to date have proved association but not causation. Therefore, in agreement with the American Society for Gastrointestinal Endoscopy, the Canadian Association of Gastroenterology recommends attaching importance to high-level reprocessing protocols and performing regular microbiological surveillance.[35] In brief, these findings are likely to limit the use of SIM. After assessing the benefits and risks, we concluded that continued use of SIM during gastrointestinal endoscopy was important to inhibit bubble formation and optimize mucosal examination. Therefore, it is important to preclean the endoscope immediately at the bedside, including postoperative rinsing and the prompt initiation of manual or machine cleaning. Moreover, more studies are needed to explore the best antifoaming dose of SIM to avoid the excessive use of it.

Strengths of this review include a comprehensive literature search, the inclusion of multiple types of polyps at different sites and adverse events as outcomes. However, there are several limitations in our study. First, the impact of technical factors and experience of endoscopists were not taken into account. Second, endoscopists used several different scale schemes and criteria to define the quality of colon cleansing. However, all these assessment scales emphasize similar aspects including the removable volume of clear liquid or fecal residue and the impact of the surplus on mucosal visibility, which greatly reduces the rate of bias. Third, with the exception of 1 article that did not mention the type of blindness, the rest were single-blinded for outcome assessment. Although it was unlikely that the blinding of outcome assessment had influenced the outcome of our analysis, we still recommend that double-blinded RCTs should be conducted to compare the effect on SIM group to that on non-SIM group.

More large double-blinded multicenter RCTs are necessary to evaluate the potential effect of SIM on colonoscopy.

CONCLUSIONS

In conclusion, adding SIM to the bowel preparation regimen improved the quality of bowel cleanliness and polyp detection rate but not ADR. No statistically significant differences were found in withdrawal time, cecal intubation time, and cecal intubation rate. Besides, we found that SIM improved the detection rate of lesions in the right colon and decreased abdominal bloating but had no effect on vomiting and abdominal pain or cramping.

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