Thieme

Impact of preprocedure simethicone on adenoma detection rate during colonoscopy: a multicenter, endoscopist-blinded randomized controlled trial

Authors
Yu Bai[1,*], Jun Fang[1,2,*], Sheng-Bing Zhao[1], Dong Wang[1], Yan-Qing Li[3], Rui-Hua Shi[4], Zi-Qin Sun[5], Ming-Jun Sun[6], Feng Ji[7], Jian-Min Si[8], Zhao-Shen Li[1]

Institutions
1 Department of Gastroenterology, Changhai Hospital, Second Military Medical University, Shanghai, China
2 Department of Gastroenterology, Zhongnan Hospital of Wuhan University; Wuhan, China
3 Department of Gastroenterology, Qilu Hospital, Shandong University, Ji'nan, Shandong Province, China
4 Department of Gastroenterology, Zhongda Hospital of Southeast University, Nanjing, Jiangsu Province, China
5 Department of Gastroenterology, General Hospital of Jinan Military Command, ShiFan Street 25, Jinan, Shandong Province 250031, China
6 Department of Gastroenterology, First Affiliated Hospital, China Medical University, Shenyang, China
7 Department of Gastroenterology, The First Affiliated Hospital of Medical College of Zhejiang University, Hangzhou, Zhejiang, China
8 Department of Gastroenterology, Sir Run Shaw Hospital, School of Medicine, Zhejiang University, Hangzhou, Zhejiang Province, China

submitted 20.2.2017
accepted after revision 9.7.2017

Bibliography
DOI https://doi.org/10.1055/s-0043-119213
Published online: 6.10.2017 | Endoscopy 2018; 50: 128–136

ISSN 0013-726X

Corresponding author
Li Zhao-Shen, MD PhD, Department of Gastroenterology, Changhai Hospital, Second Military Medical University, Shanghai, China
li.zhaoshen@hotmail.com

Scan this QR-Code for the author's interview.

ABSTRACT

Background and study aims Ideal bowel preparation for colonoscopy requires complete removal of fluid and foam from the colon. Polyethylene glycol (PEG) is widely used for bowel preparation, with antifoaming agents such as simethicone commonly used in combination with PEG. Data on the effect of simethicone on the adenoma detection rate (ADR) were limited. This study therefore aimed to investigate whether preprocedure simethicone could increase the ADR.

Patients and methods This was a prospective, multicenter, endoscopist-blinded randomized controlled trial involving consecutive patients who underwent colonoscopy in six centers in China. Patients were randomly assigned to one of two groups: PEG plus simethicone or PEG alone. The primary outcome was ADR; secondary outcomes were quality of bowel preparation, measured by the Boston bowel preparation scale (BBPS) and bubble scores.

Results 583 patients were included. More adenomas were detected in the PEG plus simethicone group than in the PEG alone group (ADR 21.0 % vs. 14.3 %, $P = 0.04$; advanced ADR 9.0 % vs. 7.0 %, $P = 0.38$). The mean number of adenomas detected was 2.20 ± 1.36 vs. 1.63 ± 0.89 ($P = 0.02$). Patients in the PEG plus simethicone group showed better bowel cleansing efficacy: BBPS ≥ 6 in 88.3 % vs. 75.2 % ($P < 0.001$) and bubble scores of 1.00 ± 1.26 vs. 3.98 ± 2.50 ($P < 0.001$). Abdominal bloating was reported less frequently in the PEG plus simethicone group (7.8 % vs. 19.7 %, $P < 0.001$) than in the PEG alone group.

Conclusion Combined use of PEG and simethicone is associated with a significantly increased ADR in a Chinese population.

Clinical.Trials.gov
NCT02540239
TRIAL REGISTRATION: Multi-center, Randomized trial NCT02540239 at clinicaltrials.gov.

* Co-first authors

Introduction

Colorectal cancer (CRC) is an important contributor to cancer-associated morbidity and mortality [1]. The incidence of colon cancer is currently increasing and is a threat to health worldwide [2]. Colonoscopy is used for screening, surveillance, and prevention of CRC [3,4]. Optimal bowel preparation for colonoscopy increases the efficacy and safety of colonoscopic examination [5]. However, the presence of fecal residue, brown liquid, and bubbles over the mucosa may lower the adenoma detection rate (ADR), prolong the procedure time, and affect patient compliance [6].

Preoperative oral intake of simethicone has been used in clinical practice to reduce bubbles within the bowel, thereby reducing the requirement for intraoperative flushing [7]. Simethicone is an effective antifoaming agent that reduces the surface tension of air bubbles; its use has been associated with improved patient satisfaction and compliance [8]. Combined use of simethicone and polyethylene glycol (PEG) as lavage solution for bowel preparation has been shown to reduce bloating, abdominal pain, and discomfort [9,10]. Moreover, it has been reported that PEG plus simethicone was superior to PEG alone in terms of mucosal visibility owing to the anti-foaming action of simethicone [11]. However, whether simethicone can increase the ADR, which is more clinically relevant to CRC prevention, remains to be elucidated. The aim of this study was therefore to determine whether the use of preprocedural simethicone as an adjunct to PEG preparation would improve the ADR.

Methods

Study design

This study was a prospective, randomized controlled, multicenter, endoscopist-blinded trial, and it was conducted according to the CONSORT guidelines. Data were collected from six tertiary endoscopy units (Changhai Hospital of Second Military Medical University, Qilu Hospital of Shandong University, Zhongda Hospital of Southeast University, General Hospital of Jinan Military Command, First Affiliated Hospital of China Medical University, and The First Affiliated Hospital of Medical College of Zhejiang University) over a 12-month period. The trial was registered at ClinicalTrials.gov (NCT02540239).

In all units, colonoscopy was performed by endoscopists with experience of > 1000 colonoscopy procedures and no trainees were involved in this study. The endoscopes used in this trial included CF-H260AI and CF-H290I (Olympus, Japan). No analgesia or sedation was used in any of the patients. Biopsies of suspected polyps and tumors were performed; final diagnosis was based on histopathological examination.

The study was conducted in accordance with the Declaration of Helsinki and Chinese clinical trials regulations. Study procedures were in compliance with the principles of Good Clinical Practice; the study protocol was approved by the Shanghai Changhai Hospital Ethics Committee. Patients were informed about the aims, procedures, benefits, and likely risks associated with their participation in the study, and gave written informed consent prior to their enrolment.

Eligible patients were randomly and blindly assigned to the study group or the control group through concealed allocation by a technician. The randomization table was centrally generated at the Center for Clinical Epidemiology and Evidence-Based Medicine of the Second Military Medical University, Shanghai, China. The randomization was stratified according to center, and a permuted block randomization with a block size of 4 was used; allocation concealment was achieved using sequentially numbered sealed opaque envelopes. The technician who generated the randomization table was not involved in the colonoscopy procedure. In each center, a technician or nurse who was not involved in the colonoscopy examinations was responsible for assigning patients to the simethicone group or the control group.

Inclusion criteria

Adult patients aged between 18 and 65 years and scheduled for outpatient colonoscopy were included.

Exclusion criteria

Patients with known or suspected heart failure, stroke, chronic obstructive pulmonary disease, or renal failure, with a history of colon surgery or hypersensitivity to any of the ingredients, along with pregnant or lactating women and those planning to become pregnant, and anyone who had participated in another clinical trial in the previous 60 days were excluded.

Procedure

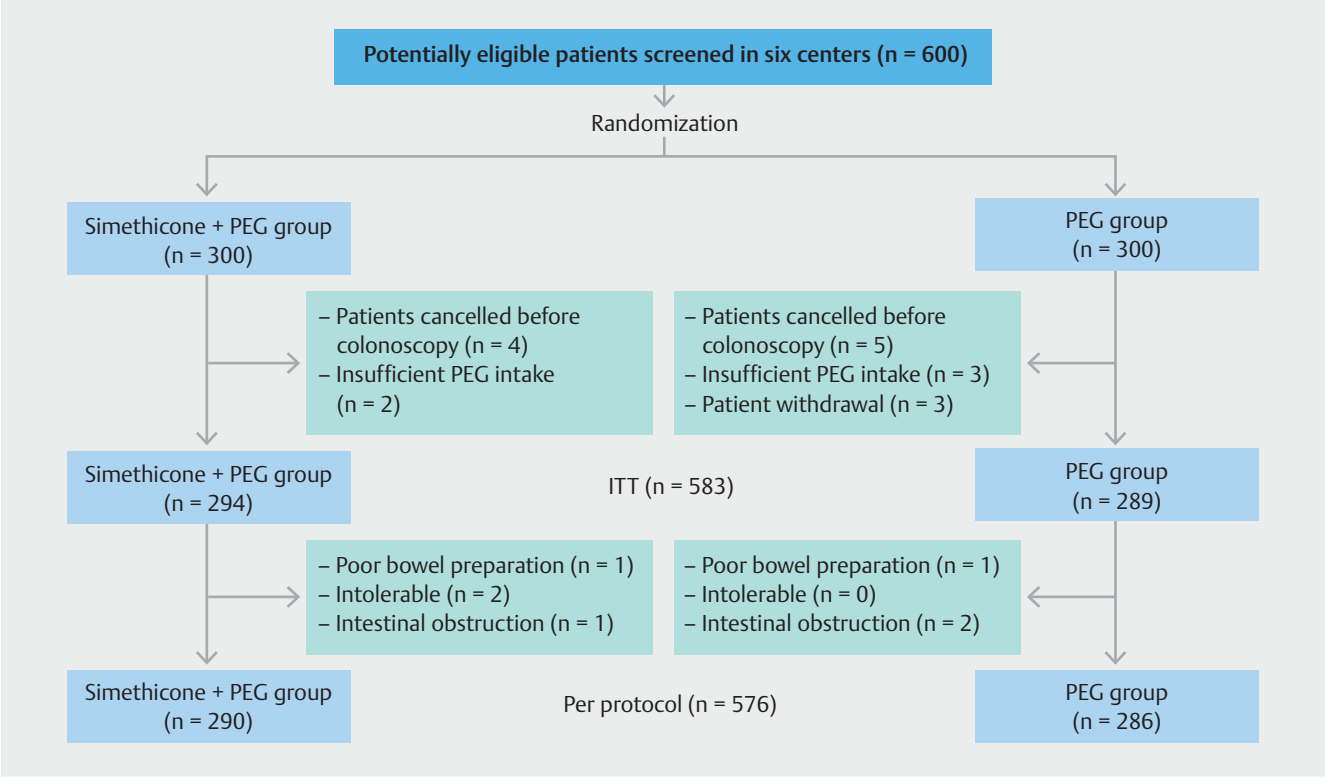
A computer-based randomization list was used to assign patients to receive one of the two bowel preparations. One group received 2 L PEG (Wanhe Pharmaceutical Co. Ltd., China; or Beaufour Ipsen [Tianjin] Pharmaceutical Co. Ltd., China) plus 30 mL simethicone (Menarini Pharmaceutical Co. Ltd., Italy) 6 – 8 hours prior to colonoscopy, with the mixture being orally administered at a dose of 250 mL every 10 – 15 minutes. Patients in the PEG alone group were given 2 L PEG. Endoscopists and nurses were blinded to the group allocation; however, the patients were informed about their treatment.

Prior to colonoscopy, patients were allowed to have a fiber-free diet comprising of meat, eggs, fish, or other dairy products. On the evening before the day of the examination, patients were required to have a clear-liquid diet only.

Outcomes

The primary outcome of this study was ADR, which was defined as the proportion of patients undergoing colonoscopy in whom at least one histologically confirmed colorectal adenoma was detected [12].

Secondary outcomes included the Boston bowel preparation scale (BBPS) score, which was developed to evaluate the quality of colon preparation and was used in our previous study [13, 14]. Each section of the colon (i. e. the right, the transverse, and the rectosigmoid colon) was rated [15]. High quality of bowel preparation was defined as a total BBPS score ≥ 6. Inadequate bowel preparation was defined as a total BBPS score < 6 [16]. In addition, the bubble score was defined on a 4-point scale according to its impact on mucosal visibility (0, no bub-



▶ **Fig. 1** Study flow diagram. PEG, polyethylene glycol; ITT, intention to treat.

bles; 1, minimal or occasional bubbles [must be actively sought]; 2, moderate or obviously present; and 3, severe or so many bubbles that vision is obscured), as has been used in previous studies [17 – 19].

Other quality indicators such as cecal intubation rate, insertion time, and withdrawal time were also recorded. Insertion time was recorded as the time for insertion of the endoscope from the anus to the cecum. Colonoscopy withdrawal time was recorded as the time from the cecum to the anus, but excluded time for biopsy performance or removal of polyps. These times were recorded by nurses or the endoscopists who performed the colonoscopy. The occurrence of gastrointestinal symptoms (nausea, vomiting, abdominal pain, and bloating) during the process of bowel preparation was also recorded.

Sample size calculation

According to our previous trials [13, 20], the ADR is about 15 % – 20 % in Chinese patients, so an estimated sample size of 273 patients in each arm would provide a power of 80 % to detect a 10 % increase in the ADR from the PEG alone group to the PEG plus simethicone group, but when a 5 % dropout rate was considered, at least 287 patients were needed in each arm.

Statistical analysis

The chi-squared test was used for categorical data. Mean (± standard deviation [SD]) and range were calculated for continuous variables and between-group differences were assessed by using Student's *t* test. Regression analysis with generalized estimating equations was used to determine the influence of body mass index (BMI), bubble score, BBPS, sex, age, and endoscopy center on ADR. *P* values < 0.05 were considered statistically significant. Statistical software from SPSS (Version 16.0, SPSS Inc., Chicago, Illinois, USA) was used for data analysis.

Results

The process of patient screening, inclusion, and exclusion is illustrated in ▶ **Fig. 1**. From July 2015 to July 2016, a total of 600 consecutive patients were screened. There were 17 patients who were not included in the final analysis, therefore 583 patients (294 PEG plus simethicone vs. 289 PEG alone) were analyzed in the intention-to-treat (ITT) and 576 patients (290 PEG plus simethicone vs. 286 PEG alone) in the per-protocol analysis. The baseline clinical and demographic characteristics were comparable between the two groups (▶ **Table 1**).

For the primary endpoint, the ADR was significantly improved in the PEG plus simethicone group (21.0 % vs. 14.3 %; *P* = 0.04), as was the polyp detection rate (37.6 % vs. 29.7 %; *P* = 0.046). There was no significant difference in terms of intubation rate or intubation time between the PEG plus simethicone group and the control group (▶ **Table 2**), but the withdrawal time was significantly shorter in the PEG plus simethicone group (6.47 ± 1.80 minutes vs. 6.87 ± 2.03 minutes; *P* = 0.03).

The characteristics of all adenomas are shown in ▶ **Table 3**, and it is notable that the mean number of adenomas detected was significantly higher in the PEG plus simethicone group (2.20 ± 1.36 vs. 1.63 ± 0.89; *P* = 0.02), although the detection rates for advanced adenomas in the two groups were similar

▶ **Table 1** Baseline characteristics of patients included in the intention-to-treat (ITT) analysis.

	PEG + simethicone (n = 294)	PEG alone (n = 289)	*P*
Age, mean ± SD, years	50.13 ± 11.37	50.73 ± 12.06	0.54
Sex, n (%)			0.66
▪ Male	160 (54 %)	152 (53 %)	
▪ Female	134 (46 %)	137 (47 %)	
Body mass index, mean ± SD, kg/m^2	23.06 ± 3.19	23.23 ± 3.45	0.54
Indication, n (%)			
▪ Diarrhea	51 (17 %)	56 (19 %)	0.53
▪ Constipation	35 (12 %)	36 (12 %)	0.84
▪ Bloating	29 (10 %)	21 (8 %)	0.26
▪ Abdominal pain	81 (28 %)	64 (22 %)	0.13
▪ Bleeding	16 (5 %)	17 (6 %)	0.82
▪ Weight loss	1 (0.3 %)	3 (1 %)	0.60
▪ Increased CEA level	4 (1 %)	7 (3 %)	0.35
▪ Change in bowel habits	12 (4 %)	6 (2 %)	0.16
▪ Post-polypectomy	21 (8 %)	13 (4 %)	0.17
▪ Others	44 (15 %)	66 (23 %)	0.02
Cecal intubation rate, n (%)	290 (99 %)	286 (99 %)	1.00
Failed colonoscopy, n	4	3	1.00
Reason for failed colonoscopy, n			
▪ Poor bowel preparation	1	1	
▪ Lack of tolerance	2	0	
▪ Colon obstruction	1	2	

PEG, polyethylene glycol; SD, standard deviation; CEA, carcinoembryonic antigen.

▶ **Table 2** Colonoscopy procedure-associated parameters by study group.

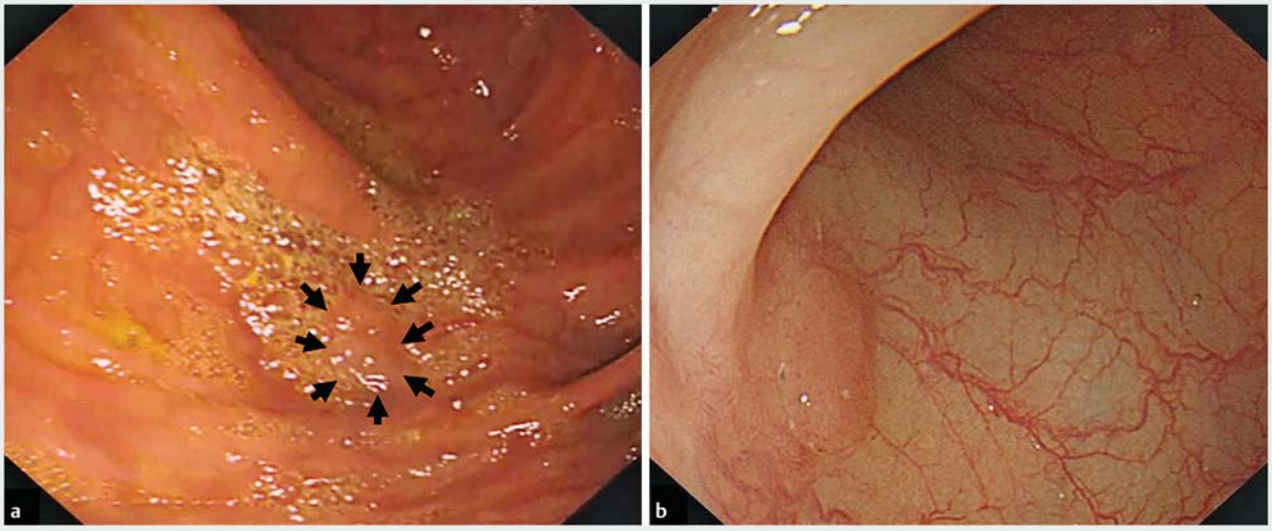
	PEG + simethicone (n = 290)	PEG alone (n = 286)	*P*
Cecal intubation time, mean ± SD, minutes	7.84 ± 5.12	7.55 ± 4.19	0.86
Withdrawal time, mean ± SD, minutes	6.47 ± 1.80	6.87 ± 2.03	0.03
Diagnosis, n (%)			
▪ Normal	162 (56 %)	181 (63 %)	0.07
▪ Polyp	109 (38 %)	85 (30 %)	0.046
▪ Adenoma	61 (21 %)	41 (14 %)	0.04
▪ Carcinoma	3 (1 %)	6 (2 %)	0.49
▪ IBD	3 (1 %)	7 (2 %)	0.33
▪ Others	14 (5 %)	7 (2 %)	0.13

PEG, polyethylene glycol; SD, standard deviation; IBD, inflammatory bowel disease.

▶ **Table 3** Comparison of the adenomas detected in the two groups.

	PEG + simethicone (n = 290)	PEG alone (n = 286)	*P*
Total number of adenomas detected	134	67	–
Mean number of adenomas detected	2.20 ± 1.36	1.63 ± 0.89	0.02
Colonoscopies with advanced adenomas detected, n (%)	26 (9 %)	20 (7 %)	0.38
Adenoma size, n (%)			
▪ ≤ 5 mm	94 (70 %)	40 (60 %)	0.14
▪ 6 – 9 mm	28 (21 %)	20 (30 %)	0.16
▪ ≥ 10 mm	12 (9 %)	7 (10 %)	0.73
Histology of adenoma, n (%)			
▪ Tubular adenoma	112 (84 %)	54 (81 %)	0.60
▪ Tubulovillous adenoma	14 (10 %)	9 (13 %)	0.53
▪ Villous adenoma	5 (4 %)	3 (4 %)	1.00
▪ High grade dysplasia	1 (0.7 %)	0	1.00
▪ Sessile serrated adenoma	2 (1 %)	1 (1 %)	1.00
Adenoma location, n (%)			0.03
▪ Proximal	85 (63 %)	32 (48 %)	
▪ Distal	49 (37 %)	35 (52 %)	

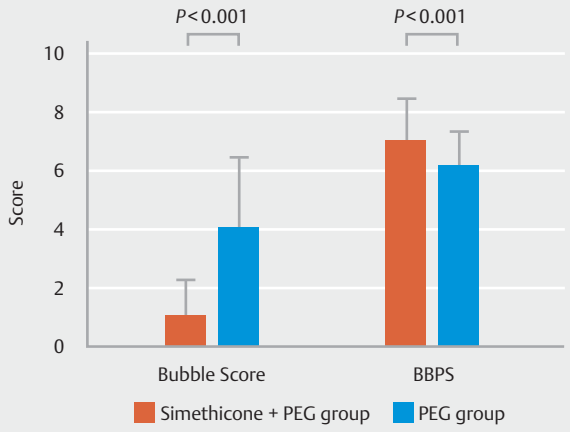
PEG, polyethylene glycol.



▶ **Fig. 2** Endoscopic images of adenomas in the proximal colon in: **a** the PEG alone group; **b** the PEG plus simethicone group.

(9.0 % vs. 7.0 %; *P* = 0.38). The size and histology of adenomas in the two groups were comparable, although more small adenomas were detected in the PEG plus simethicone group. In addition, significantly more proximal adenomas were detected in the PEG plus simethicone group (63.4 % vs. 47.7 %; *P* = 0.03) (▶ **Fig. 2**).

There was a significantly lower score for bubbles and its overall impact on mucosal visibility in the PEG plus simethicone group than in the PEG alone group (1.00 ± 1.26 vs. 3.98 ± 2.50; *P* < 0.001) (▶ **Fig. 3**). The use of simethicone reduced bubbles and foam in all colon segments. The BBPS score in the PEG plus simethicone group was significantly higher than in the PEG alone group (6.99 ± 1.47 vs. 6.12 ± 1.22; *P* < 0.001), which sug-



▶ **Fig. 3** Comparison of bowel cleansing efficacy for the two regimens assessed by bubble score and Boston bowel preparation scale (BBPS).

gested a higher quality of bowel preparation in the PEG plus simethicone group (BBPS ≥ 6 in 88.3 % vs. 75.2 %; $P<0.001$) (▶ **Table 4**).

The results of regression analysis with generalized estimating equations analyzing the influence of BMI, bubble score, BBPS, sex, age, and endoscopy center on ADR are shown in ▶ **Table 5**. The independent predicators for ADR were shown to be use of simethicone, bubble score, age, and sex, but other parameters were not associated with improved ADR.

There were no severe complications in either group. The incidence of side effects (abdominal pain 3.7 % vs. 3.1 %, $P=0.68$; nausea 13.3 % vs. 13.1 %, $P=0.97$; vomiting 10.2 % vs. 9.3 %, $P=0.73$) was comparable between the two groups. However, significantly fewer patients in the PEG plus simethicone group complained of bloating (7.8 % vs. 19.7 %, $P<0.001$) (▶ **Table 6**).

Discussion

The results of this multicenter, randomized controlled trial suggest that the combination of PEG and simethicone is associated with a significantly increased ADR and mean number of adenomas detected, less bowel foam production, and improved bowel preparation. Overall, simethicone is a useful addition to standard bowel preparation with PEG.

Colonoscopy is very important for diagnosis and treatment of colorectal disease, in particular CRC, and adequate bowel preparation is a key determinant of its efficacy, with the success of the colonoscopy procedure depending on the bowel being as clean as possible. However, patient compliance with colonoscopy is typically low because of the unpleasant bowel preparation procedure and the fear of pain or discomfort associated with the colonoscopy examination, these being major obstacles to a wider uptake of colonoscopy for CRC screening [21, 22].

High quality colonoscopy could reduce the incidence and mortality of CRC, and the ADR has been recognized as the most useful indicator for quality of colonoscopy. In the consensus statement by the American Society for Gastrointestinal Endoscopy (ASGE), the American Society of Colon and Rectal Surgeons (ASCRS), and the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES), PEG was recommended as the first choice for bowel preparation [23]. However, up to 25 % of patients have been shown to have poor quality of bowel preparation, with 4 % – 5 % of patients having to undergo a repeat procedure [24]. Researchers have therefore been trying to find a way to enhance the quality of bowel preparation and to improve patient compliance.

Simethicone has been used in clinical practice for decades; in recent studies, combined use of PEG and simethicone signif-

▶ **Table 4** Comparison of Boston bowel preparation scale (BBPS) and bubble scores in the two groups.

	PEG + simethicone (n = 290)	PEG alone (n = 286)	*P*
Bubble score	**1.00 ± 1.26**	**3.98 ± 2.50**	**< 0.001**
▪ Caecum	0.07 ± 0.26	0.52 ± 0.64	< 0.001
▪ Ascending colon	0.35 ± 0.49	1.07 ± 0.70	< 0.001
▪ Transverse colon	0.13 ± 0.36	0.84 ± 0.63	< 0.001
▪ Descending colon	0.07 ± 0.26	0.52 ± 0.64	< 0.001
▪ Rectosigmoid colon	0.03 ± 0.20	0.37 ± 0.62	< 0.001
BBPS score	**6.99 ± 1.47**	**6.12 ± 1.22**	**< 0.001**
▪ Right-side colon	2.16 ± 0.61	1.88 ± 0.49	< 0.001
▪ Transverse colon	2.43 ± 0.59	2.08 ± 0.52	< 0.001
▪ Left-side colon	2.40 ± 0.56	2.15 ± 0.58	< 0.001
Patients with BBPS ≥ 6, %	**88.3 %**	**75.2 %**	**< 0.001**

PEG, polyethylene glycol.

▶ **Table 5** Generalized estimating equations analyzing the influence of BMI, bubble score, BBPS, sex, age, and endoscopy center on ADR.

Parameters	Odds ratio	95 % confidence interval	*P*
(Intercept)	0.02	0.003 – 0.21	< 0.001
Center			
▪ Center 1	0.54	0.20 – 1.45	0.22
▪ Center 2	0.87	0.31 – 2.46	0.79
▪ Center 3	0.57	0.23 – 1.44	0.23
▪ Center 4	1.09	0.38 – 3.17	0.86
▪ Center 5	0.63	0.23 – 1.71	0.36
▪ Center 6	Ref		
Treatment group			
▪ PEG + simethicone	3.31	1.43 – 7.69	< 0.001
▪ PEG alone	Ref		
Sex			
▪ Male	2.65	1.77 – 3.97	< 0.001
▪ Female	Ref		
Bubble score	0.83	0.76 – 0.91	0.02
BBPS	0.97	0.83 – 1.13	0.68
BMI	1.00	0.94 – 1.07	0.92
Age	1.06	1.04 – 1.07	< 0.001

BMI, body mass index; BBPS, Boston bowel preparation scale; ADR, adenoma detection rate; PEG, polyethylene glycol.

▶ **Table 6** Adverse events in the two groups.

	PEG + simethicone (n = 294)	PEG alone (n = 289)	*P*
Nausea, n (%)	39 (13 %)	38 (13 %)	0.97
Vomiting, n (%)	30 (10 %)	27 (9 %)	0.73
Bloating, n (%)	23 (8 %)	57 (20 %)	< 0.001
Abdominal pain, n (%)	11 (4 %)	9 (3 %)	0.68

icantly reduced bowel foam (67.0 % vs. 100.0 %; $P < 0.005$) and stool residue (5.3 % vs. 38.9 %; $P < 0.05$) [10], which allowed better visualization of the bowel during colonoscopy. However, there is an ongoing argument as to whether simethicone can improve the ADR. Several studies [24 – 26] have shown that ADR was associated with the quality of bowel preparation, and that better bowel preparation could enhance the ability to detect smaller lesions and, thereby, improve the ADR. However, a meta-analysis by Wu et al. [27] revealed no significant improvement in bowel preparation quality with the use of simethicone, although significantly reduced foam production was observed.

Other studies have shown a positive effect of simethicone in inhibiting residual bubbles and in enhancing visualization of the colonic mucosa [28 – 30]. For instance, Matro et al. [7] found no significant difference in overall cleansing quality with or without simethicone (whole colon 94 % vs. 89 % [$P = 0.53$]; right colon 94 % vs. 88 % [$P = 0.37$]), but more patients in the PEG plus simethicone group showed excellent rather than good bowel preparation (whole colon 53 % vs. 28 % [$P = 0.004$]; right colon 53 % vs. 35 % [$P = 0.044$]). So, the effect of simethicone on bowel preparation remains unclear. In addition, although guidelines suggest that adding simethicone to standard bowel preparation may reduce foaming and improve tolerability, its effect on lesion detection has not been confirmed [23, 31].

In the present study, it was shown that simethicone could not only reduce the bowel residual foam, but was also associated with significantly improved bowel preparation. The proportion of patients with high quality bowel preparation improved from 75.2 % to 88.3 %. This could be attributed to the effect of simethicone in reducing foam formation in the colon, which lowers the adhesion of residual stool to the mucosa and facilitates its expulsion, as is also indicated by fewer patients reporting bloating during the preparation process. Although the quality of bowel preparation was improved in the PEG plus simethicone group, an increased ADR was not correlated with the quality of bowel preparation on regression analysis.

It is notable more small adenomas were detected in the PEG plus simethicone group, although the difference was not significant, and that these potentially precancerous lesions were numerically higher in the PEG plus simethicone group. It was also

found that, in the PEG plus simethicone group, many more proximal adenomas were detected, and we suppose the reason for this may be that bubbles are more commonly present in the proximal colon, especially the ascending colon, so that the elimination of bubbles was associated with increased detection of small proximal adenomas.

Additionally, in the PEG plus simethicone group, the need for repeated washes was greatly reduced; as a result, the amount of accumulated fluid was remarkably decreased, and this may contribute to better visualization of the colon and a higher mucosal lesion detection rate.

In a prospective study by Yoo et al. [28], the use of PEG plus simethicone was associated with a higher BBPS score and reduced withdrawal time, but did not increase the ADR. Although the majority of previous studies have suggested better bowel preparation with simethicone, few studies have reported that the ADR was increased and we suppose the small sample size in previous trials may be one of the reasons, given that the present study is the largest to investigate the effect of simethicone on the performance of colonoscopy and the findings indicate that preprocedure simethicone was associated with higher quality of bowel preparation and improved ADR. However, although regression analysis suggested the effect of simethicone was not related to better bowel preparation, it is possible that, through fewer bubbles and less fecal residue, simethicone could further increase the detection of small and proximal colorectal lesions.

Clear visualization of the colon, with detection and removal of adenomas during colonoscopy, is vital to reduce the incidence of CRC. However, we should also emphasize the importance of patient compliance, which directly affects the uptake of the colonoscopy procedure. Recent guidelines have endorsed that simethicone can reduce air accumulation in the gastrointestinal tract, and reduce abdominal bloating, distension, and pain [23,31]. This effect was also observed in our study, wherein use of simethicone was associated with a lower incidence of bloating, which will improve the patients' experience of the colonoscopy procedure.

We have shown that simethicone can significantly reduce withdrawal time because fewer patients needed washing during colonoscopy. It is well known that repeated washes of the mucosa because of the presence of foam prolong the withdrawal time; moreover, the accumulated fluid is liable to interfere with the examination of the colon and contribute to missed lesions.

Some limitations of our study are worth noting. Firstly, the patient population was entirely comprised of patients undergoing a diagnostic colonoscopy rather than a screening colonoscopy, which is because screening colonoscopy has not been adopted in China for colon cancer prevention. Secondly, as this is a multicenter study, interobserver variability among endoscopists may have affected our results, but we used the BBPS to evaluate the quality of bowel cleansing, as has been commonly used in our previous study [13,14] and other Chinese studies [32], which has shown excellent interobserver agreement. Finally, the overall ADR was lower than that in Western populations, but in line with that of Asian populations. Therefore, whether the conclusion of this trial will be generalizable in a population with a higher prevalence of adenomas, such as in Western countries, needs further studies to be performed.

In conclusion, combined use of PEG and simethicone is associated with significantly increased ADR and improved bowel preparation in a Chinese population.

Acknowledgments

Dr. Bai Yu is supported by the National Natural Science Foundation of China (Grant No. 81670473) and Research Doctor Fund of Changhai Hospital (B Type).

Competing interests

None

References

[1] Torre LA, Bray F, Siegel RL et al. Global cancer statistics, 2012. CA Cancer J Clin 2015; 65: 87 – 108

[2] Arnold M, Sierra MS, Laversanne M et al. Global patterns and trends in colorectal cancer incidence and mortality. Gut 2017; 66: 683 – 691

[3] Meester RG, Doubeni CA, Lansdorp-Vogelaar I et al. Variation in adenoma detection rate and the lifetime benefits and cost of colorectal cancer screening: a microsimulation model. JAMA 2015; 313: 2349 – 2358

[4] Corley DA, Levin TR, Doubeni CA. Adenoma detection rate and risk of colorectal cancer and death. NEJM 2014; 370: 2541

[5] Sung JJ, Ng SC, Chan FK et al. An updated Asia Pacific Consensus Recommendations on colorectal cancer screening. Gut 2015; 64: 121 – 132

[6] Kim HW. Inadequate bowel preparation increases missed polyps. Clin Endosc 2012; 45: 345 – 346

[7] Matro R, Tupchong K, Daskalakis C et al. The effect on colon visualization during colonoscopy of the addition of simethicone to polyethylene glycol-electrolyte solution: a randomized single-blind study. Clin Transl Gastroenterol 2012; 3: e26

[8] Brecevic L, Bosan-Kilibarda I, Strajnar F. Mechanism of antifoaming action of simethicone. J Appl Toxicol 1994; 14: 207 – 211

[9] Park JJ, Lee SK, Jang JY et al. The effectiveness of simethicone in improving visibility during colonoscopy. Hepatogastroenterology 2009; 56: 1321 – 1325

[10] Shaver WA, Storms P, Peterson WL. Improvement of oral colonic lavage with supplemental simethicone. Dig Dis Sci 1988; 33: 185 – 188

[11] Pontone S, Angelini R, Standoli M et al. Low-volume plus ascorbic acid vs high-volume plus simethicone bowel preparation before colonoscopy. World J Gastroenterol 2011; 17: 4689 – 4695

[12] Rex DK, Schoenfeld PS, Cohen J et al. Quality indicators for colonoscopy. Gastrointest Endosc 2015; 81: 31 – 53

[13] Fang J, Wang SL, Fu HY et al. Impact of gum chewing on the quality of bowel preparation for colonoscopy: an endoscopist-blinded, randomized controlled trial. Gastrointest Endosc 2017; 86: 187 – 191

[14] Fang J, Fu HY, Ma D et al. Constipation, fiber intake and non-compliance contribute to inadequate colonoscopy bowel preparation: a prospective cohort study. J Dig Dis 2016; 17: 458 – 463

[15] Lai EJ, Calderwood AH, Doros G et al. The Boston bowel preparation scale: a valid and reliable instrument for colonoscopy-oriented research. Gastrointest Endosc 2009; 69: 620 – 625

[16] Calderwood AH, Jacobson BC. Comprehensive validation of the Boston Bowel Preparation Scale. Gastrointest Endosc 2010; 72: 686 – 692

[17] McNally PR, Maydonovitch CL, Wong RK. The effectiveness of simethicone in improving visibility during colonoscopy: a double-blind randomized study. Gastrointest Endosc 1988; 34: 255 – 258

[18] Lazzaroni M, Petrillo M, Desideri S et al. Efficacy and tolerability of polyethylene glycol-electrolyte lavage solution with and without simethicone in the preparation of patients with inflammatory bowel disease for colonoscopy. Aliment Pharmacol Ther 1993; 7: 655 – 659

[19] McNally PR, Maydonovitch CL, Wong RK. The effect of simethicone on colonic visibility after night-prior colonic lavage. A double-blind randomized study. J Clin Gastroenterol 1989; 11: 650 – 652

[20] Bai Y, Gao J, Zou DW et al. Distribution trends of colorectal adenoma and cancer: a colonoscopy database analysis of 11,025 Chinese patients. J Gastroenterol Hepatol 2010; 25: 1668 – 1673

[21] Pox C, Schmiegel W. Colorectal screening in Germany. Z Gastroenterol 2008; 46 Suppl 1: S31 – S32

[22] Bleiker EM, Menko FH, Taal BG et al. Screening behavior of individuals at high risk for colorectal cancer. Gastroenterology 2005; 128: 280 – 287

[23] Wexner SD, Beck DE, Baron TH et al. A consensus document on bowel preparation before colonoscopy: prepared by a task force from the American Society of Colon and Rectal Surgeons (ASCRS), the American Society for Gastrointestinal Endoscopy (ASGE), and the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES). Gastrointest Endosc 2006; 63: 894 – 909

[24] Froehlich F, Wietlisbach V, Gonvers JJ et al. Impact of colonic cleansing on quality and diagnostic yield of colonoscopy: the European Panel of Appropriateness of Gastrointestinal Endoscopy European multicenter study. Gastrointest Endosc 2005; 61: 378 – 384

[25] Chiu HM, Lin JT, Wang HP et al. The impact of colon preparation timing on colonoscopic detection of colorectal neoplasms–a prospective endoscopist-blinded randomized trial. Am J Gastroenterol 2006; 101: 2719 – 2725

[26] Harewood GC, Sharma VK, de Garmo P. Impact of colonoscopy preparation quality on detection of suspected colonic neoplasia. Gastrointest Endosc 2003; 58: 76 – 79

[27] Wu L, Cao Y, Liao C et al. Systematic review and meta-analysis of randomized controlled trials of Simethicone for gastrointestinal endoscopic visibility. Scand J Gastroenterol 2011; 46: 227 – 235

[28] Yoo IK, Jeen YT, Kang SH et al. Improving of bowel cleansing effect for polyethylene glycol with ascorbic acid using simethicone: A randomized controlled trial. Medicine (Baltimore) 2016; 95: e4163

[29] 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 constipation. Dig Liver Dis 2015; 47: 857 – 863

[30] Saltzman JR, Cash BD, Pasha SF et al. Bowel preparation before colonoscopy. Gastrointest Endosc 2015; 81: 781 – 794

[31] Hassan C, Bretthauer M, Kaminski MF et al. Bowel preparation for colonoscopy: European Society of Gastrointestinal Endoscopy (ESGE) guideline. Endoscopy 2013; 45: 142 – 150

[32] Gao Y, Lin JS, Zhang HD et al. Pilot validation of the Boston Bowel Preparation Scale in China. Dig Endosc 2013; 25: 167 – 173