Medicine®

OPEN

Effectiveness of oolong tea and simethicone solution for lens cleansing during colonoscopy
A double-blinded randomized study

Yan Song, MB, Guanyu Zhou, MM, Mengtian Tu, MM, Jiancheng Zhang, MD, Pu Wang, MD*

Abstract

Background and aims: water is an imperfect agent for lens cleansing during endoscopy due to its incompetence to clean hydrophobic dirt, whereas amphiphilic surfactants have the potential to overcome the limitation of water. The trial was aimed to evaluate the cleansing effectiveness of 2 typical surfactants (simethicone solution and oolong tea) for colonoscopic lens.

Methods: Oolong tea (O-), low concentration simethicone solution (S1-), high concentration simethicone solution (S2-) and distilled water (D-) were used as washing solutions for colonoscopic lens. Study I: The tip of the colonoscope was immersed in lard oil in order to simulate the blur, and photographs were taken toward a standard colonoscopy image in-vitro pre- and post- each cleansing procedure. The blurred areas of each image were quantified and compared. Study II: 395 consecutive patients who were due to colonoscopy examination were enrolled and randomized into O-, S2-, D-group. The volume of washing solution used and cleansing level during the examination procedure, adenoma and polyp detected per colonoscopy, insertion time and withdraw time were analyzed.

Results: Study I: There were no differences in 4 groups for the blurred areas on images before lens cleansing. The blurred areas after lens cleansing were significantly smaller in 3 groups (O- 8.47 ± 20.91 vs S1- 13.06 ± 10.71 vs S2- 6.76 ± 8.49 vs D- 38.24 ± 29.69, $P<.05$) than water. The decline range of blurred areas after lens cleansing in oolong tea, low concentration simethicone solution, high concentration simethicone solution groups were significantly higher than that in distilled water group (O- 87.35 ± 20.81 vs S1- 78.12 ± 19.24 vs S2- 89.57 ± 8.50 vs D- 53.39 ± 28.45, $P<.05$). Study II: The volume of washing solution used in S2-group was significantly smaller than that in O-group and D-group. The cleansing level of the colonoscopic lens of O-group was significantly superior than that of S2-group and D-group.

Conclusions: The in-vitro test showed oolong tea and simethicone solution can effectively cleans the colonoscopic lens. The clinical trial demonstrated that oolong tea instead of water is effective to provide better visualization during colonoscopy.

Registration: Chictr.org.cn No: ChiCTR1900025606.

Abbreviations: ADR = adenoma detection rate, APC = adenoma per colonoscopy, BBPS = Boston bowel preparation scale, EGD = esophagogastroduodenoscopy, GI = gastrointestinal, PDR = polyp detection rate, PPC = polyp per colonoscopy.

Keywords: cleansing, colonoscopy, lens, oolong tea, simethicone, surfactant

1. Introduction

Colonoscopy is the gold standard diagnostic tool for colorectal diseases. During colonoscopy, a variety of non-hydrophilic substances can blur the colonoscopic lens and thus decline image quality, which might result in a limited visualization and a subsequent miss diagnosis as well as a prolonged withdraw time and associated risk without effective lens cleansing.[1–5] Hence, effective lens cleansing should be considered an important pre-requisite to maintain a good visualization. However, distilled water as a commonly used lens cleansing agent is incompetent to clean non-hydrophilic substances which are widely existed in mucous and debris in gastrointestinal (GI) tract. Evidence has shown that saponins, a surfactant, in oolong tea has good cleansing capability for oily stains.[6,7] It has been demonstrated that oolong tea to have better cleansing effect than distilled water on lens of ultrathin transnasal esophagogastroduodenoscopy (EGD). Moreover, the application of oolong tea as a cleansing agent during transnasal EGD has also been demonstrated to reduce examine time and consumption of the cleansing agent.[8] Simethicone is anothor surfactant which is widely used as antifoaming agent in the pre-procedural management of both upper and lower gastrointestinal tract at pharmaceutical level,[9–13] we hypothesize that oolong tea and simethicone should have the potential to improve lens cleansing and maintain a better baseline visualization during colonoscopy. The aim of this study was to explore the lens cleansing effect of oolong tea and simethicone solution during colonoscopy in comparison with distilled water. We performed an in-vitro test first to find the proper concentration of simethicone and then we conducted a randomized double-blinded clinical study to assess their effectiveness in lens cleansing in real clinical setting.

2. Materials and methods

2.1. Procedures and outcome measures

In this study, an in vitro experiment (study I) and a double-blinded randomized controlled trial (Study II) were used to evaluate the cleansing effect of oolong tea and simethicone solution.

2.2. Study I

Four washing solutions were evaluated in this study, including oolong tea (O-group, Suntory Holdings Ltd., Osaka, Japan),[8] low concentration simethicone solution (S1-group, 10% concentration, 4.0 mg/mL) (Berlin-Chemie AG, German), high concentration simethicone solution (S2-group, 40% concentration, 16.0 mg/mL), and sterile distilled water(D-group). Melting lard oil was used to simulate the turbidity and stickiness of non-hydrophilic colonic mucus and debris.[8] The lard oil was melted in a constant temperature water bath at 36.8℃, the tip of colonoscope (Olympus CF-Q260, Olympus Medical Systems Co., Tokyo, Japan) was immersed in lard oil for 3 seconds. A printed high resolution colonoscopy image (210 mm × 297 mm) which contains previously photographed clear transverse colon by Olympus CF-Q260 was used as a standard testing image. Photographs toward the test image were taken after a lens-cleansing from the endoscopic jet nozzle for 3 seconds in each group, photographs were also taken right after each soiling procedure as well. Photographs were taken at a distance of 2 cm away toward the standard image. There were 20 repeated

cleansing procedures in each group respectively. All the images obtained in the cleansing test were estimated by three-senior panel simultaneously who were blinded to the grouping, the blurred areas were manually labeled on a touch-screen laptop once consensus was reached. The number of pixels in the labeled areas was quantified by using Photoshop 7.0 (Adobe Systems Inc., Mountain View, USA) (Figure S1, Supplemental Digital Content, http://links.lww.com/MD2/A295). In study I, the grouping was concealed by means of covering solution tank by a research assistant, the researcher who performed cleansing was blinded to the solutions used. Main outcomes are blurred areas after cleansing as well as decline range of blurred areas, which was calculated by subtracting the blurred areas after cleansing from blurred areas before cleansing.

2.3. Study II

After Study I, we performed a single-centered, double-blinded, randomized, controlled study to evaluate the cleansing effective-ness for colonoscopic lens of oolong tea and simethicone with higher concentration which was demonstrated to have better cleansing effect in study I. Three hundred ninety five consecutive patients presenting for diagnostic, screening and surveillance colonoscopy between October 2019 and April 2020 at the endoscopy center of Sichuan Academy of Medical Sciences & Sichuan Provincial People's Hospital, China were enrolled (Fig. 1).

Colonoscopies were performed with high image-quality colonoscopes (Olympus CF-Q260, CF-H260 and CF-H290) and high-definition monitors. Cases without successful cecum insertion were excluded. Bowel preparation method was 2L of polyethylene glycol with 6 mL simethicone solution, given in split doses.

Four experienced endoscopists from the division of gastroen-terology participated in the study as colonoscopy performers. All examinations were done with patients in the left lateral position. All enrolled patients were given intravenous anesthesia during colonoscopy.

Patients were randomly assigned, via the principle of flipping a coin, to one of 3 groups: O-Group (oolong tea), S2-Group (high concentration simethicone solution, 40% concentration, 16.0 mg/mL), and D-Group (sterile distilled water) by the research assistant. In study II, the grouping were concealed by means of covering solution tank by research assistant, the colonoscopists and patients were both blinded to group assignment.

During colonoscopy, optical biopsy instead of tissue biopsy on each polyp or non-polypoid neoplasma was performed by endoscpists according to NBI International Colorectal Endo-scopic (NICE) Classification system[14] by use of non-magnified NBI. Patients with endoscopically resectable polyps were referred for later complete resection, it is a typical endoscopy workflow in large centers in China, that not to remove lesions during first colonoscopy due to lack of preoperative preparation and bed reservation for out-patient participants. Polyp location, size and morphological features according to the Paris classification were recorded by research assistant.

Baseline demographic characteristics for each patient were recorded (Table 1). Boston bowel preparation scale (BBPS) as scored by the endoscopist were recorded by the research assistant. Insertion time to the cecum, withdraw time for each procedure were all recorded by research assistant.

After each procedure, endoscopists rated level of lens cleansing for the entire procedure from 1 to 5 using a 5-point
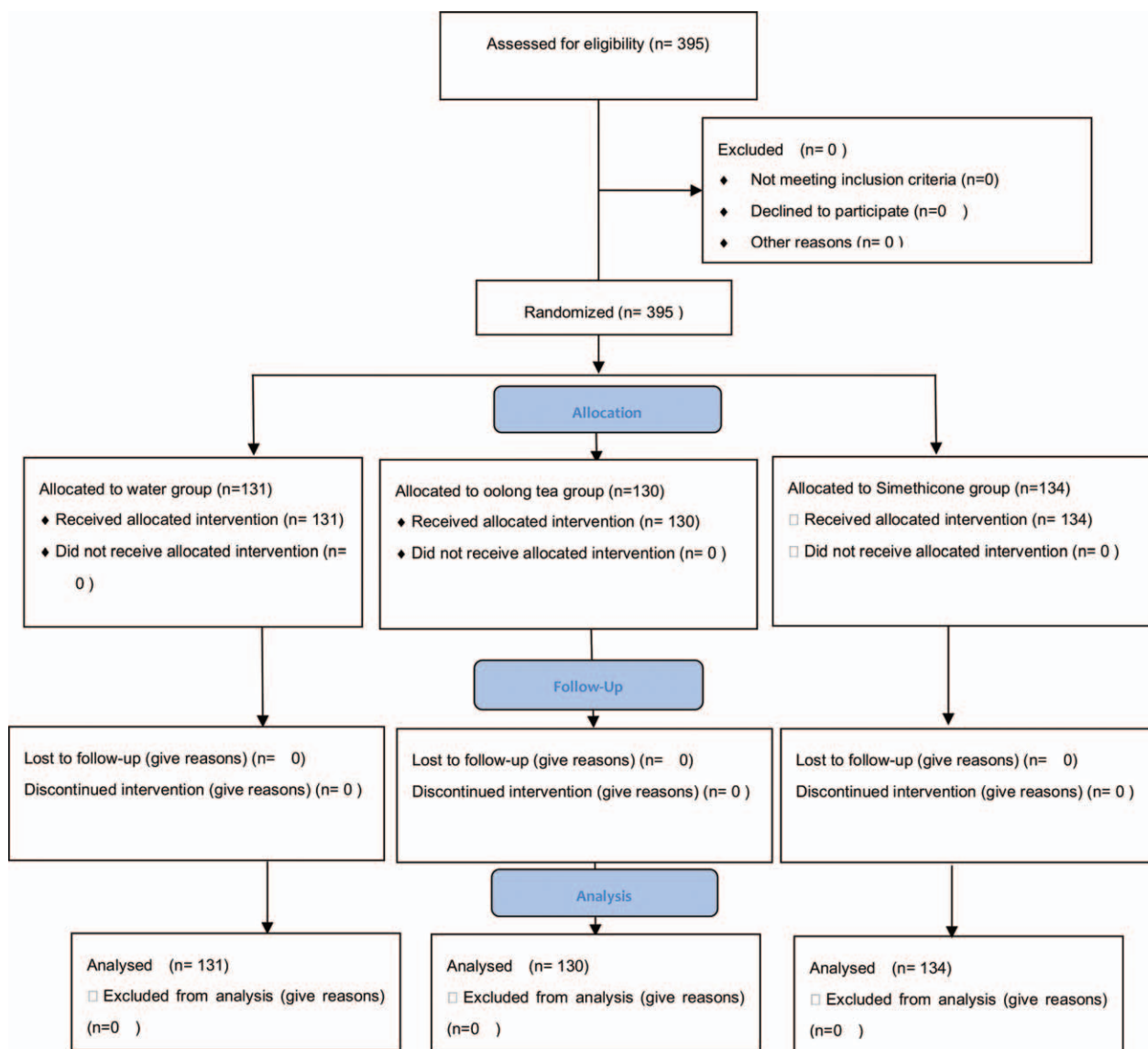
Figure 1. Enrollment.

Likert scale[5] wherein level 1 represented most of the blurred areas of the lens cannot be cleaned at once, unsatisfied cleansing effect, Level 2 represented between levels 1 and 3, level 3 represented most of the blurred areas of the lens can be cleaned, but it's not easy to do it all at once, level 4 represented between levels 3 and 5, level 5 represented all blurred areas of the lens can be easily cleaned at once, fully satisfied with the quality of the image (Figure S2, Supplemental Digital Content, http://links.lww.com/MD2/A295).

The primary outcome of study II was the volume of washing solution used during the examination procedure. Secondary outcomes include optically predicted adenoma detection rate (ADR-O) which was defined as the proportion of individuals undergoing a complete colonoscopy who had one or more Type II and Type III adenoma deemed by operating endoscopists according to NICE system. Optically diagnosed polyp detection rate (PDR-O) was defined as the proportion of individuals undergoing a complete colonoscopy who had one or more polyps deemed by operating endoscopists. Optically predicted adenoma per colonoscopy (APC-O) was defined as the total number of Type II and Type III adenomas according to NICE system divided by the total number of patients of each group. Optically diagnosed polyp per colonoscopy (PPC-O) was defined as the

Table 1

Baseline patients' characteristics.

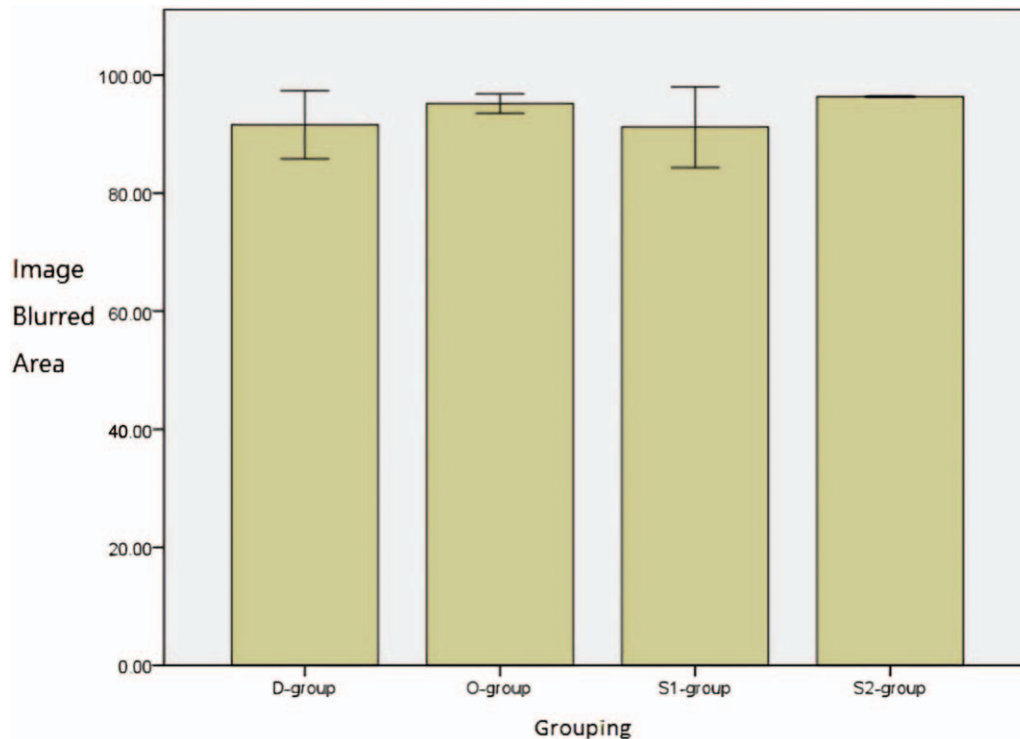|	O-group	S2-group	D-group
Age(yr)	53.20 ± 11.36	50.51 ± 12.88	51.32 ± 12.18
Sex			
Female	71 (54.6%)	77 (57.5%)	82 (62.6%)
Male	59 (45.4%)	57 (42.5%)	49 (37.4%)
BMI(kg/m^2)	23.25 ± 3.04	23.00 ± 3.31	23.14 ± 2.98
Indication			
Screening	75 (57.7%)	71 (53.0%)	80 (61.1%)
Symptomatic	48 (36.9%)	57 (42.5%)	43 (32.8%)
Surveillance	7 (5.4%)	6 (4.5%)	8 (6.1%)

BMI = body mass index.

Figure 2. Blurred area before cleansing.

total number of polyps according to endoscopist's judgment divided by the total number of patients of each group.

Cleansing level of the colonoscopic lens, BBPS, insertion time and withdraw time were also compared among groups.

This study was approved by the ethics committee of Sichuan Academy of Medical Sciences & Sichuan Provincial People's Hospital, China and registered with Chinese Clinical Trial Registry.

All authors had access to the study data and reviewed and approved the final manuscript.

2.4. Statistical analysis

The primary outcome parameter in Study II was the amount of washing solution used during colonoscopy. We referred to a primary study[8] and performed an internal exploratory test. We prospectively designed this study to allow for 80% power or more to detect a 20% decrease in requirement for washing solution (4 mL), between colonoscopy procedures with a 2 group χ^2 test with a two-sided α level of 0.05. The sample size of at least 130 patients per group was calculated based on the statistical requirement.

In vitro experiment, absolute number of pixels corresponding to blurred area of all images in 4 groups were indicated by mean ± standard deviation (X ± S). The data of each group were compared by ANOVA test. In clinical trial, the volume of washing solution, the cleansing level of colonoscopic lens, BBPS, the insertion time and withdraw time in each group were all indicated by mean ± standard deviation (X ± S). The data of each group were compared by ANOVA test. Chi-Squared test was used for comparison of ADR-O and PDR-O. When unequal variances were found in the analyzed data, a significant difference

was statistically calculated by Welch test. The difference was statistically significant when $P < .05$. All statistical data were analyzed by statistical software SPSS 22.0 (version 22.0 for the PC, Armonk, NY).

3. Results

3.1. Study I

The blurred areas right after soiling of the 4 groups were 91.64 ± 10.61 in D-group, 95.83 ± 2.15 in O-group, 91.17 ± 14.62 in S1-group and 96.33 ± 0.02 in S2-group, respectively. There was no significant difference among groups ($P > .05$) (Fig. 2).

The blurred areas after cleansing of the 4 groups were 38.24 ± 29.69 in D-group, 8.47 ± 20.91 in O-group, 13.06 ± 10.71 in S1-group and 6.76 ± 8.49 in S2-group, respectively. The blurred area of O-group, S1-group and S2-group after cleansing were significantly smaller than that of D-group (O- 8.47 ± 20.91 vs D- 38.24 ± 29.69, $P = .001$; S1- 13.06 ± 10.71 vs D- 38.24 ± 29.69, $P = .004$; S2- 6.76 ± 8.49 vs D- 38.24 ± 29.69, $P < .001$). There was no difference regarding blurred areas among O-, S1- and S2- groups. (Fig. 3).

Decline range of blurred areas were 53.39 ± 28.45 in D-group, 87.35 ± 20.81 in O-group, 78.12 ± 19.24 in S1-group and 89.57 ± 8.50 in S2-group, respectively. The decline range of blurred areas in O-group, S1-group and S2-group after cleansing were significantly higher than that of D-group (O- 87.35 ± 20.81 vs D- 53.39 ± 28.45, $P < .001$; S1- 78.12 ± 19.24 vs D- 53.39 ± 28.45, $P = .009$; S2- 89.57 ± 8.5 vs D- 53.39 ± 28.45, $P < .001$), among which, the decline range of blurred areas in S2-group was similar as in O- group, and significantly higher than that in S1-group. (O- 87.35 ± 20.81 vs S2- 89.57 ± 8.5, $P = .971$; S1- 78.12 ± 19.24 vs S2- 89.57 ± 8.5, $P = .048$) (Fig. 4).
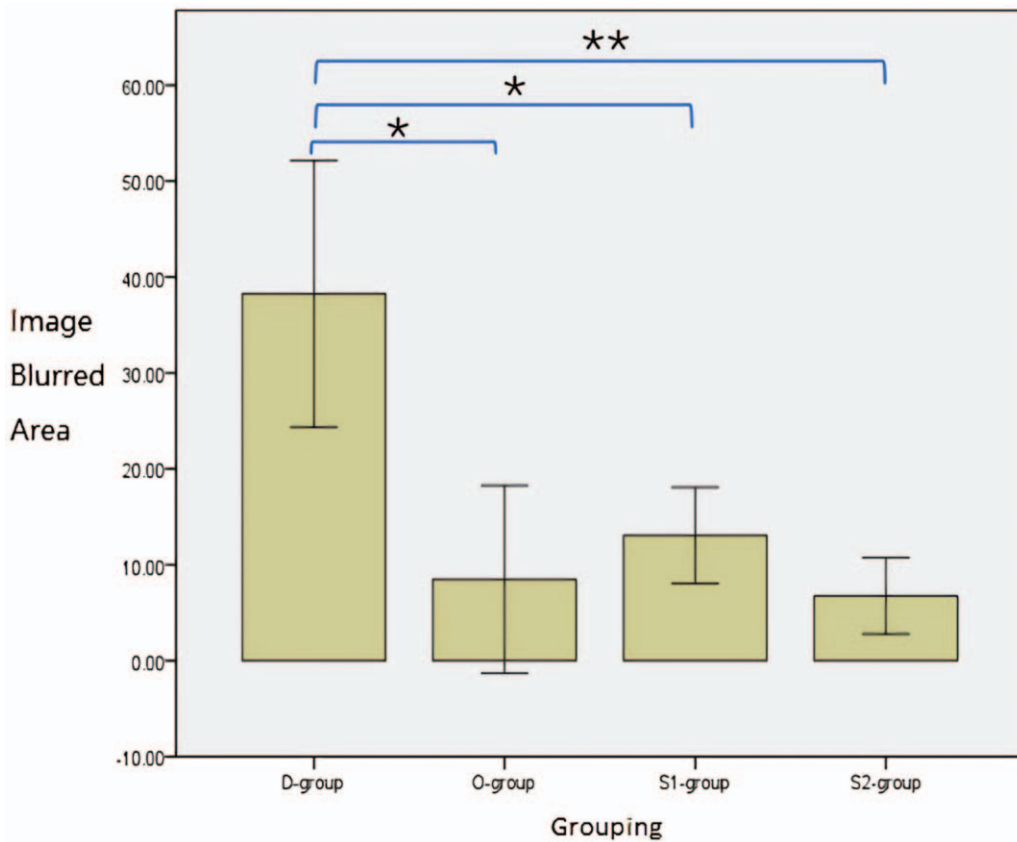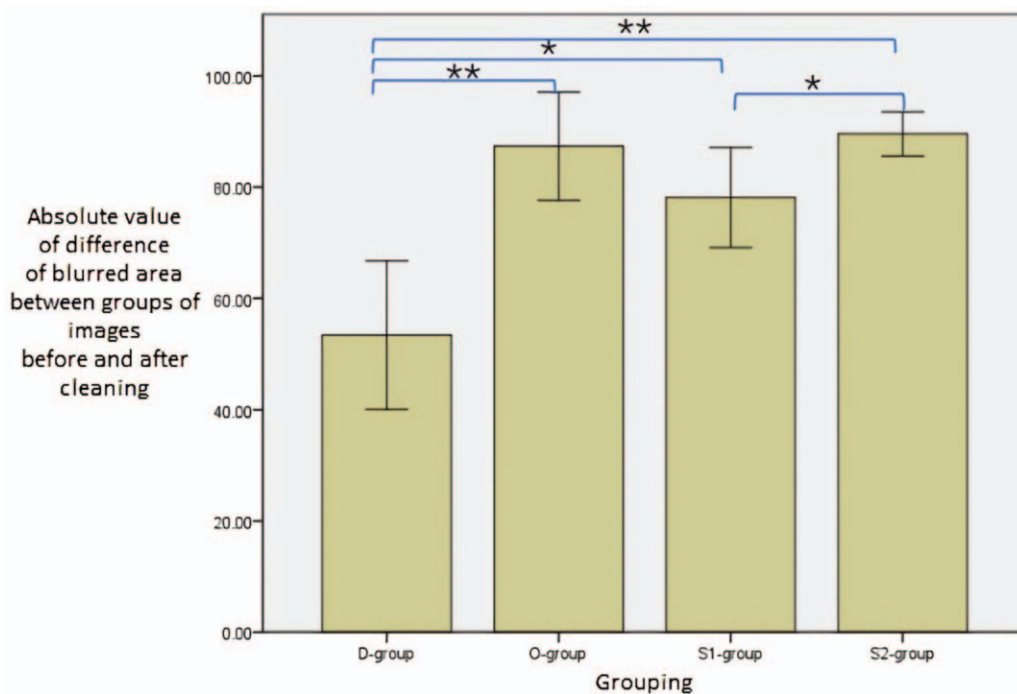
Figure 3. Blurred area after cleansing.

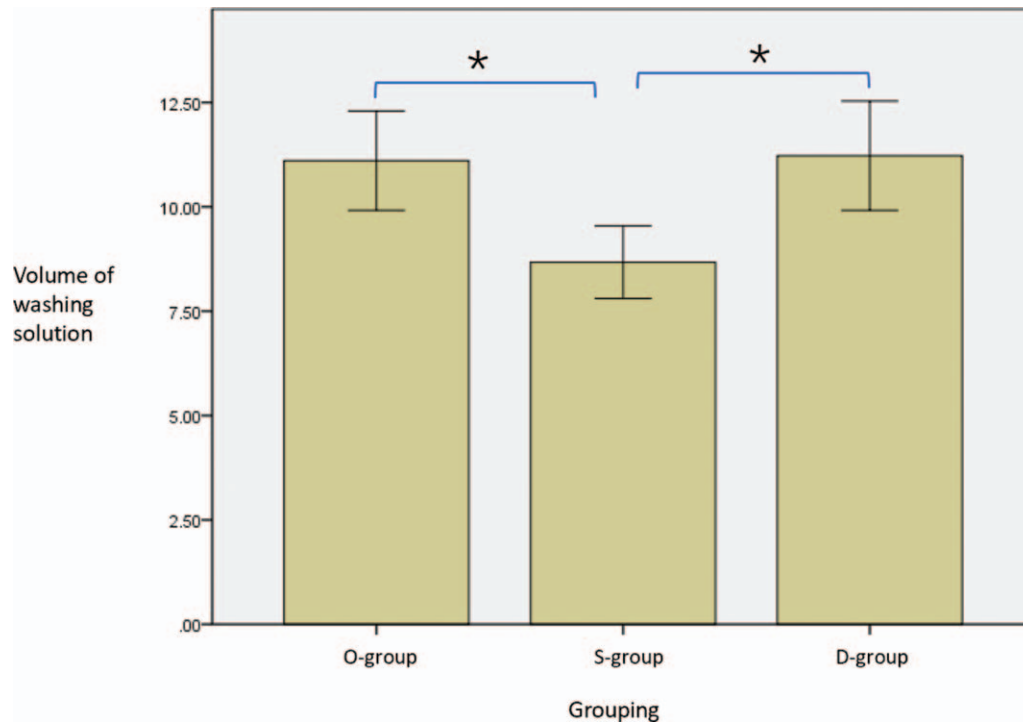**Figure 4.** Decline range of blurred areas after lens cleansing.

Figure 5. The volume of washing solution used.

3.2. Study II

Simethicone with higher concentration (40% concentration, 16.0 mg/mL) in S2- group was demonstrated with superior cleansing effect than simethicone with lower concentration in Study I. Therefore, we used higher concentration simethicone (40% concentration, 16.0 mg/mL) as S2-group in study II with the same O-group and D-group in study I.

A total of 395 eligible patients were enrolled in study II. The O-, S2-, D-groups contained 130, 134, and 131 patients, respectively. Baseline patients' characteristics of each group are shown in Table 1. No statistically significant differences of these characteristics were found among groups.

The average volume of washing solution used during each examination procedure in the O-, S2-, D-group were 11.11 ± 6.85, 8.67 ± 5.09, 11.22 ± 7.56 mL, respectively. The volume of washing solution used in S2-group was significantly smaller than that in O-group and D-group (S- 8.67 ± 5.09 vs O- 11.11 ± 6.85, $P = .003$; S- 8.67 ± 5.09 vs D- 11.22 ± 7.56, $P = .002$). There was no significant difference in the volume of washing solution used in O-group and D-group (O- 11.11 ± 6.85 vs D- 11.22 ± 7.56, $P = .886$). (Fig. 5)

The cleansing level of the colonoscopic lens in O-, S2-, D-group were 4.58 ± 0.55, 4.35 ± 0.72 and 4.32 ± 0.72, respectively. Among them, the cleansing level of the colonoscopic lens of O-group was significantly superior than that of S2-group and D-group (O- 4.58 ± 0.55 vs S2- 4.35 ± 0.72, $P = .012$; O- 4.58 ± 0.55 vs D- 4.32 ± 0.72, $P = .004$). There was no significant difference between S2-Group and D-group (S 4.35 ± 0.72 vs D 4.32 ± 0.72, $P = .937$). (Fig. 6)

The ADR-O of O-, S2-, D-group were 38.5%, 42.5% and 37.9%, respectively. The PDR-O of O-, S2-, D-groups were 54.6%, 53.7%, and 52.2%, respectively. There was no significant difference of ADR-O, PDR-O among groups.

The APC-O of O-, S2-, D-group were (O- 1.00 ± 1.70 vs D- 0.66 ± 1.28, $P = .170$; O- 1.00 ± 1.70 vs S2- 0.81 ± 1.22, $P = .538$; D- 0.66 ± 1.28 vs S2–0.81 ± 1.22, $P = .626$), There were no significant difference among groups. The PPC-O of O-, S2-, D-group were (O- 1.58 ± 2.01 vs D- 0.92 ± 1.43, $P = .007$; O- 1.58 ± 2.01 vs S2- 1.21 ± 1.48, $P = .198$; D- 0.92 ± 1.43 vs S2–1.21 ± 1.48, $P = .179$).

BBPS of O-, S2-, D-group were 6.57 ± 1.38, 6.77 ± 1.39 and 6.67 ± 1.36, respectively. There was no significant difference among groups (Figure S3, Supplemental Digital Content, http://links.lww.com/MD2/A296). The insertion time of O-, S2-, D-group were 7.60 ± 7.11, 6.66 ± 5.32 and 5.98 ± 5.07 minutes, respectively (Figure S4, Supplemental Digital Content, http://links.lww.com/MD2/A297). The withdraw time of O-, S2-, D-group were 7.22 ± 1.88, 7.17 ± 1.55 and 7.01 ± 1.42 minutes, respectively (Figure S5, Supplemental Digital Content, http://links.lww.com/MD2/A298).

4. Discussion

Distilled water is the standard cleansing agent to wash the endoscopy lens through the nozzle. However, non-hydrophilic substance contained in mucus and debris in GI tract can hardly be removed effectively from the lens by water, and thus may lead to poor visualization sometimes when the patient's bowel is not well prepared. Moreover, repeated cleansing procedures would unnecessarily prolong the examine time and waste cleansing agent.[8] Regarding the incompetence of water for cleansing non-hydrophilic substance from endoscopy lens, clinicians have tried
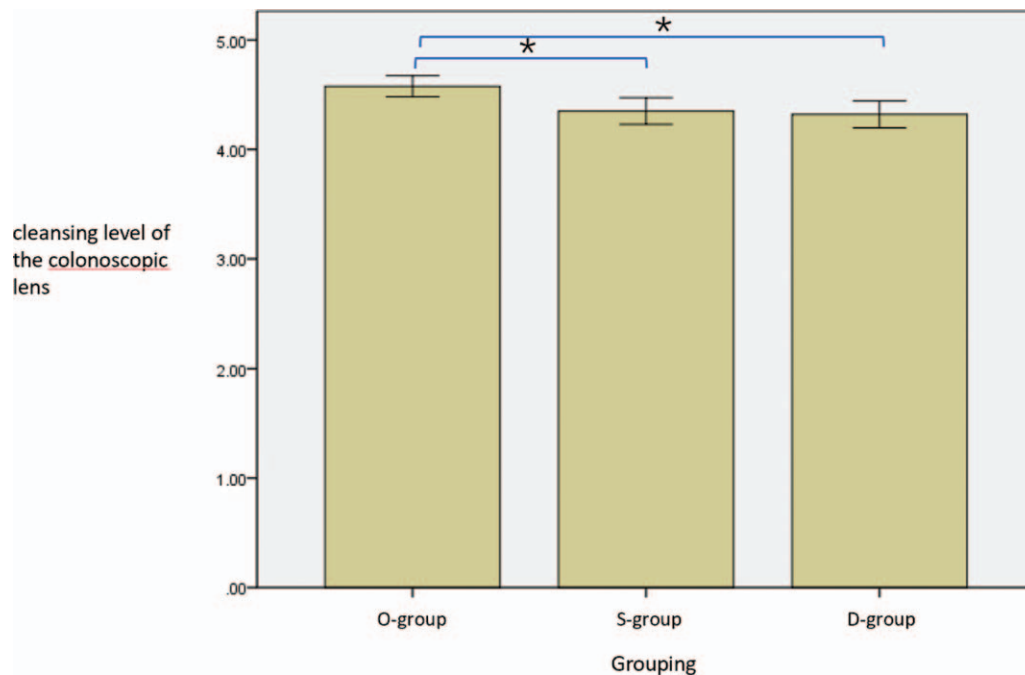
Figure 6. The cleansing level of the colonoscopic lens.

surfactant as a lens washing agent during EGD, and found oolong tea which is rich in saponins is more effective to cleans EGD lens than water in vitro, the application of oolong tea as cleansing agent was also found to improve clinical outcomes in real clinical setting in comparison with water.[8] Saponin is a surface-active substance widely exists in soaps and detergents, it is both hydrophilic and lipophilic.[15] Nevertheless, this study has 2 major limitations, firstly, the quality of lens cleansing was categorized into 5 levels[8] and assessed subjectively, that is an imprecise evaluation attributed in lacking of quantitative comparison. Secondly, the oolong tea they used was a food-grade tea beverage with complex ingredients, including caffeine[8,16] and sugar. Although the amount of tea left in the GI tract is very small, yet there is still a risk for triggering cardiovascular[17,18] and endocrine disease, the safety and applicability of non-pharmaceutical beverage should be rigorously investigated in larger trials before utilized in real clinical setting.

Simethicone is a complex of polydimethylsimethicone and silicon dioxide. It is a stable surfactant. Simethicone is non-absorptive to human GI tract. As a safe pharmaceutical-grade oral antifoaming agent,[9] simethicone could be used to treat abdominal distension[19] and in pre-procedure management of endoscopy, capsule endoscopy, abdominal ultrasound, abdominal CT.[2] The mechanism of simethicone is to reduce the surface tension of bubbles in chyme and mucus, decompose bubbles, and expel them from the body by means of belching through intestinal peristalsis.[20] The antifoaming capability of simethicone has allowed a significant increase in polyp detection rate when used as a washing solution through endoscopy channel during colonoscopy.[21] In addition, there is no evidence of simethicone induced poisoning and severe side effect from literatures.[22] Therefore, simethicone could be an ideal lens cleansing surfactant compared with oolong tea, in view of its amphiphilic nature and medical safety.

In vitro study, we demonstrated the efficacy of simethicone is similar with oolong tea for lens cleansing in colonoscopy. Moreover, results have revealed the effectiveness is concentration dependent, 16.0 mg/mL simethicone was shown equally effective as oolong tea and superior to 4.0 mg/mL simethicone. Although the high concentration simethicone is a suspension solution which is slightly sticky and not completely transparent, it would not remain on the lens for too long and does no harm to the endoscopic nozzle or vapor tube. The double-blinded quantitative analysis in this study provides solid evidence than the preliminary study[8] which deployed subjective evaluation.

Then we used high concentration simethicone solution (16.0 mg/mL), oolong tea and distilled water for further double-blinded, randomized controlled clinical trial. In this trial, there was no significant difference of insertion and withdraw time, BBPS and all baseline data among groups. The volume of simethicone solution used for cleansing of colonoscopic lens was significantly smaller than that of oolong tea and distilled water, however, the subjective evaluated level of lens cleansing for the entire procedure of simethicone was lower than oolong tea (O- 4.58±0.55 vs S2- 4.35±0.72, $P = .012$). After a post-hoc analysis on video records in S2- group, we found the reason why operating endoscopists rated a lower score for simethicone. Because simethicone is not completely soluble in water, it is a suspension at the 16.0 mg/mL concentration. After each cleansing procedure, although the blur was washed as clean as that in oolong tea group, there will be some fine white particles left on the lens for a short time, which leads to a lower score. Therefore, the cleansing level of simethicone was slightly underestimated, regardless fine white particle does no harm to the observation of lesions during colonoscopy which was demonstrated with an equal ADR-O, PDR-O, APC-O, PPC-O between oolong tea and simethicone group. Although there would left some tiny white

particles, the cleansing speed of simethicone is fast, so the volume used is small.

Better cleansing effect may lead to improved clinical outcomes. The PPC-O in O- group was significantly higher than that in D-group (O- 1.58 ± 2.01 vs D- 0.92 ± 1.43, $P = .007$). Other metrics, such as ADR-O, PDR-O, APC-O were all showed increasing trends in O- and S2 group than those in D- group, although there was no statistically significant difference which may due to limited sample size and corresponding statistical power for these secondary outcomes. These should be warranted larger trials which aim at revealing whether the major quality control metrics could be improved by use of advanced lens cleansing agent.

There are several limitations in this study. First, lard oil can not completely represent the dirt pattern by debris and mucous with various components in colon, however, to use lard oil to mimic the lens blur was a commonly used and widely accepted method in previous studies.[8] Second, the sample size of study II was not estimated on ADR or APC which are important clinical metrics that reflect the quality of colonoscopy, larger trials are need to investigate the impact of advanced lens cleansing agent on major clinical outcomes. Third, adenomas were optically diagnosed according to NICE system instead of by pathology, thus the ADR-O, APC-O could not completely reflect the true ADR and APC, however, optical biopsy according to NICE or other classification systems are acknowledged as an indirect yet feasible method for "diagnose and leave" or "resect and discard" strategies in real clinical setting,[23] thus we believe our results are representative and meaningful. Fourth, we did not carry out detailed experiments according to the concentration gradient of simethicone, but chose the larger and the smaller concentrations which was based on the literature and our internal exploratory test, to observe a trend, thus, the optimal concentration of simethicone needs to be further studied.

In conclusion, this study showed that oolong tea and simethicone used as a lens cleansing agent can effectively cleans the lens either in in-vitro test or during real life colonoscopy. These surfactants are promising to reduce miss diagnosis and improve major clinical outcomes during colonoscopy by reducing lens blur and offering optimal visualization.

Acknowledgment

Author contributions

Conceptualization: Yan Song, Pu Wang.
Investigation: Yan Song, Jiancheng Zhang.
Methodology: Guanyu Zhou, Pu Wang.
Writing – original draft: Guanyu Zhou.
Writing – review & editing: Mengtian Tu, Pu Wang.

References

[1] Sunny S, Cheng G, Daniel D, et al. Transparent antifouling material for improved operative field visibility in endoscopy. Proc Natl Acad Sci 2016;113:11676–81.

[2] Tatsuki H, Yokobori T, Katayama C, et al. A novel one-step lens cleaning device using air and water flow for endoscopic surgery. PLoS One 2018;13:e0200749.

[3] Cassera MA, Goers TA, Spaun GO, et al. Efficacy of using a novel endoscopic lens cleaning device: a prospective randomized controlled trial. Surg Innov 2011;18:150–5.

[4] Kreeft D, Arkenbout EA, Henselmans PWJ, et al. Review of techniques to achieve optical surface cleanliness and their potential application to surgical endoscopes. Surg Innov 2017;24:509–27.

[5] Yong N, Grange P, Eldredevans D. Impact of laparoscopic lens contamination in operating theaters: a study on the frequency and duration of lens contamination and commonly utilized techniques to maintain clear vision. Surg Laparosc Endosc Percutan Tech 2016; 26:286–9.

[6] Lee VS, Chen CR, Liao YW, et al. Structural determination and DPPH radical-scavenging activity of two acylated flavonoid tetraglycosides in Oolong tea (Camellia sinensis). Chem Pharm Bull 2008;56:851–3.

[7] Ozlem G, Giuseppe M. Saponin: properties, applications and processing. Crit Rev Food Sci Nutr 2007;47:231–58.

[8] Komazawa Y, Amano Y, YuKi M, et al. Oolong tea is useful for lens cleansing in transnasal small-caliber esophagogastroduodenoscopy. Endoscopy 2010;42:104–8.

[9] Devereaux BM, Taylor ACF, Athan E, et al. Simethicone use during gastrointestinal endoscopy: position statement of the gastroenterological society of Australia. J Gastroenterol Hepatol 2019;doi: 10.1111/ jgh.14757. [Epub ahead of print].

[10] Hassan C. Bowel preparation for colonoscopy: European society of gastrointestinal endoscopy (ESGE) guideline. Endoscopy 2013;45: 142–55.

[11] Di Nardo G, Aloi M, Cucchiara S, et al. Bowel preparations for colonoscopy: an RCT. Pediatrics 2014;134:249–56.

[12] Peng P, Sheng-Bing Z, Bing-Han L, et al. Effect of supplemental simethicone for bowel preparation on adenoma detection during colonoscopy: a meta-analysis of randomized controlled trials. J Gastroenterol Hepatol 2019;34:314–20.

[13] Amrein R, Keller R, Joos H, et al. Impact of preprocedure simethicone on adenoma detection rate during colonoscopy: a multicenter, endoscopist-blinded randomized controlled trial. Endoscopy 2018;50:128–36.

[14] Hayashi N, Tanaka S, Hewett DG, et al. Endoscopic prediction of deep submucosal invasive carcinoma: validation of the narrow-band imaging international colorectal endoscopic (NICE) classification. Gastrointest Endosc 2013;78:625–32.

[15] Bottger S, Hofmann K, Melzig MF. Saponins can perturb biologic membranes and reduce the surface tension of aqueous solutions: a correlation? Bioorg Med Chem 2012;20:2822–8.

[16] Hursel R, Westerterp-Plantenga MS. Catechin- and caffeine-rich teas for control of body weight in humans. Am J Clin Nutr 2013;98:1682S–93S.

[17] Voskoboinik A, Koh Y, Kistler PM. Cardiovascular effects of caffeinated beverages. Trends Cardiovasc Med 2018;29:345–50.

[18] Doepker C, Franke K, Myers E, et al. Key findings and implications of a recent systematic review of the potential adverse effects of caffeine consumption in healthy adults, pregnant women, adolescents, and children. Nutrients 2018;10:1536.

[19] Ingold CJ, Akhondi H. Simethicone. Treasure Island (FL): StatPearls Publishing, 2021: 1-5. Bookshelf ID: NBK555997.

[20] Tongprasert S, Sobhonslidsuk A, Rattanasiri S. Improving quality of colonoscopy by adding simethicone to sodium phosphate bowel preparation. World J Gastroenterol 2009;15:3032–7.

[21] Kutyla M, O'Connor S, Gurusamy SR, et al. Influence of simethicone added to the rinse water during colonoscopies on polyp detection rates: results of an Unintended Cohort Study. Digestion 2018;98: 217–21.

[22] Zhang LY, Li WY, Ji M, et al. Efficacy and safety of using premedication with simethicone/pronase during upper gastrointestinal endoscopy examination with sedation: a single center, prospective, single blinded, randomized controlled trial. Dig Endosc 2018;30:57–64.

[23] Rex DK, Hardacker K, MacPhail M, Rahmani F, et al. Determining the adenoma detection rate and adenomas per colonoscopy by photography alone: proof-of-concept study. Endoscopy 2015;47:245–50.