

The Efficacy of Simethicone Plus N-Acetylcysteine Versus Water in Improving Mucosal Visualization During Gastroscopy Using Total Mucosal Visibility Scoring (TMVS): A Meta-analysis

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Abstract

Background/Aim: To determine the efficacy of Simethicone plus N-acetylcysteine (NAC) versus water prior to Gastroscopy in improving mucosal visualization.

Materials and Methods: With the search of relevant studies conducted from Pubmed and Web of science database for randomized clinical trials regarding Simethicone plus NAC as pre procedural medication prior to Gastroscopy in improving mucosal visualization. A random effects meta-analysis was done to determine the difference in total mucosal visibility score (TMVS) between the experimental and control group.

Results: Four randomized clinical trials involving 632 patients who fulfilled the inclusion criteria were pooled into a meta-analysis. Simethicone plus NAC showed better total mucosal visibility score versus water as control with computed mean difference of -2.46 (-3.99, -0.93) which showed significant result with a P value of <0.00001 in total mucosal visibility scoring (TMVS).

Conclusions: Simethicone plus N-Acetylcysteine as a premedication prior to gastroscopy improves mucosal visibility using TMVS.

Keywords: Simethicone; N-acetylcysteine; Premedication; Preparation; Gastroscopy

Introduction

Esophagogastroduodenoscopy (EGD) is one of the most common methods for the diagnosis and treatment of upper gastrointestinal diseases [1]. It also helps to identify early neoplastic lesions. However, accumulation of foam, bubbles and mucus in the upper gastrointestinal tract interfere with the mucosal visualization, which may possibly increase the risk of missing subtle lesions, decreases diagnostic accuracy, and reduces patient's comfort. There are clearing mechanisms applied to create good endoscopic visualizations for the upper gastrointestinal tract using mucolytic agents, antifoaming agents, proteolytic enzymes and neutralizers [2-4].

Simethicone or activated Dimethicone was proved and one of the widely used antifoaming agents for pre-endoscopic usage for bubble and mucus removal [5,6]. It has also been studied to be used in colonoscopy as an additive agent to other bowel preparations to eliminate bubbles [7,8]. It lowers the surface tension of air bubbles, dispersing them without any significant absorption in the GI system. N-acetylcysteine (NAC), a mucolytic agent that has been used to improve endoscopic visualization by breaking the disulfide bonds that stabilize extracellular proteins in the mucus *in vitro*, thus reducing the thickness of the gastric mucosal barrier.

The aim of this study is to determine the effectiveness of Simethicone plus N-acetylcysteine as premedication in improving mucosal visualization in an unselected group of patients.

Methods

Inclusion criteria

Type of study

The type of studies included were randomized controlled clinical trials published in the English language regardless of year.

Types of participants

1. Participants were adults (18 - 89 years old) 2. Patients undergoing routine or outpatient upper gastrointestinal endoscopy (UGE) 3. Patients who are not pregnant, no known stricture, not breastfeeding women, participants who have no known upper gastrointestinal malignancy, no pharyngeal weakness/paralysis bulbar or pseudobulbar palsy, no any previous esophageal or gastric surgery, no known allergy to NAC or Simethicone, no gastrointestinal bleeding, no caustic ingestion, no diabetes, no asthma, not emergency cases and with stable vital signs.

Outcome measures

The outcome that was evaluated in this study was the mucosal visibility score using the total mucosal visibility score (TMVS).

Data source and search strategy

Eligible studies regardless of their publication year. Studies were identified by a comprehensive search in the following databases: PubMed and Web of science database. All type of studies included were randomized controlled trial published using Simethicone, N-acetylcysteine, Simethicone plus N-acetylcysteine in improving the mucosal visualization during gastroscopy using Total mucosal visibility scoring (TMVS) published in English Language. Searches were conducted by combining the following keywords (“Simethicone”) or (“Dimethicone”), (“N-acetylcysteine”) or (“NAC”), (“Gastroscopy”) or (“Esophagogastroduodenoscopy”) or (“Upper endoscopy”) and (“premedication”) or (“pre procedural medication”).

Study selection

After the process of identification of databases, duplicates were removed and all the identified studies were carefully screened by two independent authors (J Ortiz and D Sevilleja). Abstracts which met the inclusion criterias as described were selected. Other study conflicts encountered was resolved by a third author (E Amatong). Studies included in qualitative and quantitative analysis were reviewed and determined for eligibility inclusion and for every conflict encountered, it was resolved with concensus.

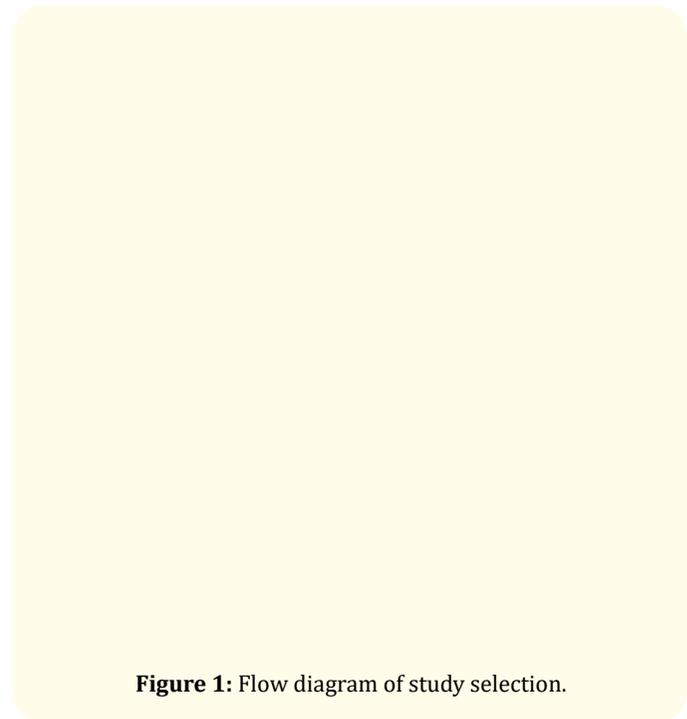


Figure 1: Flow diagram of study selection.

Data extraction

Data extraction was independently done by two authors as mentioned from the studies screened and selected which includes gathering information pertaining to the author, year of publication, study participants, sample size, study design, intervention used and outcomes measure using TMVS. Data extracted are shown in table 1.

Study	Population	Intervention	Control	Outcome
Prasit., <i>et al.</i> (2020)	128	A. Water 100 ml B. Water 100 ml w/Sim 100 mg C. Water 100 ml w/Sim 100 mg + NAC 600 mg D. Water 100 ml w/Sim 100 mg + NAC 600 mg + Na HCO ₃ 1000 mg, peppermint oil 85 mg	E. Water 100 ml	TMVS

Monroy, <i>et al.</i> (2017)	230	A. Sim 200 mg in 100 ml water B. Sim 200 mg and NAC 500 in 100 ml water	C. 100 ml water	TMVS
Basford, <i>et al.</i> (2016)	126	A. Sim 60 mg and NAC 1000 mg in 50 ml water	B. 50 ml water	TMVS
Asl, <i>et al.</i> (2011)	148	A. Dim 100 mg in 100 water B. Dimethicone 100 + NAC 600 in 100 ml water	C. 100 ml water	TMVS

Table 1: Summary of all studies included in the systematic review. Sim: Simethicone; NAC: N-Acetylcysteine; Dim: Dimethicone; TMVS: Total Mucosal Visibility Score.

Risk of bias and validity assessment

Validity of eligible trials were ascertained using the Cochrane Collaboration’s tool for assessing risk of bias. Risk of bias was analyzed through 6 domains pertaining to random sequence generation, allocation concealment, blinding of participants and person-

nel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias. A checklist was generated and included studies were given an assessment of low risk, unclear risk, and high risk. A summary of the checklist is provided on table 2.

Study	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Asl, <i>et al.</i> (2011)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Basford, <i>et al.</i> (2016)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Monroy, <i>et al.</i> (2017)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Prasit, <i>et al.</i> (2020)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk

Table 2: Validity Assessment of Included RCT’s using Cochrane Collaboration Tool.

Statistical analysis

Statistical analysis was performed using Review Manager (Rev-Man) Version 5.4 freeware program developed by the Cochrane Collaboration. Heterogeneity among studies was assessed in terms of both clinical and statistical aspect. Quantification was done using the I² test to ascertain that differences between studies are not due to chance. Considering that the included studies presented were continuous variables, data was depicted as mean with its respective standard deviations. An inverse variance statistical method was used in this meta-analysis with mean difference as its effect measure at 95% confidence interval. A forest plot was generated by combining the mean differences of included study using a random effects model.

Results

A total of 632 randomized participants were included in the study who were scheduled to undergo Gastroscopy. Out of 632 patients, 155 participants were given Simethicone plus NAC as experimental while 156 were given water as control group. In figure 2, it was determined that the combination of Simethicone plus N-Acetylcysteine versus control (Water) was assessed in four studies, namely Asl, *et al.* 2011, Basford, *et al.* 2016, Monroy, *et al.* 2017, and Prasit, *et al.* 2020 which revealed a mean difference of -3.34 with a 95% confidence interval of -3.92 to -2.76. The Z statistics for the overall effect size were 11.26 and was statistically significant, with a P-value of <0.00001 and heterogeneity as evidenced by the I² of 41%.

Figure 2: Total Mucosal Visibility Score (Simethicone + NAC) and control.

Discussion

Gastroscopy or Esophagogastroduodenoscopy (EGD) is widely used as a standard diagnostic test to detect upper gastrointestinal tract (UGI) diseases. However, due to mucus secretion and bubble formation, it may impair mucosal visualization and reduce diagnostic accuracy therefore using pre procedural medications should be considered.

Simethicone plus N-acetylcysteine are anti bubble and mucolytic agents and is statistically more effective than water alone with regards to total mucosal visibility scoring and with regards to mucosal visibility it is one of the important elements for gastroscopy especially in early screening for Upper gastrointestinal malignancies. The aim of this review was to evaluate the efficacy of simethicone plus NAC as premedication for gastroscopy.

The findings of the study showed that Simethicone plus NAC is statistically more effective than water alone when used as premedication in Gastroscopy.

Conclusion

The study showed that mucolytic agent such as NAC plus simethicone are useful and more effective when combined and used as premedication for gastroscopy, as it showed significant improvement in the mucosal visibility using the TMVS scoring which may increase the diagnostic yield of upper gastrointestinal examination.

Recommendation

It is recommended to include the procedural time used in each studies and the amount of water used in flushing during the procedure. Limitations of this meta-analysis should also be addressed by including studies with more similar sample size. Future meta-analyses should also consider inclusion of studies with more similar interventional dose regimen to minimize clinical heterogeneity.

Conflicts of Interest

There are no conflicts of interest.

Bibliography

1. Cohen J., *et al.* "Quality indicators for esophagogastroduodenoscopy". *American Journal of Gastroenterology* 101 (2006): 886-891.
2. Keeratichananont S., *et al.* "The role of liquid simethicone in enhancing endoscopic visibility prior to esophagogastroduodenoscopy (EGD): a prospective, randomized, double-blinded, placebo-controlled trial". *Journal of the Medical Association of Thailand* 93.8 (2010): 892-897.
3. Wu L., *et al.* "Systematic review and meta-analysis of randomized controlled trials of Simethicone for gastrointestinal endoscopic visibility". *Scandinavian Journal of Gastroenterology* 46.2 (2011): 227-235.
4. Chen HW., *et al.* "Pre-medication to improve esophagogastroduodenoscopic visibility: a meta-analysis and systemic review". *Hepatogastroenterology* 61.134 (2014): 1642-1648.
5. McDonald GB., *et al.* "Pre-endoscopic use of oral simethicone". *Gastrointestinal Endoscopy* 24 (1978): 283.
6. Banerjee B., *et al.* "Effectiveness of pre-procedure simethicone drink in improving visibility during esophagogastroduodenoscopy: a double-blind, randomized study". *Journal of Clinical Gastroenterology* 15 (1992): 264-265.
7. McNally PR., *et al.* "The effectiveness of simethicone in improving visibility during colonoscopy: a double-blind randomized study". *Gastrointestinal Endoscopy* 34 (1998): 255-258.
8. Tongprasert S., *et al.* "Improving quality of colonoscopy by adding simethicone to sodium phosphate bowel preparation". *World Journal of Gastroenterology* 15 (2009): 3032-3037.

9. Chang WK, *et al.* "Efficacy of simethicone and N-acetylcysteine as premedication in improving visibility during upper endoscopy". *Journal of Gastroenterology and Hepatology* 29 (2014): 769-774.
10. Mahawongkajit P and Kanlerd A. "A prospective randomized controlled trial comparing simethicone, N-acetylcysteine, sodium bicarbonate and peppermint for visualization in upper gastrointestinal endoscopy". Springer Science+Business Media, LLC, part of Springer Nature (2020).
11. Asl SMK and Sivandzadeh GR. "Efficacy of premedication with activated Dimethicone or N-acetylcysteine in improving visibility during upper endoscopy". *World Journal of Gastroenterology* 17.37 (2011): 4213-4217.
12. Basford PJ, *et al.* "A randomized controlled trial of pre-procedure simethicone and N-acetylcysteine to improve mucosal visibility during gastroscopy-NICEVIS". *Endoscopy International Open* 04 (2016): E1197-E1202.
13. Monroy H, *et al.* "Use of N-acetylcysteine plus simethicone to improve mucosal visibility during upper GI endoscopy: a double blind, randomized controlled trial". 2017 by the American Society for Gastrointestinal Endoscopy 0016-5107.
14. Neale J, *et al.* "Premedication with N-acetylcysteine and simethicone improves mucosal visualization during gastroscopy: a randomized, controlled, endoscopist-blinded study". *European Journal of Gastroenterology and Hepatology* 25 (2013): 778-783.

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