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Original Article

Efficacy and Safety of Bowel Cleansing with Mini S-Oral Sulfate Tablet versus the Conventional Oral Sulfate Tablet: A Prospective, Randomized, Investigator-Blinded, Multicenter, Noninferior, Phase 3 Trial

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Background/Aims: Conventional oral sulfate tablets (OSTs) and mini-OSTs have gained popularity for bowel preparation in South Korea. This study aimed to evaluate the efficacy, tolerability, and safety of mini S-OSTs, which have fewer tablets and include simethicone compared to the mini-OSTs.

Methods: This was a prospective, randomized, investigator-blinded, multicenter, and noninferior phase 3 trial conducted between August 2023 and January 2024. The efficacy, safety, and tolerability were compared among a mini S-OST split dose group, mini S-OST non-split dose group and conventional OST group. To evaluate the occurrence of gastric mucosal lesions, gastroscopy was also performed.

Results: High-quality preparation was achieved in the mini S-OST split dose group and conventional OST group according to both the full analysis set and per-protocol set analyses, without significant differences. Tolerability metrics were more favorable in the mini-OST group. The hematin content tended to decrease and the number of erosions was reduced in the mini S-OST split dose group compared with the conventional OST group according to the gastroscopy results. Adverse events were comparable between the conventional OST and mini S-OST split dose groups. The mini S-OST non-split dose group showed no difference in overall successful cleaning, but the proportion of high-quality cleaning in the ascending colon was lower than that in the mini S-OST split dose group and conventional OST group.

Conclusions: Compared with conventional OST, the mini S-OST split dose showed excellent efficacy, comparable safety and tolerability, with less gastric injury (ClinicalTrial.gov identifier NCT06287606). **(Gut Liver, 2026;20:294-304)**

Key Words: Cathartics; Colonoscopy; Treatment outcome; Bowel preparation

INTRODUCTION

Colonoscopy is considered a highly effective procedure for screening of colorectal cancer and removal of precancerous polyps, leading to a long-term reduction in colorectal cancer incidence and mortality.[1-3] The effectiveness of colonoscopy strictly depends on adequate bowel cleansing. However, many preparation solutions require the ingestion of large volumes of up to 4 L, which may reduce patient compliance.[4] Therefore, many low-volume preparation agents, including oral sulfate solution, have been introduced and have showed similar safety and efficacy to large volume agents.[5]

Recently, oral sulfate tablets (OSTs) have been introduced

as an attractive solution to overcome the taste barriers of oral sulfate solution. OST was noninferior to 2-L polyethylene glycol with ascorbic acid (PEG/Asc) in terms of preparation efficacy, was better tolerated, and had a similar safety profile to 2-L PEG/Asc.[6-9] However, the dissolution of the OST in the stomach may be delayed, which can result in acute gastropathy due to prolonged contact with the gastric mucosa.[10]

Novel mini-OST (CTP 0303, Suprepmini) was developed with 1/10 size of conventional OST. Recently, randomized controlled trial showed that mini-OST had a similar efficacy, tolerability, and safety compared with conventional OST.[11] As three observational studies reported a high rate of erosive gastritis associated with the use of conventional OST preparation,[10,12,13] additional prospective studies comparing the potential protective effect against acute gastric mucosal lesions between mini-OST and conventional OST are required.

Very recently, the original mini-OST was improved with fewer tablets and simethicone ingredient as mini S-OST. In this study, we compared the efficacy, tolerability, and safety as well as occurrence of gastric mucosal lesions of bowel preparation between the mini S-OST and the conventional OST.

MATERIALS AND METHODS

1. Study design and population

This was a phase 3, prospective, randomized, investigator- and central reader-blinded, parallel, multicenter, noninferiority study conducted at five academic hospitals in Korea between August 2023 and January 2024. Clinical research coordinators at each participating center randomized the enrolled subjects to either (1) the conventional OST (Orafang; Pharmbio Korea, Chungju, Korea) with split dose group; (2) mini S-OST (CTP 0302; Taejoon Pharm Co., Ltd., Korea) split dose group; or (3) mini S-OST non-split dose group. Randomization was stratified by site, with fixed block sizes concealed from investigators, and generated by an independent statistician (Sukyoung Kwon, The Catholic University of Korea, Seoul, Korea) using SAS software (SAS Institute Inc., Cary, NC, USA). Randomization codes were securely maintained until assignment, and investigators were blinded to upcoming allocations throughout the enrollment process.

Eligible subjects were consecutive adult outpatients aged >19 years who were willing to undergo screening, surveillance, or diagnostic colonoscopy. The overall study design was similar to those of previous study with mini-OST, including same inclusion and exclusion criteria.[11] All enrolled subjects received comprehensive information regarding the study, and written informed consent was obtained prior to the initiation of any study-related processes. This study was approved by all institutional ethics committees (KHNMC IRB number: 2023-03-023) and was registered under NCT06287606 at ClinicalTrials.gov.

2. Bowel preparation protocol

All subjects were instructed to have a low-residue diet for 3 days prior to colonoscopy and were restricted to a soft or liquid diet for breakfast and lunch and fasting for dinner on the day before colonoscopy. All colonoscopies were performed by site colonoscopists, who were highly experienced board-certified gastroenterologists (>10,000 colonoscopies).

Comparison of the composition and dosage between mini S-OST, mini-OST and conventional OST are shown in Supplementary Table 1. Conventional OST (Orafang, 1.5 g/per tablet) comprises 28 tablets, with containing sodium sulfate anhydrous, potassium sulfate, magnesium sulfate and simethicone per one box (28 tablets, a size of 17.2×8.2×6.4 mm per tablet). Mini S-OST (169 mg/per tablet) comprises 300 mini tablets, with containing sodium sulfate anhydrous, potassium sulfate, sodium chloride, potassium chloride and simethicone per one box (300 tablet, a size of 7.4×3.9×3.6 mm per tablet). Compared with previous mini-OST (Suprepmini), mini S-OST has a slightly reduced total number (from 320 to 300), and added ingredient simethicone.

Group 1 was mini S-OST with split dose regimen. On the day before colonoscopy, subjects were requested to take 150 mini tablets with 420 mL of water, and then take two additional doses of 420 mL of water over the next hour. Subsequently, the remaining 150 mini tablets were taken in the same way on the day of colonoscopy. Group 2 was mini S-OST with non-split dose regimen. On the day of colonoscopy, subjects were requested to take 150 mini tablets with 420 mL of water, and then take two additional doses of 420 mL of water over the next hour. Subsequently, after 1 to 2 hours, the remaining 150 mini tablets were taken in the same way. Group 3 was conventional OST with split dosing regimen. On the day before colonoscopy, subjects were requested to take 14 tablets with 425 mL of water and to take two additional doses of 425 mL of water over the next hour; subsequently, the remaining 14 tablets were taken in the same way on the day of colonoscopy. In the groups 1 and 3, the first dose was administered at 16:00 to 21:00 on the day before colonoscopy, whereas the second dose was administered on the day of colonoscopy, 10 to 12 hours after first dose administration. In all groups, bowel preparation should be completed 2 to 5 hours prior to the colonoscopy, which will be performed to evaluate the effectiveness of the bowel preparation.

3. Assessment of outcomes

Assessment of outcomes was performed with the same methods as in the previous study with mini-OST.[11] The three trained central readers, who were blinded to the initial cleansing scores, subsequently analyzed the video recordings to minimize inter-colonoscopist assessment variability.

The primary outcome of this study was the bowel cleansing efficacy using the Harefield Cleansing Scale (HCS), and the overall HCS grade was categorized into four, as follows: A (all segments scored 3 or 4), B (≥1 segment scored 2), C (≥1 segment scored 1), and D (≥1 segment scored 0). Secondary outcomes were (1) high-quality bowel preparation, which was defined as an overall HCS grade of A, whereas successful overall bowel preparation was defined as an overall HCS grade of A or B; (2) colonoscopy outcome, including the polyp detection rate and adenoma detection rate in the entire colon, procedure/withdrawal time, cecal intubation rate, and residual bubble score. Residual bubble score defined as follows:[14] no or minimal bubble; score 0, bubbles covering at least half the luminal diameter; score 1, bubbles covering the circumference of the lumen; score 2, bubbles filling the entire lumen; score 3.

Exploratory assessment outcomes were (1) response time from completion of preparation agent to first bowel movement; and (2) gastroscopy outcome, including acute gastropathy score and endoscopic finding. In this study, we compared the detection rate of acute gastric mucosal lesions in individuals undergoing gastroscopy, based on the acute gastropathy evaluation criteria.[15] In summary, gastric lesions were assessed by following criteria: blackish color (3 points), fundic localization (2 points), multiple lesions (1 point), no gastrotoxic drug intake (1 point), no gastric symptoms (1 point), and negative *Helicobacter pylori* test (3 points). A total score of 0–2 indicated imputability, 3–5 indicated doubtful, 6–7 indicated possible, and 8–9 indicated very likely. In the patients who had hematin is found, grading of hematin was conducted based on the gastroscopy rating scale:[16] grade 1, 1 to 3 hematins (localized area only); grade 2, 4 to 9 hematins (localized area only); grade 3, 10 or more hematins or hematins found in multiple areas.

4. Evaluation of tolerability and safety

Tolerability and safety were also evaluated with the same methods as in the previous study with mini-OST (CTP 0303).[11] Tolerability was evaluated using a "Patient-reported Satisfaction Scale" (0-400, where lower values reflect greater satisfaction) together with diary-based documentation of adherence (defined as ingestion of ≥75% of each schedule dose). Participants were also asked two questions regarding their willingness to reuse the same regimen in the future.

Safety monitoring included collection of adverse events (AEs) through clinical examination, laboratory tests, vital signs, and physical assessments performed at screening, after preparation, and at follow-up. Any new symptom or diagnosis was counted as an AE irrespective of causality. Blood chemistry was obtained to check electrolytes and overall physiologic status. Adverse drug reactions—whether anticipated or unexpected—were categorized by severity (mild, moderate, or severe), and common bowel-preparation–related complaints were systematically documented.

5. Statistical analysis

The sample size was determined to evaluate whether the colon cleansing efficacy of the investigational regimen (mini S-OST) was noninferior to that of the comparator regimen (conventional OST). Calculation was based on previously published data[9] in which the overall cleansing success rate was 95% for OST preparation. Assuming an overall cleansing success rate of 95% for both groups, a non-inferiority margin of 15%–derived from prior bowel preparation studies[17-21] and considered clinically acceptable in those contexts–and a one-sided alpha level of 2.5%, a sample size of 45 subjects per group was determined. A gatekeeping testing procedure was implemented to sequentially assess the primary hypotheses while controlling the family-wise type I error rate. Gate 1 compared the mini S-OST split-dose group with the conventional OST group, and Gate 2 compared the mini S-OST non–split-dose group with the conventional OST group, contingent upon noninferiority being established in Gate 1. Each gate was powered at 90%, yielding an overall power of approximately 81%. To account for an anticipated dropout rate of 15%, the final target enrollment was set at 53 participants per group.

The full analysis set (FAS) was defined as all randomized participants who received the investigational product on more than one occasion and were assessable for the primary efficacy outcome. The per-protocol set (PPS) comprised individuals who satisfied all eligibility requirements, adhered to the dosing schedule by taking at least 75% of each dose, and had no major protocol deviations. The safety set comprised all subjects for whom it could not be ruled out that they had received the investigational product at least once (based on subjects diaries).

Continuous variables are presented as mean ± standard deviation and were compared using the analysis of variance for three groups and the Wilcoxon rank-sum test for two groups. Categorical variables are presented as percentage and using the chi-square test or the Fisher exact test for comparing groups. Changes in laboratory profiles from baseline to post-preparation were presented as numbers

and percentages. Within-group changes were assessed with McNemar's test, while comparisons across groups were evaluated using either the chi-square test or Fisher exact test when appropriate. The Kaplan-Meier approach was employed to estimate the median time, along with the 95% confidence interval, from administration of the study drug to the first bowel movement. All analyses were conducted using two-sided tests, and results were regarded as statistically significant when the p-value was below 0.05. Statistical analyses were performed using SAS version 9.4 64-bit (SAS Institute Inc.).

RESULTS

1. Baseline characteristics

The flowchart of the study is shown in Fig. 1. Five academic sites screened 163 subjects; of these, 161 were randomized to receive either mini S-OST split dose (n=55), mini S-OST non-split dose (n=52) or conventional OST (n=54). The three groups did not significantly differ in terms of baseline characteristics (Table 1). Of these subjects, two were excluded from the analysis as they did not receive the investigational product. Consequently, the FAS consisted of 54 and 51 subjects receiving the mini S-OST split and non-split dose, respectively, and 54 subjects receiving the conventional OST split dose. Among them, one participant had major protocol violations. Finally, PPS was composed of 158 subjects (54, 50, and 54 in the mini S-OST split dose, non-split dose and conventional OST split dose, respectively), who completed the entire preparation process.

2. Efficacy

In all three groups, high rate of successful overall preparation (defined as an overall HCS grade of A or B) was observed in both FAS (all 100% for three groups) and PPS analyses (all 100% for three groups) (Table 2, Fig. 2). In the comparison between split dose groups, overall high-quality preparations were comparable between mini S-OST and conventional OST groups in both FAS (96.3% vs 98.2%, p=1.000) and PPS analyses (96.3% vs 98.2%, p=1.000) (Fig. 2). However, proportion of overall high-quality preparation was lower in mini S-OST non-split dose group than split dose group in both FAS and PPS analyses (both p<0.001) (Fig. 2). Colonoscopy outcomes, including procedure time, withdrawal time, cecal intubation rate, adenoma detection rate and polyp detection rate were all comparable between three groups (Table 3). Total score of residual bubble was lower in conventional OST group compared with mini S-OST split group (p=0.001) (Table 3). However, clinically significant residual bubble, grade 1–3, were comparable in two groups (p=0.118). In the first bowel movement after taking the preparation agent, median response time was significantly more rapid in mini S-OST group, regardless of split or non-split dose, than conventional OST group (62.5 minutes, 37.5 minutes vs 90.0 minutes, p=0.040, p<0.001, respectively) (Fig. 3).

In the gastroscopy outcome, there were no significant difference between three groups for the acute gastropathy in total score, total score ≥6 and total score ≥8 (Table 3). However, acute gastropathy score did not reflect the severity of hematin, so we also evaluate hematin based on the gastroscopy rating scale. For the severity of hematin, grade

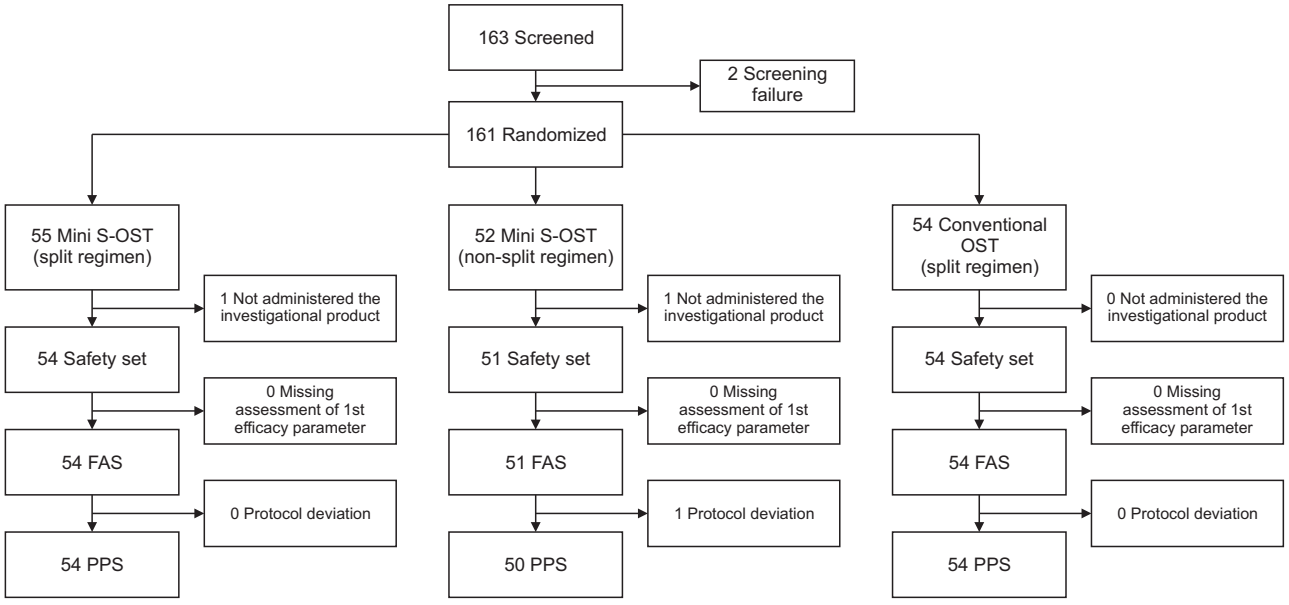

Fig. 1. Flowchart of the study population. OST, oral sulfate tablet; FAS, full analysis set; PPS, per-protocol set.

Table 1. Baseline Characteristics of the Study Population

Characteristic	Mini S-OST		OST split (n=54)	p-value
	Split (n=55)	Non-split (n=52)		
Age, yr	44.1±13.2	43.2±13.2	43.3±14.4	0.932*
Sex				0.116†
Male	17 (30.9)	23 (44.2)	27 (50.0)	
Female	38 (69.1)	29 (55.8)	27 (50.0)	
Body mass index, kg/m^2	23.1±3.0	24.0±3.0	24.0±3.0	0.235*
Previous history of colonoscopy	27 (49.1)	27 (51.9)	26 (48.2)	0.660†
Previous abdominal surgery	13 (23.6)	11 (21.2)	9 (16.7)	0.669‡
Comorbid disease§	29 (52.7)	32 (61.5)	25 (46.3)	0.288†
Metabolism/nutrition disease	14 (25.5)	8 (15.4)	13 (24.1)	
Gastrointestinal disease	10 (18.2)	14 (26.9)	10 (18.5)	
Cardiovascular disease	6 (10.9)	8 (15.4)	8 (14.8)	
Infectious disease	5 (9.1)	3 (5.8)	2 (3.7)	
Hepatobiliary disease	3 (5.5)	2 (3.9)	4 (7.4)	
Endocrine disease	4 (7.3)	3 (5.8)	1 (1.9)	
Musculoskeletal disease	1 (1.8)	2 (3.9)	5 (9.3)	
Respiratory disease	1 (1.8)	4 (7.7)	2 (3.7)	
Renal and urinary disease	1 (1.8)	1 (1.9)	3 (5.6)	
Eye disease	1 (1.8)	3 (5.8)	0	
Current medications‖	51 (92.7)	51 (98.1)	48 (88.9)	0.188‡
Alimentary tract/metabolism	49 (89.1)	47 (90.4)	47 (87.0)	
Cardiovascular system	12 (21.8)	11 (21.2)	11 (20.4)	
Respiratory system	3 (5.5)	2 (3.9)	3 (5.6)	
Systemic hormonal therapy	5 (9.1)	2 (3.9)	1 (1.9)	
Anti-infectious for systemic use	4 (7.3)	2 (3.9)	0	
Nervous system	3 (5.5)	1 (1.9)	1 (1.9)	
Dermatologic system	2 (3.6)	3 (5.8)	0	

Data are presented as mean±SD or number (%).
OST, oral sulfate tablet.
*p-value from analysis of variance; †Pearson chi-square test; ‡Fisher exact test; §Comorbid diseases and ‖current; medications were presented when their percentage of case is more than 5%.

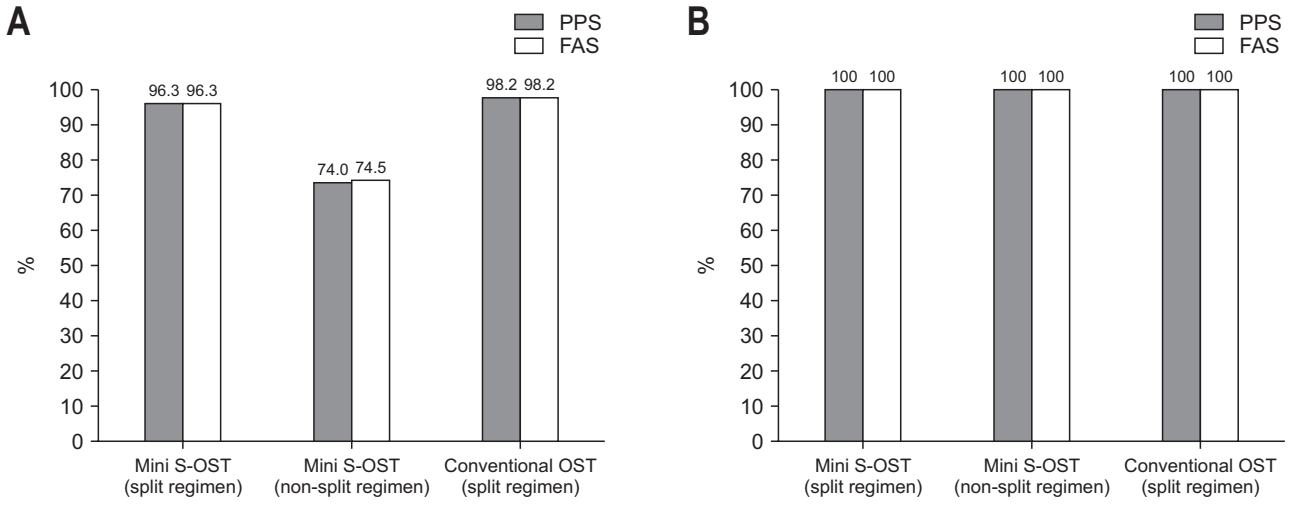

Fig. 2. Overall high-quality cleansing (A) and successful cleansing (B) in three groups: the mini S-OST split-dose group, mini S-OST non-split-dose group, and conventional OST group. Data are shown for both the FAS and PPS analyses. (A) Overall high-quality preparations were comparable between the mini S-OST and conventional OST groups in both the FAS (96.3% vs 98.2%, p=1.000) and the PPS analyses (96.3% vs 98.2%, p=1.000). (B) High rate of successful overall preparation (defined as an overall HCS grade of A or B) was observed in both the FAS (all 100% for three groups) and PPS analyses (all 100% for three groups). PPS, per-protocol set; FAS, full analysis set; OST, oral sulfate tablet; HCS, Harefield Cleansing Scale.

Table 2. Efficacy of Bowel Preparation Using the HCS

Variable	Mini S-OST		OST split	p-value*	p-value†
	Split	Non-split			
Full analysis set	54	51	54		
Successful cleansing‡	54 (100)	51 (100)	54 (100)	-	-
High-quality cleansing§	52 (96.3)	38 (74.5)	53 (98.2)	1.000	0.003
In each segment					
Ascending colon/cecum	52 (96.3)	39 (76.5)	53 (98.2)	1.000	0.006
Transverse colon	54 (100)	51 (100)	53 (98.2)	1.000	-
Descending colon	54 (100)	49 (96.1)	53 (98.2)	1.000	1.000
Sigmoid colon	54 (100)	51 (100)	53 (98.2)	1.000	-
Rectum	54 (100)	48 (94.1)	53 (98.2)	1.000	0.947
Per-protocol set	54	50	54		
Successful cleansing‡	54 (100)	50 (100)	54 (100)	-	-
High-quality cleansing§	52 (96.3)	37 (74.0)	53 (98.2)	1.000	<0.001
In each segment					
Ascending colon/cecum	52 (96.3)	38 (76.0)	53 (98.2)	1.000	0.006
Transverse colon	54 (100)	50 (100)	53 (98.2)	1.000	-
Descending colon	54 (100)	48 (96.0)	53 (98.2)	1.000	0.441
Sigmoid colon	54 (100)	50 (100)	53 (98.2)	1.000	-
Rectum	54 (100)	47 (94.0)	53 (98.2)	1.000	0.214

Data are presented as number (%).
HCS, Harefield Cleansing Scale; OST, oral sulfate tablet.
*p-value means comparison between split regimen of mini S-OST and conventional OST; †p-value means comparison between split regimen and non-split regimen of mini S-OST, p-value from the Pearson chi-square test; ‡Successful cleansing means HCS grade of A or B (≥1 segment with a score 2); §High-quality cleansing means HCS grade of A (all segments with scores of 3 or 4).

Table 3. Colonoscopy and Gastroscopy Outcomes (Per-Protocol Set)

Variable	Mini S-OST		OST split	p-value*	p-value†
	Split	Non-split			
Colonoscopy outcomes	54	50	54		
Procedure time, min	12.8±3.0	13.5±4.4	14.0±5.0	0.403‡	0.651‡
Withdrawal time, min	8.5±1.9	8.5±1.7	8.5±2.6	0.549‡	0.850‡
Cecal intubation rate	54 (100)	50 (100)	54 (100)	-	-
Polyp detection rate	15 (27.8)	18 (36.0)	18 (33.3)	0.531§	0.490§
Adenoma detection rate	7 (13.0)	13 (26.0)	13 (24.1)	0.137§	0.150§
Residual bubble					
Total score (0-3)	1.2±2.8	1.0±2.5	0.1±0.3	0.001‡	0.660‡
Grade 1-3 at any segment	4 (7.4)	3 (6.0)	0	0.118‖	1.000‖
Gastroscopy outcomes	49	50	53		
Acute gastropathy probability					
Total score (0-9)	5.9±2.7	5.7±2.9	6.3±2.2	0.341‡	0.896‡
Total score ≥6	19 (38.8)	23 (46.0)	21 (39.6)	0.930§	0.600§
Total score ≥8	19 (38.8)	16 (32.0)	18 (34.0)	0.614§	0.620§
Endoscopy findings					
Hematin	19 (38.8)	24 (48.0)	21 (39.6)	0.778§	0.469§
Hematin grade				0.051§	0.299§
Grade 1	3 (15.8)	4 (16.7)	2 (9.5)		
Grade 2	6 (31.6)	3 (12.5)	1 (4.8)		
Grade 3	10 (52.6)	17 (70.8)	18 (85.7)		
Fundus localization	5 (10.2)	3 (6.0)	3 (5.7)	0.476‖	0.487‖
Multiple erosions	9 (18.4)	17 (34.0)	18 (34.0)	0.038§	0.190§

Data are presented as mean±SD or number (%).
OST, oral sulfate tablet.
*p-value means comparison between split regimen of mini S-OST and conventional OST; †p-value means comparison between split regimen and non-split regimen of mini S-OST; p-value from ‡Wilcoxon's rank sum test, §Pearson chi-square test, and ‖Fisher exact test.

3 hematin (10 or more hematins or hematins in multiple areas) tended to be less frequently observed in mini S-OST split dose group than conventional OST group (52.6% vs 85.7%, p=0.051). The between-group difference was 33.1% (95% CI, –2.5% to 62.8%). In addition, multiple erosions tended to be observed less in mini S-OST split dose group than conventional OST group (18.4% vs 34.0%, p=0.038).

3. Tolerability

Dose adherence was similarly high in three groups (Table 4); however, one participant in the mini S-OST non-split dose group took 72% of the total dose due to nausea and vomiting. The FAS analysis showed that the mean total "Patient Satisfaction Scale" score did not significantly differ between the two split-dose groups (p=0.481). Most tolerability variables were similar between mini S-OST and conventional OST in split dose, however, more subjects expressed that they would ask for the mini S-OST again on the next colonoscopy than conventional OST (94.4% vs 81.5%, p=0.038) (Table 4).

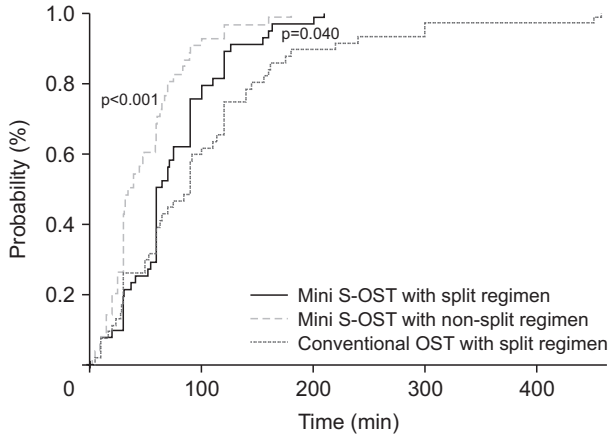

Fig. 3. Kaplan-Meier analysis for the response time (median, minutes) from completion of preparation agents to first bowel movement in the three study groups: the mini S-OST split-dose group, mini S-OST non-split-dose group, and conventional OST group. Median response time was significantly faster in the mini S-OST group, regardless of the split or non-split regimen, than in the conventional OST group (62.5 minutes, 37.5 minutes vs 90.0 minutes, p=0.040, p<0.001, respectively). OST, oral sulfate tablet.

4. Safety

Both solicited events and unsolicited events did not significantly differ between the three groups (Table 5). Abdominal distension was the most common among solicited mild AEs. In unsolicited AEs, one subject in mini S-OST split-dose group was diagnosed with rectal cancer (T2N0M0) and completely resected through surgical treatment. Another subject in mini S-OST non-split dose group was diagnosed with early gastric cancer (T1aN0M0) and completely resected through endoscopic submucosal dissection. Both cases were counted as unsolicited severe AEs. The laboratory results checked at the screening visit (pre-preparation) and on the day of colonoscopy (post-preparation) are summarized in Supplementary Table 2. Changes in some electrolytes, chloride, and magnesium were all sub-clinical and returned to baseline levels.

DISCUSSION

This phase 3, randomized, controlled, investigator- and central reader-blinded, multicenter, non-inferiority trial

Table 4. Tolerability According to the Patient Satisfaction Scale (Full Analysis Set)

Variable	Mini S-OST		OST split (n=54)	p-value*	p-value†
	Split (n=54)	Non-split (n=51)			
Patient satisfaction scale‡					
Total score	88.0±50.6	128.4±75.8	97.2±61.6	0.481§	0.005§
Domain 1 (opinion for current colonoscopy)					
Easy to consume	27.8±22.1	41.2±25.4	30.6±26.9	0.700§	0.010§
Ability to consume (yes)	54 (100)	45 (88.2)	53 (98.2)	1.000‖	0.379‖
Overall experience	28.2±19.5	34.8±24.0	31.0±19.4	0.412§	0.226§
Taste	31.9±20.3	40.7±21.8	33.8±22.3	0.611§	0.037§
Domain 2 (opinion for future colonoscopy)					
Ask for the same agent	51 (94.4)	38 (74.5)	44 (81.5)	0.038¶	0.010¶
Refuse the same agent	1 (1.9)	10 (19.6)	6 (11.1)	0.113‖	0.003‖
Adherence of dose					
Yes (≥75%)	54 (100)	50 (98.0)	54 (100)	-	0.977¶

Data are presented as mean±SD or number (%).
OST, oral sulfate tablet.
*p-value means comparison between split regimen of mini S-OST and conventional OST; †p-value means comparison between split regimen and non-split regimen of mini S-OST; ‡Patient Satisfaction Scale ranges from 0 to 400, with lower scores indicating higher satisfaction; p-value from §Wilcoxon's rank sum test, ‖Fisher exact test, and ¶Pearson chi-square test.

Table 5. Clinical Safety of Bowel Preparation (Safety Set Analysis)

Variable	Mini S-OST		OST split (n=54)	p-value*	p-value†
	Split (n=54)	Non-split (n=51)			
Solicited event					
Adverse event	24 (44.4)	25 (49.0)	20 (37.0)	0.557‡	0.697‡
Adverse drug reaction§	24 (44.4)	25 (49.0)	20 (37.0)	0.557‡	0.697‡
Severe adverse event	0	0	0	-	-
Severe adverse drug reaction	0	0	0	-	-
Unsolicited event					
Adverse event	23 (42.6)	30 (58.8)	29 (53.7)	0.336‡	0.119‡
Adverse drug reaction†	0	2 (3.9)	1 (1.9)	1.000‡	0.233‡
Severe adverse event	1 (1.9)	1 (2.0)	0	1.000‡	1.000‡
Severe adverse drug reaction	0	0	0	-	-

Data are presented as number (%).
OST, oral sulfate tablet.
*p-value means comparison between split regimen of mini S-OST and conventional OST; †p-value means comparison between split regimen and non-split regimen of mini S-OST; ‡p-value from Fisher exact test; §Adverse drug reaction included nausea, vomiting, thirst, weakness, bloating, abdominal pain, headache and dizziness.

evaluates the efficacy, tolerability, and safety of mini S-OST compared to a conventional OST during both gastroscopy and colonoscopy procedures. The mini S-OST split dose preparation had excellent bowel cleansing efficacy similar to the conventional OST preparation without severe AE or adverse drug reactions. In terms of reusability, tolerability was superior in mini S-OST split dose group and in the aspect of gastroscopy findings, there was a slight tendency for a lower grade of hematin and fewer multiple erosions in mini S-OST split dose group.

In the comparison between mini S-OST split dose group and conventional OST group, high rates of successful preparation (all 100%) and high-quality preparation (all>96%) without significant differences between the two groups were observed on both FAS and PPS analyses. The rate of high-quality preparation was not significantly different from those of previous studies with conventional OST,[6,8,22] and our previous study with original mini-OST.[11] Excellent successful cleansing in overall and in each segments, including the right colon, was observed in both groups and did not significantly differ. As this study was conducted with the upgraded mini S-OST (CTP 0302), which included the addition of simethicone compared to the previous mini-OST (CTP 0303), we compared residual bubbles as secondary colonoscopy outcome. Although the mean residual bubble score was lower in the conventional OST group compared with the mini S-OST split-dose group, the proportion of clinically relevant residual bubbles (grade 1–3) did not differ significantly between the two groups, and both polyp detection rate and adenoma detection rate were comparable. These findings suggest that the observed difference in bubble scores is unlikely to have a meaningful clinical impact on colonoscopy quality outcomes. Considering the results of other studies evaluating bubble levels in PEG-based preparations, where the proportion of "no air bubbles" or "minimal bubbles" was approximately 65% to 70%,[23] the grade 0 rate in the study group (92.6% and 94.0% for mini S-OST with split and non-split dose groups) is deemed an adequate level for endoscopic examination.

There were several indicators suggesting potential superiority of mini S-OST. The first bowel movement, response time were significantly more rapid in mini S-OST split dose group than conventional OST group. Tolerability, in terms of reusability was superior in mini S-OST split dose group than conventional OST group. In addition, in the gastroscopy finding, high-grade hematin and multiple erosions tended to less likely be observed in mini S-OST split dose group than conventional OST group. Although the absolute numbers for high-grade hematin (19/36 vs 18/21 in evaluable cases) resulted in wide confidence intervals, limiting statistical significance, the observed percentage difference was substantial (>30%).

Recent observations with OSTs have raised a safety concern regarding acute gastropathy.[10,12,13] Since most clinical trials for bowel preparation agents lack data on gastroscopy, the prevalence of acute gastropathy linked to these agents might be underestimated.[6,7] Similar to pill-induced esophagitis, delayed dissolution of OSTs in the stomach may lead to acute gastropathy, presenting as mucosal erosion or ulceration caused possibly by prolonged contact of the OST with the gastric mucosa. In the previous large observational study,[12] the rates of acute gastric mucosal abnormalities, including blood staining/clots, erosions on the greater curvature of the antrum/body, multiple erosions, and mucosal erythema or edema, were significantly higher in the conventional OST group compared to the

1 L PEG/Asc group (all p<0.001) in healthy subjects who underwent both gastroscopy and colonoscopy screening during routine health checkups. Moreover, high and indeterminate probability scores for preparation agent-induced gastropathy were observed more frequently in the conventional OST group (p=0.001). In our previous study, dissolving time of original mini-OST was about 2-fold rapid than that of conventional OST (7 minutes vs 15 minutes) by the laboratory test (unpublished data). Thus, in this study, we focused on comparing the mini S-OST and conventional OST with gastropathy. The tendency for less high-grade hematin and multiple erosions suggests that the smaller-sized mini S-OST (approximately 7.4×3.9×3.6) or mini-OST (Suprepmini, 7.4×4.0×2.8) may cause less gastric injury compared to conventional OST (Orafang, 17.2×8.2×6.4 mm).

This study also investigated the efficacy and tolerability of the mini S-OST non-split dose group. The non-split regimen was included as a secondary, exploratory comparison to evaluate feasibility in specific clinical scenarios. In the mini S-OST non-split dose group, although successful cleansing was 100%, the proportion of high-quality cleaning in the ascending colon was lower and comparable with previous studies that split-dose is better than non-split dose.[24] Potential factors include a longer interval between preparation completion and colonoscopy, especially affecting the proximal colon, and overnight stool stasis. In addition, mini S-OST non-split dose group showed significantly lower satisfaction scores than mini S-OST split dose group, and the incidence of AEs in mini S-OST non-split dose group was approximately 5% to 12% higher than split dose groups, although the difference was not statistically significant, similar to finding from other studies.[25] To compile the above information, the mini S-OST non-split dose regimen can be considered in cases where non-split-dose administration is necessary, for example, afternoon colonoscopy.

This study, however, has several limitations. First, the number of participants included in this study was relatively small compared to similar trials. The 15% non-inferiority margin was based on previous bowel preparation studies; however, given the limited number of direct comparative trials, establishing a margin on robust scientific evidence was challenging. This margin may also be considered clinically suboptimal. Second, as participants were recruited solely on a voluntary basis, younger individuals predominantly applied, resulting in a mean age of 43 to 44 years across all groups. The relatively young age distribution of participants may have contributed to the marginal statistical differences observed in gastric mucosal injury between groups. Moreover, the study population consisted exclusively of Korean participants, which limits the generalizability of our findings to older individuals, patients with significant comorbidities, and non-Asian populations. Third, while the non-split mini S-OST regimen may be useful for afternoon colonoscopies, its efficacy in such settings warrants further evaluation. Fourth, patient perceptions and acceptance of the tablet burden may differ in regions outside Korea, where familiarity with OSTs is lower. Given the higher prevalence of colorectal cancer and widespread colonoscopy use in the elderly, further large-scale studies with a greater representation of elderly participants and a more clinically relevant non-inferiority margin are necessary to validate our findings across broader patient populations

In conclusion, the mini S-OST split dose regimen showed excellent efficacy, comparable tolerability and safety, with less gastric injury compared with conventional OST regimen.

CONFLICTS OF INTEREST

This study was supported by Taejoon Pharm Co., Ltd., Seoul, Korea, the manufacturer of the investigational product. The sponsor provided financial support and was involved in the initial study design and monitoring. However, the sponsor had no role in patient recruitment, data collection, central image assessment, statistical analysis, data interpretation, manuscript drafting, or the decision to submit the manuscript.

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AUTHOR CONTRIBUTIONS

Study concept and design: J.M.C. Data acquisition: all authors. Data analysis and interpretation: all authors. Drafting of the manuscript: S.K.P. Critical revision of the manuscript for important intellectual content: S.R.J.,

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SUPPLEMENTARY MATERIALS

Supplementary materials can be accessed at https://doi.org/10.5009/gnl250291.

DATA AVAILABILITY STATEMENT

Data analyzed in this study are available from the corresponding author upon reasonable request.

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