

The Role of Simethicone in Upper Gastrointestinal Endoscopy and Functional Dyspepsia



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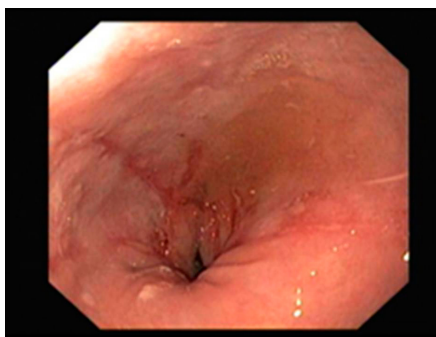
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Simethicone for upper gastrointestinal endoscopy

Nowadays, the esophagogastroduodenoscopy (EGD) still remains, not only the standard diagnostic test for the upper gastrointestinal (UGI) tract diseases, (figure 1) but also has been used as a therapeutic procedure for many conditions for example; stopping of UGI bleeding, tumor removals, dilation or stenting for significant luminal strictures¹⁻². However, food retention, or obscuring foam and bubbles (that originate by the mixing of intraluminal gas with gastric mucus or bile juice, figure 2)³ could cause abdominal discomfort, impaired mucosal visualization and have an impact on the diagnostic accuracy.⁴⁻⁶ Therefore, fasting for at least 6 to 8 hours and/or using of prokinetic drugs (intravenous erythromycin) or anti-foaming agents (oral simethicone) before the procedure should be considered⁷⁻¹⁰.

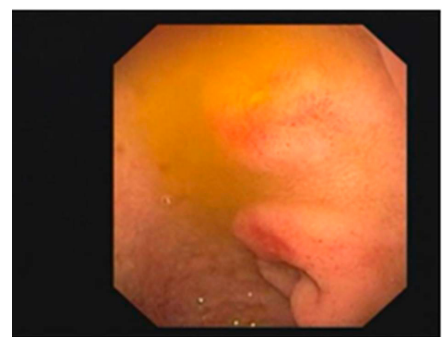
Figure 1: Images of the upper GI mucosa (esophagus, stomach and duodenal diseases) during the esophagogastroduodenoscopy (EGD).



Erosive esophagitis

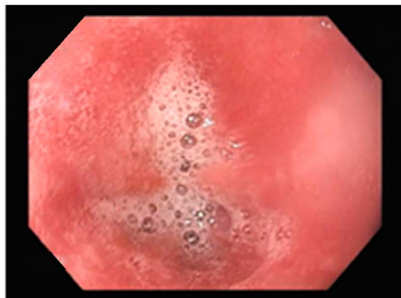


Gastric ulcer

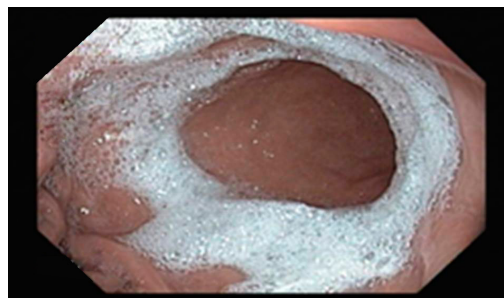


Duodenitis

Figure 2: Intraluminal foam, bubbles which decrease endoscopic visibility during the EGD.



Foam in esophagus



Stomach bubbles



Duodenal foam



Simethicone (polydimethylsiloxane, plus silicon dioxide) is a defoaming agent, which is tasteless, odorless, unabsorbed through GI mucosa, rarely has drug-drug interactions and can be taken up to 900 mg/day without any systemic toxicity¹¹⁻¹⁶. Simethicone acts mainly in the GI lumen with both anti-foaming and gastric mucosal protective properties^{8, 12, 17-20}. It acts by decreasing the surface tension of air bubbles causing small bubbles to coalesce and are then able to be easily removed from the GI tract¹⁷⁻²¹. Therefore, usage of simethicone washing during the EGD showed good efficacy in clearing such obscuring foam and bubbles (figure 3).

Figure 3: Efficacy between the adjunctive simethicone washing vs. water jet for removing duodenal foam, bubbles during the EGD.



In the 1950's, oral liquid simethicone has been mentioned as a pre-procedural anti-foaming agent in uncontrolled studies²²⁻²⁵. After that, two small randomized, double-blind studies were conducted in 1967 and 1978, which showed pre-endoscopic simethicone could significantly reduce the number of obscuring foam and bubbles^{4, 26}. In 1992 Berton, et al. conducted a randomized double-blinded placebo-controlled study in 330 participants, and revealed that liquid simethicone 65 or 195 mg in 90 ml of water taken 15 min prior to EGD enhanced endoscopic visibility by diminishing obscuring foam and bubbles in the stomach and duodenum. The results also showed that simethicone significantly reduced the number of patients who needed adjunctive simethicone washing³.

Subsequently, in 2009, a prospective randomized, double-blind placebo-controlled trial carried out by Keeratichananont and colleagues with 121 participants of EGD, received liquid simethicone (2 ml equivalent to 133.3 mg) or a placebo with 60 ml of water, 15-30 min prior to EGD²⁷. The investigators showed that liquid simethicone significantly enhanced endoscopic visibility within all areas of the UGI tract better than the placebo, which was demonstrated by the reduction of mean cumulative scores of foam and bubbles (6.83 ± 2.4 vs. 11.05 ± 2.6 , $p < 0.001$). Furthermore, the number of patients who needed adjunctive simethicone washing was significantly lower (17.5% vs. 74.1%, $p < 0.001$) and the median of adjunctive washing times for residual obscuring foam were shorter (0 vs. 19 seconds, $p < 0.001$) in the simethicone group, respectively. Moreover, the results revealed that simethicone enhanced endoscopist satisfaction significantly by showing higher proportions of a good to very good endoscopic visibility scale in this group compared to the placebo group (70.0% vs. 15.4%, $p < 0.001$). In addition, the patients self-reports in the severity of abdominal pain, nausea and vomiting after the procedure were also lower in the simethicone group, as well as there being no significant differences in the adverse effects between the study groups.²⁷

Later, in 2011 Ahsan, et al. conducted a randomized, placebo-controlled, double-blinded trial in 173 patients, which was aimed to evaluate the efficacy of pre-procedural simethicone chewable tablets (40 mg) taken with 30 ml of water within 15-30 min before EGD. They observed simethicone could significantly decrease the amount of gastric foam and shortened the endoscopy time better than the placebo²⁸. In 2014, Chang, et al. conducted a prospective study in 1,849 patients to assess the efficacy of pre-medication with 100 mg simethicone suspension alone versus a combination of 100 mg simethicone and 200 mg N-acetylcysteine in 100 ml of water prior to EGD. The study demonstrated that 100 mg of simethicone suspension alone could significantly improve endoscopic visibility comparable to the combination of these two drugs²¹. Recently, a meta-analysis as well as a systemic review from ten prospective studies, involving 1,541 patients made by Chen, et al. confirmed that there was a statistically significant improvement in endoscopic visibility with pre-medication using simethicone in at least 30 ml of water before EGD²⁹.

Conclusions

Intra-procedural simethicone washing demonstrated good efficacy in clearing obscuring foam and bubbles during the EGD. Moreover, pre-endoscopic simethicone could enhance endoscopic visibility in all areas of the UGI tract, improving both endoscopist and patient satisfaction, whilst additionally shortening the duration of adjunctive simethicone washing. Therefore, oral simethicone has been proven as a good anti-foaming agent for an UGI endoscopy.

Simethicone for functional dyspepsia

Functional dyspepsia (FD), a disorder, thought to originate from the gastroduodenum, is one of the most common final diagnosis in patients presenting with chronic dyspeptic symptoms. The current popular diagnostic criteria for FD is based on The Rome III criteria as shown in table 1³⁰⁻³¹.

Table 1: The Rome III diagnostic criteria for functional dyspepsia (FD).

At least 3 months with onset at least 6 months previously of one, or more of the following.	
1.	Bothersome postprandial fullness, occurring after ordinary-sized meals, at least several times per week.
2.	Early satiation that prevents finishing a regular meal, at least several times per week.
3.	Epigastric pain localized to the epigastrium of at least moderate severity, at least once per week.
4.	Epigastric burning sensation.
5.	No evidence of structural disease (including at upper GI endoscopy) that is likely to explain the symptoms.

FD is a chronic, fluctuating disease with periods of time when the patient is asymptomatic followed by episodes of symptom relapse, and only 50% of cases achieved long-term disease remission. Although, FD is not a life-threatening condition, and it has not been shown to be associated with any increase in mortality, FD has a strong negative impact on patients' health-related quality of life compared to the general population³²⁻³⁴.

The underlying pathophysiology in FD is probably multifactorial, involving a combination of dysregulation of the brain-gut interaction, gastroduodenal hypersensitivity to hydrochloric acid (HCL), fatty meals, or distension from food & gas, food intolerance or allergy, impaired fundus relaxation, delayed gastric emptying time, *H. pylori* infection, drugs and also emotional stress³⁵⁻³⁸. Therefore, the understanding in all pathophysiology, disease progression, useful medications and lifestyle modifications are essential to the effectiveness of treatment response.

As we know, acid suppression therapy with proton pump inhibitors or H2-receptor antagonists, prokinetic agents, anxiolytic/anti-depressant drugs and simethicone are all useful medications for FD³⁷⁻⁴¹. However, the best curative drug is now unavailable, thus treatment is on the basis of individual patient characteristics, this being the preferred strategy.

Simethicone reduces gastric foam and bubbles so, may attenuate gastric hyperdistension from stomach gas. Additionally, simethicone may stimulate gastrointestinal motility, (by accelerate transit of intestinal gas) as well as having a gastric mucosal protective property (prevents gastric injury from HCL acid and bile salts)^{8, 12, 17-20}. In 1999, Holtmann, et al. conducted the first prospective randomized, double-blinded study in 177 FD patients, with the aim to compare the efficacy of simethicone 84 mg tid with a prokinetic agent (cisapride) 10 mg tid for 4 weeks. The study revealed that simethicone tablet relief in global dyspeptic symptoms is comparable to cisapride without any adverse events. Furthermore, simethicone could improve dyspeptic symptoms during the first 2 weeks of treatment significantly better than cisapride (global symptom scores decrease from 14.0 ± 3.7 to 5.4 ± 3.0 in simethicone group vs. from 14.1 ± 3.3 to 7.7 ± 3.4 in cisapride group, $p < 0.001$)⁴². After this study, in 2002, a prospective randomized, double-blind placebo-controlled trial was carried out by Holtmann, et al. 185 patients with FD were randomized and treated using a double-dummy technique with simethicone 105 mg tid, cisapride 10 mg tid or a placebo for 8 weeks. The results showed that treatment with simethicone tablets or cisapride was significantly (all p -value < 0.0001) better than the placebo for symptom control, and that used together, simethicone was also significantly superior to prokinetic cisapride in the first 2 weeks of treatment ($p = 0.0007$)⁴³.

In the context of a combination with other drugs, two recently prospective, placebo-controlled studies confirmed that the combination between simethicone (45-90 mg tid) with either, activated charcoal or magnesium oxide, was significantly more effective than a placebo on overall symptom intensity in patients with functional dyspepsia⁴⁴⁻⁴⁵.

Conclusions

Functional dyspepsia is still the most common stomach disease with chronicity in natural course. To date, there are many classes of therapeutic medications, but the best drug and regimens are not yet known. Simethicone showed a significant efficacy in therapeutic for relief the global dyspeptic symptoms. Therefore, simethicone alone, or a combination, with other useful drugs is beneficial, and should be considered as a good treatment option for patients presenting with functional dyspepsia.

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