PREMEDICATION WITH ORAL SOLUTION OF SIMETHICONE PLUS N-ACETYLCYSTEINE TO IMPROVE THE QUALITY UPPER GI ENDOSCOPY: INITIAL EXPERIENCE

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ABSTRACT

Introduction*: To assess the efficacy and safety of simethicone with or without N-acetylcysteine (NAC) as premedications before gastroscopy.*

Materials and methods*: Patients were randomized into 5 groups. Endoscopic visibility was evaluated in 4 districts (esophagus, gastric body, fundus and antrum) using a visual scale, graduating from 1 to 4 points.*

Results*: There was no significant difference on the rate of positive findings when comparing simethicone with simethicone plus NAC and with water, respectively. Simethicone plus NAC showed better total mucosal visibility score than simethicone alone. Both simethicone plus NAC and simethicone alone offer more benefit than water. The procedure time in simethicone group was shorter than that in water group. Regarding adverse events, there was no significant difference in simethicone and water group.*

Conclusions*: As premedication of gastroscopy, simethicone plus NAC offers more benefit on positive findings and total mucosal visibility score.*

Keywords*: Quality, Gastroscopy, N-acetylcysteine, premedication, simethicone.*

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Introduction

Upper gastrointestinal endoscopy (UGE) requires optimal visualization of the mucosa, but the endoscopist's view is often hampered by the presence of bubbles and foam: it also requires multiple aspirations of the foam and intraprocedural lavages, which maybe lengthen the time required for endoscopic examination. Simethicone (S) is frequently used to improve visibility during endoscopy, and has been suggested by some clinical trials[1,2], as well as N-acetylcysteine (NAC)is a long-known mucolytic[3].

Aim of our study is to evaluate the use of oral simethicone (S) plus NAC before UGE, comparing differences in the visualization of the gastric mucosa in patients prepared with simethicone or NAC plus simethicone with water alone or no intervention

Materials and methods

Patients were randomized into 5 groups:

- no intervention;
- 50 mL of water (W);
- W + simethicone (S) 150 mg + NAC (S) 250 mg;
- W + simethicone (S) 100 mg + NAC (S) 300 mg;
- W + simethicone (S) 100 mg + NAC (S) 200 mg (table 1).

Patients, technical staff, endoscopists, nurses and data collectors have been blinded. For this purpose, all liquid solutions were prepared in opaque containers of similar appearance. The participants received the assigned solution 30 minutes before the procedure under the supervision of a doctor.

	Group 1 (no prep)	Group 2 (water 50 ml)	Group 3 S 150 mg + NAC 250 mg	Group 4 S 100 mg + NAC 300 mg	Group 5 S 100 mg + NAC 200 mg
Numebr	10	10	10	10	10
Mean age (years)	45.3 ± 8.7	46.1 ± 7.9	44.9 ± 7.5	48.3 ± 6.8	45.3 ± 8.7
M:F ratio	1.4:1	1.5:1	1:1	1:1	1.5:1
Dyspepsia	50%	60%	80%	60%	80%
Pirosis	90%	80%	90%	90%	80%
GERD	60%	70%	60%	80%	50%
PPI use	100%	90%	100%	100%	90%
prokinetics use	50%	60%	40%	50%	40%

Table 1: Clinical-demographic characteristics of the patients enrolled for the study.

All patients received standard recommendations before the procedure: at least 8 hours of liquid and solid fasting and 72 hours of suspension of anti-secretory medications. Local pharyngeal anesthetic solution has been used immediately before the procedure.

Endoscopic visibility was evaluated in 4 districts (esophagus, gastric body, fundus and antrum) using a visual scale, graduating from 1 to 4 points:

• no adherent mucus on the mucosa examined;

• a small amount of mucus on the mucosa that does not hinder vision;

• a large amount of mucus on the mucosa, which can be washed thoroughly with less than 50 mL of water;

• a large amount of mucus, which cannot be cleaned completely with up to 50 mL of water, and would require more water for washing[4].

Results

No adverse reaction attributable to the procedure was detected during the study. No allergic reactions or upper respiratory tract aspirations were noted. There were no cardiovascular or endoscopic adverse events in the patients during study period, from administration of the study drug to at least 120 minutes after the UGE procedure was completed. No late adverse reactions has been reported.V Integral results are reported in table 2.

	Group 1 (no prep)	Group 2 (water 50 ml)	Group 3 (S 150 mg + NAC 250 mg	Group 4 (S 100 mg + NAC 300 mg)	Group 5 (S 100 mg + NAC 200 mg)
Satisfaction px	Not valutable	8/10	8/10	9/10	8/10
Vision quality	4/10	5/10	9/10	9/10	9/10
EGDS duration	6 ± 3 minutes	6 ± 4 minutes	6 ± 2 minutes	6 ± 2 minutes	5 ± 1 minutes
Bubbles	+ + +	+ + -	+ - -	Absence	Absence
Esoohagitis	30%	40%	40%	30%	30%
Gastritis	60%	30%	20%	40%	40%
Duodenitis	20%	20%	30%	30%	30%
Lesions < 5 mm	0	0	30%	20%	20%

Table 2: results.

From the data in the table it can be seen how the use of the solution with 100 mg of simethicone and a quantity of NAC between 200 mg and 300 mg effectively favors vision during the endoscopic procedure, reducing the number of bubbles and ultimately the duration of the examination, and increasing the number of lesions <5 mm diagnosed.

Discussion

Simethicone, dimethicone and NAC are widely used as anti-bubble premedication before gastroscopy, colonoscopy and capsule endoscopy[5,6].

The aim of our sperimental study was to summarize and evaluate the effect and safety of simethicone or dimethicone ± NAC as preprocedural preparation of gastroscopy.

Not only simethicone plus NAC, but also simethicone alone was statistically more effective than water for mucosal visibility, with substantial heterogeneity, whereas the evidence quality was moderate. Mucosal visibility by simethicone plus NAC is significantly better, than simethicone alone, with moderate level of evidence[4].

However, the result did not maintain consistency when sensitivity analysis was performed. Mucosal visibility is one of the important elements for gastroscopy, especially for screening for early upper gastrointestinal cancer. Since early upper gastrointestinal neoplasia is superficial, detection of minor elevations or depressions in the mucosal surface and subtle changes in color is difficult when bubbles and foam exist in esophagus and stomach. Bubbles and foam may cover superficial and minor lesions, which can easily be missed during gastroscopic procedure. Simethicone plus NAC, as anti-bubble and mucolytic agents, is an appropriate option before gastroscopy. These defoamers and mucolytic agents are widely used in Japan and China[7].

In our experience, adequate endoscopic visualization helps us screen entire upper gastrointestinal mucosa and increase the rate of positive findings. Procedure time in simethicone group was shorter than water without substantial heterogeneity. Mean procedure time in the included studies ranged from 5.1 to 10.5 min[7]. The main cause for prolonged time is flushing time and aspiration. Actually, for patients without sedation, tolerability of the procedure might influence overall mucosal screening. Shorter procedure time may be suitable for patients with poor tolerance without sedation. However,

there is considerable debate about procedure time. The study by Teh et al.[8] in 2015 showed a three-fold increase in findings for a with procedure time of >7 min compared with those who were spending less time on their examination. A minimum 7-min procedure time for diagnostic EGD was recommended by European Society of Gastrointestinal Endoscopy in 2016[9]. In our opinion, if the patient prefers unsedated procedure, we suggest taking oral simethicone ± NAC before gastroscopy in order to decrease flushing times and provide enough time to screen. If the patient prefers sedation, procedure time of at least 7 min will be better for first diagnostic EGD. Additionally, adverse events were also reported[10]. The most common adverse events were nausea, vomiting and bloating, which were within the acceptable range. Simethicone did not result in more adverse events than water.

Conclusions

Our study has some obvious limitations: we cannot compare endoscopic visibility measurements for each patient before premedication to assess the impact of the individual preparations (only 2 subjects, excluded from the study, underwent 2 upper endoscopy, one before and one after the solution was administered: the results, although not statistically significant, suggest a better visualization of the mucosa after the administration of S + NAC).

Our results suggest that the lesion detection rate should improve with the use of adequate preparation with mucolytic agent s before UGE, even if this needs to be investigated prospectively.

In conclusion, our findings show that the oral use of NAC + S before UGE improves the visibility of the mucosa and reduces near to zero the need of water, which may increase the diagnostic yield of the UGE examination.

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Statements
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Autorship
All authors have made substantial contributions to all of the following:
(1) the conception and design of the study: GG, GGDV
(2) acquisition of data: GG, SF, BDO
(3) analysis and interpretation of data: SF, BDO
(4) drafting the article or revising it critically for important intellectual content: GG, AILM, GGDV
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