# Efficacy and Safety of Pre-Endoscopy Regimens for Mucosal Visualization During Sedated Esophagogastroduodenoscopy: A Randomized Controlled Trial

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## ABSTRACT

***Background**: Optimal mucosal visibility during esophagogastroduodenoscopy (EGD) is critical for diagnostic accuracy but is often impaired by the presence of mucus and bubbles. This study aimed to compare the efficacy and safety of four premedication regimens for mucosal visualization during sedated EGD.* ***Methods**: A double-blind randomized controlled trial was conducted at the Endoscopy Unit of Dr. Zainoel Abidin General Hospital, Banda Aceh, Indonesia, from January to December 2024. Patients scheduled for elective diagnostic EGD were randomly assigned to: Group 1 (simethicone 40 mg at 30 minutes before the procedure), Group 2 (simethicone 40 mg + 100 mL 5% sodium bicarbonate at 2 hours), Group 3 (simethicone 40 mg + N-acetylcysteine 600 mg in 100 mL water at 2 hours), or Group 4 (all three agents at 2 hours). Primary outcomes were mucosal visibility (6-site, 3-point scoring system with lower scores indicating superior mucosal visibility); procedural metrics (irrigation volume and duration); and safety (the lowest recorded $SpO_2$%). Data were analyzed using ANOVA or Kruskal–Wallis for continuous variables, and Chi-square or Fisher's exact test for categorical variables, with post hoc testing as applicable.* ***Results**: A total of 168 patients were randomized into four groups (n=42 each). Groups 3 and 4 showed superior mucosal visibility compared to Groups 1 and 2 (p=0.004), with no significant difference between Groups 3 and 4. Irrigation volume differed significantly (p=0.018), lowest in Group 4. Group 3 had the shortest procedure time (3.1 ± 1.2 minutes), significantly more efficient than Groups 1 and 2, but similar to Group 4. Oxygen saturation was slightly lower in Group 3 (p<0.005), though all groups remained within safe clinical limits.* ***Conclusions**: Simethicone and N-acetylcysteine given two hours before endoscopy effectively enhanced mucosal visibility and procedural efficiency without compromising safety, offering a practical alternative to more complex regimens.*

***Keywords:** esophagogastroduodenoscopy; mucosa visibility; premedication; simethicone; N-acetylcysteine.*

## INTRODUCTION

Esophagogastroduodenoscopy (EGD) is a cornerstone procedure for the diagnosis and management of upper gastrointestinal (GI) disorders, including dysphagia, peptic ulcer disease, gastroesophageal reflux disease (GERD), and upper GI bleeding. It also serves as a critical screening tool for detecting early esophageal and gastric malignancies in high-risk populations.[1-7] When performed correctly, EGD is safe and well-tolerated, but its diagnostic accuracy heavily depends on optimal mucosal visualization.[2,8,9]

A key challenge in EGD is the presence of mucus, froth, and air bubbles, which obscure mucosal details and may lead to missed lesions,

prolonged procedural time, and increased healthcare costs.[2,10,11] Studies found that inadequate mucosal visibility contributed to diagnostic errors, particularly for subtle lesions such as early gastric cancer or Barrett's esophagus.[12-14] To address this issue, various premedication strategies, including defoaming agents (e.g., simethicone), alkalinizing agents (e.g., sodium bicarbonate), mucolytics (e.g., N-acetylcysteine), antispasmodics (e.g., hyoscine butylbromide), and sedatives, have been employed.[9,15-18] However, the efficacy of these agents varies widely, and global practices remain inconsistent due to a lack of standardized protocols.[18-21] Therefore, this study aimed to evaluate the mucosal visibility, procedural efficiency, and safety of different premedication regimens, including variations in composition and timing. In this study, the efficacies of simethicone alone, simethicone in combination with sodium bicarbonate or N-acetylcysteine, and a combination of all three agents were assessed.

## METHODS

A double-blind, randomized controlled trial (RCT) was conducted at the Endoscopy Unit of Dr. Zainoel Abidin General Hospital in Banda Aceh, Indonesia, between January and December 2024. Ethical approval was obtained from the Institutional Ethical Committee of Dr. Zainoel Abidin General Hospital (Approval No: 053/ETIK-RSUDZA/2024; Protocol No 24-02-040), with written informed consent acquired from all patients. This study adhered to the CONSORT guidelines for conducting and reporting randomized trials.[22] The study compared the effects of four pre-endoscopy preparation regimens (simethicone alone; simethicone plus sodium bicarbonate; simethicone plus N-acetylcysteine; and a combination of all three agents) on mucosal visibility, procedural efficiency, and patient safety during sedated diagnostic EGD. Primary outcomes included mucosal visibility scores, volume of irrigation fluid required, total procedure duration, and oxygen saturation levels during the examination. Sample size calculation using G*Power 3.1 (one-way ANOVA, four groups) indicated 160 patients were required to detect a medium effect size (Cohen's f=0.25) with 80% power at $\alpha$=0.05. Accounting for a 5% dropout, the target enrollment was set at 168 patients.

### Patient's Criteria and Randomization

Eligible patients were adults (>18 years) scheduled for elective diagnostic EGD under sedation. Inclusion criteria included clinical referral for diagnostic upper endoscopy, ability to comply with pre-procedure instructions, and provision of written informed consent. Patients with prior upper GI surgery, active GI bleeding, pregnancy, planned therapeutic interventions during EGD (e.g., biopsy or polypectomy), and known hypersensitivity to simethicone, sodium bicarbonate, or N-acetylcysteine were excluded from the study. Dropout criteria included development of adverse drug reactions (e.g., nausea, vomiting, or allergic reactions), protocol violations, or voluntary withdrawal of consent at any study stage.

Randomization was performed using a computer-generated block randomization scheme (block size of 8), stratified by age and sex to ensure balanced allocation. Group assignments were sealed in sequentially numbered, opaque envelopes prepared by an independent statistician. Envelopes were opened by trained study nurses after obtaining informed consent.

### Intervention

Patients were randomly assigned to one of four premedication regimens before undergoing sedated EGD. Group 1 (control) received simethicone 40 mg (chewed) 30 minutes before the procedure, in accordance with the hospital's standard protocol. Group 2 received simethicone 40 mg plus 100 mL of 5% sodium bicarbonate solution, administered two hours pre-procedure. Group 3 received simethicone 40 mg combined with N-acetylcysteine 600 mg dissolved in 100 mL of water, also given two hours before EGD. Group 4 received a triple combination of simethicone 40 mg, sodium bicarbonate 500 mg, and N-acetylcysteine 600 mg in 100 mL of water, administered two hours before endoscopy. All patients were instructed to fast for a minimum of eight hours for solids and two hours for clear fluids.

### Data Collection

Baseline demographic and clinical characteristics were recorded for all patients before the procedure, including sex distribution (male/female), mean age (± standard deviation), and primary indications for EGD (dyspepsia, upper GI bleeding, epigastric mass, dysphagia, cirrhosis hepatis, epigastric pain, and anemia). Standardized laboratory parameters obtained during pre-procedure evaluation included hemoglobin (g/dL), hematocrit (%), platelet count ($\times 10^3$ cells/µL), leukocyte count ($\times 10^3$ cells/µL), urea (g/dL), creatinine (g/dL), glucose (g/dL), prothrombin time (PT), activated partial thromboplastin time (aPTT), and albumin (g/dL). All laboratory tests were performed at the hospital's clinical pathology laboratory using Sysmex XN-Series Automated Hematology Analyzer (Sysmex Corporation, Kobe, Japan) and Roche Cobas 6000 Analyzer Series (Roche Diagnostics, Basel, Switzerland). Study outcomes included mucosal visibility scores, volume of irrigation fluid required, total procedure duration, and oxygen saturation levels during the examination, which were assessed and recorded.

### Study Outcomes

Study outcomes assessed in this investigation were mucosal visibility scores, volume of irrigation fluid required, total procedure duration, and oxygen saturation levels during the examination. EGDs were performed by two board-certified endoscopists with over five years of experience in therapeutic endoscopy. All procedures were conducted using Olympus EVIS EXERA III GIF-H190 high-definition video endoscopes (Olympus Corporation, Tokyo, Japan) and followed a standardized examination protocol, systematically evaluating the esophagus, stomach, and duodenum in sequence.

Mucosal visibility score was evaluated using a standardized 3-point scale across six anatomical regions: esophagus, gastric fundus, gastric body, gastric angle, gastric antrum, and duodenum. Each site was scored independently based on the following criteria: score 1 indicated no adherent mucus with clearly visible mucosa; score 2 represented a thin coating of mucus with preserved visibility; and score 3 denoted adherent mucus partially or completely obscuring the mucosa. The total mucosal visibility score (TMVS) was calculated as the sum of individual scores across all six regions (range: 6−18), with lower scores indicating superior mucosal visibility. All endoscopic evaluations were performed by the procedure endoscopist, with random video recordings reviewed by another blinded endoscopist to ensure scoring consistency.

Procedural metrics included precise measurement of irrigation fluid volume using the endoscopy pump's built-in volume counter (recorded in mL) and documentation of total procedure duration, timed in minutes from initial scope insertion to final withdrawal. Patient safety was monitored through continuous pulse oximetry, with the lowest recorded oxygen saturation ($SpO_2$%) during the procedure documented as a safety parameter.

### Statistical Analysis

Data normality was assessed with the Shapiro–Wilk test. Continuous variables were presented as mean ± standard deviation (SD) for normally distributed data or median (min–max) for non-normally distributed data. Group comparisons were performed using one-way ANOVA (parametric) or Kruskal–Wallis test (non-parametric), depending on data distribution. Post hoc analyses were conducted using the Tukey test (following ANOVA) or pairwise the Mann–Whitney U tests with Bonferroni correction (following Kruskal–Wallis). Categorical variables were compared using the Chi-squared test or Fisher's exact test. A $p$-value $<0.05$ was considered statistically significant. Data were analyzed using SPSS Statistics version 26 (IBM Corp., Armonk, NY, USA).

## RESULTS

### Enrollment Process and Characteristics of the Patients

A total of 185 patients were initially assessed for eligibility. Seventeen patients were excluded before randomization due to not meeting inclusion criteria (n=11), declining to participate (n=4), or incomplete clinical data (n=2). The remaining 168 eligible patients were enrolled and randomized equally into four

intervention groups (n=42 per group): Group 1 (simethicone only), Group 2 (simethicone plus sodium bicarbonate), Group 3 (simethicone plus N-acetylcysteine), and Group 4 (triple combination of simethicone, sodium bicarbonate, and N-acetylcysteine).

All randomized patients received their allocated interventions and underwent the scheduled EGD without any protocol deviations or losses to follow-up. However, several patients were excluded from the final analysis due to intra-procedural findings requiring therapeutic or diagnostic interventions. Specifically, Group 2 had two exclusions (one due to biopsy, one due to esophageal variceal ligation), Group 3 had five exclusions (two biopsies, three ligations), and Group 4 had eight exclusions (three biopsies, three ligations). Group 1 had no exclusions. These participants were removed from analysis to ensure that mucosal visualization outcomes were evaluated exclusively in diagnostic, non-therapeutic procedures. The detailed patient enrollment process is illustrated in **Figure 1**.

The Baseline demographic and clinical characteristics of the patients are summarized in **Table 1**. The mean age ranged from 48.6 ± 15.1 to 52.6 ± 12.9 years across the groups. The sex distribution was relatively balanced, with a slight male predominance in Groups 1 to 3 and a female predominance in Group 4. The most common indication for EGD was dyspepsia with alarm symptoms, reported most frequently in Groups 1, 3, and 4. A significantly lower proportion was observed in Group 2 ($p$=0.001). Significant intergroup differences were also noted in the incidence of epigastric mass ($p$=0.009), epigastric pain ($p$=0.035), and anemia ($p$=0.030). Other indications were evenly distributed across groups. Among laboratory parameters, leukocyte count, creatinine, and blood glucose levels differed significantly between groups, with $p$<0.001, $p$=0.001, and $p$=0.027, respectively. Other parameters, including hemoglobin, hematocrit, platelet count, renal function markers, coagulation profile, and serum albumin, were comparable across groups.

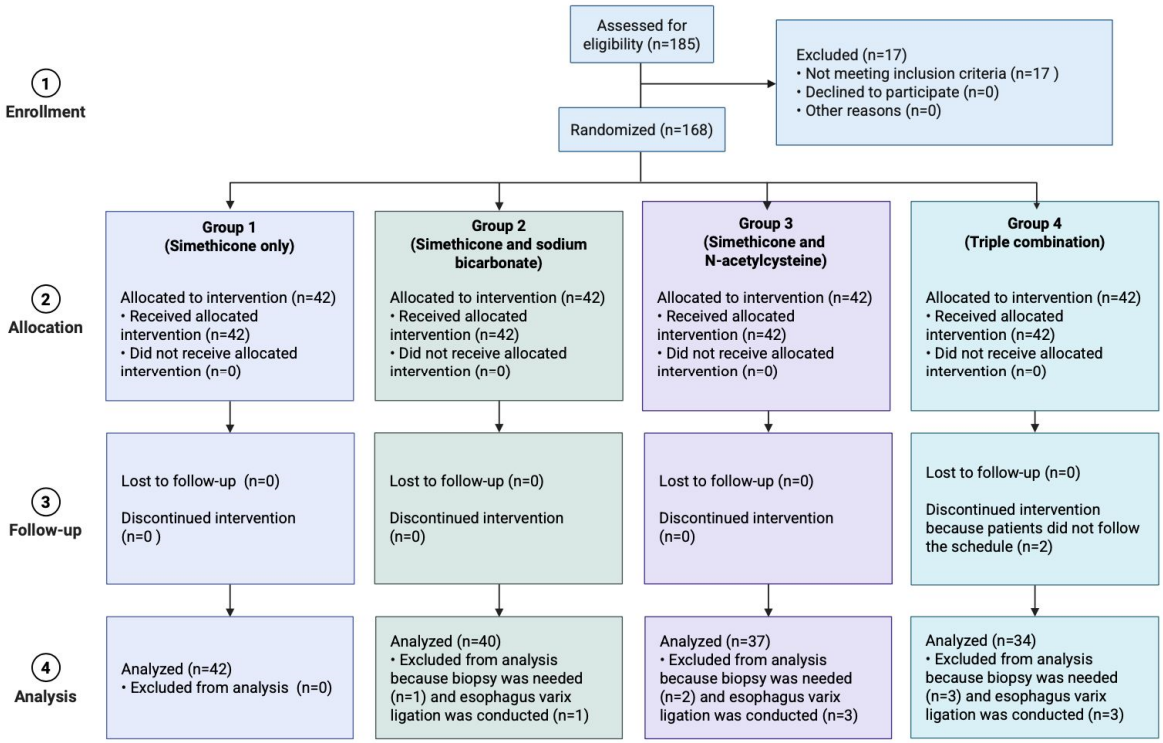


**Figure 1.** CONSORT flow diagram of the patient enrollment process.

**Table 1. Baseline demographic and laboratory characteristics of patients undergoing elective EGD**

| Characteristics | Groups, mean±SD | | | | *p*-value |
|---|---|---|---|---|---|
| | Simethicone only (Group 1) (n=42) | Simethicone and sodium bicarbonate (Group 2) (n=40) | Simethicone and N-acetylcysteine (Group 3) (n=37) | Triple combination (Group 4) (n=34) | |
| Age (years) | 48.6 ± 15.1 | 52.1 ± 13.0 | 52.6 ± 12.9 | 50.6 ± 15.8 | 0.548[b] |
| Sex, n (%) | | | | | |
| Male | 24 (57.1%) | 26 (65%) | 25 (67.5%) | 14 (41.1%) | |
| Female | 18 (42.9%) | 14 (35%) | 12 (32.4%) | 20 (58.8%) | 0.104[c] |
| Indications for EGD, n (%) | | | | | |
| Dyspepsia with alarm signs | 26 (61.9%) | 13 (32.5%) | 26 (70.3%) | 24 (70.6%) | 0.001[c*] |
| Upper GI bleeding | 9 (21.4%) | 16 (40%) | 9 (24.3%) | 6 (17.6%) | 0.122[c] |
| Epigastric mass | 0 (0.0%) | 4 (10%) | 0 (0.0%) | 0 (0.0%) | 0.009[b*] |
| Dysphagia | 0 (0.0%) | 1 (2.5%) | 0 (0.0%) | 0 (0.0%) | 0.419[b] |
| Cirrhosis hepatis | 2 (4.8%) | 3 (7.5%) | 2 (5.4%) | 2 (5.9%) | 0.960[b] |
| Epigastric pain | 0 (0.0%) | 3 (7.5%) | 0 (0.0%) | 0 (0.0%) | 0.035[b*] |
| Anemia | 5 (11.9%) | 0 (0.0%) | 0 (0.0%) | 2 (5.9%) | 0.030[b*] |
| Laboratory markers | | | | | |
| Hemoglobin (g/dL) | 11.7 ± 1.6 | 10.9 ± 2.0 | 11.1 ± 2.3 | 11.7 ± 1.9 | 0.124[a] |
| Hematocrit (%) | 35.1 ± 5.4 | 32.0 ± 5.6 | 34.3 ± 7.1 | 35.1 ± 5.5 | 0.079[a] |
| Platelet (×10³/µL) | 282.3 ± 117.3 | 258.9 ± 112.7 | 291.8 ± 121.8 | 238.4 ± 106.1 | 0.194[b] |
| Leukocyte (×10³/µL) | 9.6 ± 3.7 | 6.8 ± 2.8 | 10.1 ± 6.8 | 7.3 ± 3.1 | <0.001[b*] |
| Urea (g/dL) | 31.6 ± 26 | 30.7 ± 25.3 | 39.9 ± 28.9 | 31.85 ± 26.5 | 0.220[b] |
| Creatinine (g/dL) | 0.7 ± 0.7 | 1.1 ± 1.1 | 1.2 ± 1.1 | 0.9 ± 0.8 | 0.001[b*] |
| Glucose (g/dL) | 156.2 ± 84.7 | 137.1 ± 49.6 | 125.7 ± 51.2 | 114.9 ± 40.4 | 0.027[b] |
| PT (s) | 0.9 ± 0.4 | 1.1 ± 0.1 | 1.1 ± 0.1 | 1.1 ± 0.2 | 0.143[b] |
| aPTT (s) | 0.7 ± 0.3 | 0.9 ± 0.3 | 0.9 ± 0.2 | 0.9 ± 0.3 | 0.646[b] |
| Albumin (g/dL) | 3.4 ± 0.6 | 3.2 ± 0.7 | 3.1 ± 0.6 | 3.3 ± 0.5 | 0.230[b] |

* Statistically significant at $p<0.05$, [a] Analyzed using one-way ANOVA, [b] Analyzed using Kruskal-Wallis test, [c] Analyzed using chi-square test

### Effect of Premedication Regimens on Mucosal Visibility

Mucosal visibility was generally acceptable across all anatomical regions. There were no statistically significant differences among the groups in the esophagus or gastric antrum. However, significant differences were observed in the gastric fundus ($p=0.006$), gastric angle ($p<0.001$), gastric body ($p=0.003$), duodenum ($p=0.030$), and in the total mucosal visibility score ($p = 0.004$) (**Table 2**).

Post hoc analysis showed that Group 2 had significantly higher scores than Group 1 in the gastric fundus and angle, and significantly higher scores than both Group 3 and Group 4 in the gastric angle, gastric body, and TMVS, indicating lower mucosal visibility in these regions. Group 1 had higher scores than Group 3 in the gastric body and duodenum, and higher scores than Group 4 in the same regions, suggesting inferior visibility compared to the other two groups. In the gastric antrum, Group 4 demonstrated significantly lower scores than Group 3, indicating clearer visualization. Overall, Groups 3 and 4 exhibited the most favorable mucosal visibility, with lower TMVS values indicating superior clarity. Group 4 achieved the lowest TMVS, suggesting it provided the best overall mucosal visualization among the four premedication regimens (**Table 2**).

### Effect of Premedication Regimens on Irrigation Fluid Volume During EGD

Significant differences in irrigation fluid volume were observed among the groups across several anatomical regions. No statistically significant differences were found in the esophagus ($p=0.160$) or duodenum ($p=0.186$). However, irrigation volumes differed significantly in the gastric fundus ($p=0.006$), gastric angle ($p<0.001$), gastric body ($p=0.004$), gastric antrum ($p<0.001$), and total volume ($p=0.018$). Although overall differences were statistically significant in several regions, post hoc analysis did not reveal any significant pairwise differences between the groups in any region (**Table 3**).

**Table 2. Comparison of mucosal visibility scores across anatomical regions among groups, with post hoc analysis**

| Region | Mucosal visibility score, mean±SD | | | | *p*-value |
|---|---|---|---|---|---|
| | Simethicone only (Group 1) (n=42) | Simethicone and sodium bicarbonate (Group 2) (n=40) | Simethicone and N-acetylcysteine (Group 3) (n=37) | Triple combination (Group 4) (n=34) | |
| Esophagus | 1.1 ± 0.3[a] | 1.3 ± 0.5[a] | 1.1 ± 0.3[a] | 1.2 ± 0.4[a] | 0.579 |
| Gastric fundus | 1.1 ± 0.3[a] | 1.3 ± 0.5[b] | 1.0 ± 0.1[a] | 1.1 ± 0.3[ab] | 0.006* |
| Gastric angle | 1.1 ± 0.2[a] | 1.3 ± 0.5[b] | 1.0 ± 1.0[a] | 1.0 ± 1.0[a] | <0.001* |
| Gastric body | 1.3 ± 0.5[b] | 1.3 ± 0.5[b] | 1.1 ± 0.3[a] | 1.1 ± 0.2[a] | 0.003* |
| Gastric antrum | 1.3 ± 0.5[a] | 1.3 ± 0.5[a] | 1.3 ± 0.5[a] | 1.1 ± 0.3[a] | 0.159 |
| Duodenum | 1.3 ± 0.5[b] | 1.4 ± 0.6[b] | 1.1 ± 0.3[a] | 1.1 ± 0.3[a] | 0.030* |
| Total score | 7.3 ± 1.4[b] | 8.2 ± 2.7[b] | 6.8 ± 0.8[a] | 6.5 ± 0.9[a] | 0.004* |

* Statistically significant at $p<0.05$, analyzed using Kruskal-Wallis test

[a],[b] Different superscripts indicate statistically significant differences between groups ($p<0.05$) based on Mann-Whitney post hoc tests. Same or shared letters ([ab]) indicate no significant difference.

**Table 3. Comparison of irrigation fluid volume required during esophagogastroduodenoscopy (EGD) across anatomical regions among groups, with post hoc analysis**

| Region | Irrigation fluid volume (mL), mean±SD | | | | *p*-value |
|---|---|---|---|---|---|
| | Simethicone only (Group 1) (n=42) | Simethicone and sodium bicarbonate (Group 2) (n=40) | Simethicone and N-acetylcysteine (Group 3) (n=37) | Triple combination (Group 4) (n=34) | |
| Esophagus | 0.9 ± 2.6[a] | 0.2 ± 1.1[a] | 0.5 ± 3.3[a] | 0.4 ± 1.9[a] | 0.160 |
| Gastric fundus | 0.9 ± 2.6[a] | 0 ± 0 | 0 ± 0 | 1.5 ± 5.5[a] | 0.006* |
| Gastric angle | 1.3 ± 2.9[a] | 0.5 ± 2.2[a] | 0 ± 0 | 0 ± 0 | <0.001* |
| Gastric body | 1.9 ± 3.3[b] | 3.2 ± 6.5[b] | 1.7 ± 5.9[b] | 0.3 ± 1.7[b] | 0.004* |
| Gastric antrum | 2.0 ± 4.1[a] | 7.0 ± 7.2[a] | 6.3 ± 11.2[a] | 0.6 ± 2.0[a] | <0.001* |
| Duodenum | 1.4 ± 3.3[b] | 1.2 ± 3.9[b] | 1.8 ± 6.9[b] | 0.6 ± 3.4[b] | 0.186 |
| Total fluid volume | 8.4 ± 16.6[b] | 12.5 ± 15.9[b] | 9.8 ± 17.7[b] | 3.4 ± 7.6[b] | 0.018* |

* Statistically significant at $p<0.05$, analyzed using Kruskal-Wallis test

### Effect of Premedication Regimens on Procedure Time During EGD

The mean duration of EGD was under five minutes across all groups, with a statistically significant difference in procedure time among the groups ($p=0.003$). Group 3 had the shortest mean procedure duration (3.1 ± 1.2 minutes), followed by Group 4 (3.5 ± 1.2), Group 1 (4.0 ± 1.4), and Group 2 (4.0 ± 1.4). Post hoc analysis revealed that Group 3 had a significantly shorter procedure time compared to Groups 1 and 2. No statistically significant differences were observed between the other pairwise comparisons (**Table 4**).

**Table 4. Comparison of EGD procedure duration across anatomical regions among groups, with post hoc analysis**

| Group | EGD procedure duration (minutes), mean±SD | | | | *p-value* |
|---|---|---|---|---|---|
| | Simethicone only (Group 1) (n=42) | Simethicone and sodium bicarbonate (Group 2) (n=40) | Simethicone and N-acetylcysteine (Group 3) (n=37) | Triple combination (Group 4) (n=34) | |
| Duration (min) | 4.0 ± 1.4[b] | 4.0 ± 1.4[b] | 3.1 ± 1.2[a] | 3.5 ± 1.2[ab] | 0.003* |

* Statistically significant at $p<0.05$, analyzed using one-way ANOVA

[a],[b] Different superscripts indicate statistically significant differences between groups ($p<0.05$) based on Tukey tests. Same or shared letters ([ab]) indicate no significant difference.

### Effect of Premedication Regimens on Patient Safety (Oxygen Saturation)

All groups maintained clinically safe oxygen saturation levels throughout the procedure, with no recorded desaturation events. However, statistically significant differences in $SpO_2$% were observed during examination across all anatomical regions (*p*-values ranging from 0.001 to 0.004). Post hoc analysis showed that Group 3 had significantly lower $SpO_2$% than the other groups across all anatomical regions (**Table 5**).

## DISCUSSION

This study demonstrates that the combined regimen of simethicone 40 mg chewable tablet and N-acetylcysteine 600 mg tablet dissolved in 100 mL of water (Group 3) resulted in significantly improved mucosal visualization compared to simethicone alone (Group 1) or simethicone combined with sodium bicarbonate (Group 2). The lack of additional benefit from sodium bicarbonate suggests that the mucolytic properties of N-acetylcysteine are the primary contributors to enhanced visibility. These results are consistent with previous studies indicating that combining mucolytic and anti-foaming agents yields superior gastric mucosal clarity when administered 20–30 minutes before EGD.[23-29] Although certain studies have reported that sodium bicarbonate and peppermint may improve mucosal visualization,[17, 27, 30] our findings suggest their effect is limited when N-acetylcysteine is already part of the regimen. This supports the notion that the mucolytic mechanism, through disulfide bond disruption and mucus thinning, is more impactful than alkalinization alone in this setting.[31] Importantly, our protocol maintained efficacy despite the premedication being administered two hours before EGD. This contrasts with earlier protocols that relied on shorter pre-procedure intervals (10–30 minutes),[32-34] demonstrating the feasibility and clinical practicality of a longer interval within sedated EGD workflows, where earlier administration may be preferred for procedural logistics and patient preparation.

Procedural efficiency outcomes further highlight the advantages of N-acetylcysteine-containing regimens. Group 3 (simethicone + N-acetylcysteine) required no irrigation in the gastric fundus and angle, while Group 4 (triple combination) had the lowest total fluid use. These findings contrast with reports suggesting no added benefit of N-acetylcysteine over simethicone alone,[35,36] likely attributable to methodological differences, particularly in visibility scoring or timing of drug administration. Notably, Group 3 also achieved the shortest mean EGD duration (3.1 minutes), compared to 4.0 minutes in the simethicone alone group, implying that improved mucosal clarity facilitates faster examinations. While a study has reported simethicone alone as the fastest option,[36] our results suggest that combination regimens offer an optimal balance between procedural speed and visibility enhancement.

**Table 5. Comparison of the lowest recorded oxygen saturation ($SpO_2$%) across anatomical regions among groups, with post hoc analysis**

| Region | Lowest recorded oxygen saturation ($SpO_2$%), mean±SD | | | | *p*-value* |
|---|---|---|---|---|---|
| | Simethicone only (Group 1) (n=42) | Simethicone and sodium bicarbonate (Group 2) (n=40) | Simethicone and N-acetylcysteine (Group 3) (n=37) | Triple combination (Group 4) (n=34) | |
| Esophagus | 98.6 ± 1.8[b] | 98.7 ± 1.9[b] | 98.3 ± 0.5[a] | 98.8 ± 1.1[b] | 0.004 |
| Gastric fundus | 98.7 ± 1.7[b] | 98.7 ± 1.8[b] | 98.3 ± 0.4[a] | 98.8 ± 0.9[b] | 0.001 |
| Gastric angle | 98.7 ± 1.7[b] | 98.8 ± 1.8[b] | 98.3 ± 0.4[a] | 98.8 ± 0.9[b] | <0.001 |
| Gastric body | 98.7 ± 1.7[b] | 98.8 ± 1.8[b] | 98.3 ± 0.4[a] | 98.8 ± 1.0[b] | 0.001 |
| Gastric antrum | 98.7 ± 1.7[b] | 98.8 ± 1.8[b] | 98.3 ± 0.4[a] | 98.6 ± 1.8[b] | 0.001 |
| Duodenum | 98.7 ± 1.7[b] | 98.7 ± 1.9[b] | 98.3 ± 0.4[a] | 98.6 ± 1.8[b] | 0.002 |

* Statistically significant at $p<0.05$, analyzed using one-way ANOVA

[a,b] Different superscripts indicate statistically significant differences between groups ($p<0.05$) based on Tukey tests. Same or shared letters ([ab]) indicate no significant difference.

Safety evaluations confirmed that all regimens were well-tolerated, with no clinically significant differences in oxygen saturation; all groups maintained $SpO_2$ >98%, and no aspiration events were observed. These findings support the safety of administering premedication two hours before sedated EGD without increasing airway risk. [24, 28]. The absence of adverse events, including in groups receiving sodium bicarbonate, despite its potential to increase gastric volume, is especially reassuring and supports the clinical applicability of these regimens.

Several limitations should be considered when interpreting the findings of this study. First, the single-center design may limit generalizability to other practice settings with different patient populations or endoscopic protocols. Second, the fixed-dose regimens (e.g., 600 mg N-acetylcysteine) did not account for potential dose-response relationships that might optimize outcomes further. Third, while we standardized the sedation protocol, unmeasured variations in individual patient responses to sedation could have influenced procedure duration and mucosal visibility assessments. Finally, the study was not powered to detect rare adverse events, although the absence of safety concerns across all groups is reassuring. Future multicenter studies should validate these findings while exploring optimal administration timing and dosing strategies, particularly for non-sedated procedures.

## CONCLUSION

All four premedication regimens demonstrated acceptable safety and efficacy and may be selected based on clinical context and availability. Among them, the combination of simethicone 40 mg chewable tablet and N-acetylcysteine 600 mg tablet dissolved in 100 mL of water, administered two hours before endoscopy, showed significantly improved mucosal visibility and reduced procedure time, with safety outcomes comparable to more complex regimens. Given its performance and simplicity, this two-agent regimen may serve as a preferred option to enhance endoscopic quality and procedural efficiency. Future multicenter studies are warranted to validate these findings and assess broader applicability.

## CONFLICTS OF INTERESTS

The authors declare no conflicts of interest.

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