Reviewer 3646555; reviewed 2016-07-01 02:06:

To the authors: Many outstanding errors need to be rectified. However I would be happy for this article to be published if these errors are satisfactorily corrected. As most of these errors are minor, I hope that this process will not be very onerous for the authors. GRAMMATICAL ERRORS 1. In abstract: "surgical resection to the upper gastrointestinal tract" should read "surgical resection of the upper gastrointestinal tract" 2. In third paragraph of introduction: "over the counter" should be "over-the-counter" 3. In third paragraph of introduction: "scope elderly patients" should be "perform endoscopy on elderly patients" (scope is not an appropriate verb in medical terminology) 4. Patient selection paragraph: "Patients who were incarcerated, had prior history of surgical resection to the esophagus, stomach, or duodenum, had known hypersensitivity to simethicone, or required gastroscopy for urgent indications such as suspected gastrointestinal bleeding, were all excluded from the study" should read "Patients who were incarcerated; had prior history of surgical resection of the esophagus, stomach, or duodenum; had known hypersensitivity to simethicone; or required gastroscopy for urgent indications such as suspected gastrointestinal bleeding were all excluded from the study" 5. Study design paragraph: "After the endoscopist has completed an adequate inspection of the mucosal surfaces, the endoscopist withdraws the tip of the gastroscopy up to the gastroesophageal junction and the research coordinator notes the time. The procedure time is defined" should read "After the endoscopist completed an adequate inspection of the mucosal surfaces, the endoscopist withdrew the tip of the gastroscopy up to the gastroesophageal junction and the research coordinator noted the time. The procedure time was defined" 6. Study design paragraph: "After this, the endoscopist will advance the gastroscope back into the stomach and proceed to do any interventions deemed necessary such as biopsies of detected lesions" should read "After this, the endoscopist advanced the gastroscope back into the stomach and proceeded to do any interventions deemed necessary such as biopsies of detected lesions" 7. Endoscopic scoring system of mucosal visibility paragraph: "the endoscopists will evaluate and note the McNally" should read "the endoscopists evaluated and noted the McNally" 8. In Discussion paragraph, "which is compared against a placebo using the McNally scoring method" should read "which was compared against a placebo using the McNally scoring method" 9. Discussion first paragraph, "their 100ml solution consisted of mucolytic and anti-foaming agent resulted in the best mucosal visibility scores" should read "their 100ml solution consisting of mucolytic and anti-foaming agent resulted in the best mucosal visibility scores" 10. In Discussion first paragraph: "This is turn, resulted in a significantly shorter procedure time" should read "This, in turn, resulted in a significantly shorter procedure time" 11.

Final sentence of discussion: "such volumes are routinely used as modified water swallowing test" should read "such volumes are routinely used as modified water swallowing tests" 12. Figure 4: the word "simethicone" needs to be capitalised MORE EVIDENCE NEEDED IN CERTAIN AREAS 1. Third paragraph of introduction: "Singapore has an aging population"- this paper would be improved with a reference showing evidence of this. 2. Discussion first paragraph :You have stated "There was also significantly lower volume of additional flushes required during gastroscopy if simethicone was given. This in turn, resulted in a significantly shorter procedure time for mucosal inspection". Whilt it seems intuitive, you have not proven any statistical correlation between these two outcomes. Could you provide this (perhaps a scatterplot graph with flush volume on the x axis and procedure time on the y axis, with a r-squared.

Reply to reviewer 3646555:

All grammatical errors were corrected. Additional reference added for the aging population of Singapore. A scatter plot between total volume of additional water flushed during gastroscopy and the procedure time is done showing a positive correlation. Many thanks for the detailed review and helpful suggestions.

Reviewer 61678; reviewed 2016-07-01 06:47:

Dear Editor, Authors Thank you for sending the paper entitled "Efficacy of small-volume simethicone given at least 30 minutes before gastroscopy "for revision - It is a good practical idea - I think the importance of search could be more applicable if the study done for enteroscopy not upper endoscopy. - The paper is well written, well organised . - Minor language correction needed. Thanks.

Reply to reviewer 61678:

Thank you for the review.

Reviewer 70280; reviewed 2016-07-20 01:15:

This is an interesting article on an interesting topic it can accepted.

Reply to reviewer 70280:

Thank you very much.

Reviewer 2979057; reviewed 2016-07-22 14:21:

This manuscript by Dr. Song et al evaluated the efficacy of a low volume (5mls) simethicone solution compared to a placebo by TMVS, showing that a low volume of simethicone solution with adequate premedication time was still effective in terms of mucosal visibility. The overall structure of this manuscript is basically complete, and preliminarily answers the scientific question about the efficacy of low-volume defoaming agent for the preparation of gastroscopy examination. This RCT research was a randomized, placebo-controlled, endoscopist-blinded study, and the source of the data presented was basically reliable. And the results showed some obvious improvement in TMVS in the low-volume simethicone group. From these findings, the authors came to the conclusion that with a premedication time of at least 30 min, 5mls simethicone can significantly decrease gastric foam, decrease the volume of additional flushed and shorten the examination time. This research was based on some recent and relevant researches, and its design was similar to that of those researches. In all, this clinical research may provide more information on personalized preparation plan before gastroscopy examination since such a small volume is more suitable for patients with swallowing difficulties and the formulation has excellent patient compliance with no adverse effects. The title of the manuscript contains key words and could attract our attention, and the main topic falls within the scope of this magazine. The language of this manuscript reaches the standard of publishing. I think the paper contains some interesting observations and great application value but there are a few points for author's clarifications: 1. According to the CONSORT statement for RCT, a table showing baseline demographic and clinical characteristics for each group is necessary. In table 1, the authors only listed and compared age, gender and mean premedication time which seems not concrete and comprehensive enough, and I think it would be nice to take some more factors into consideration such as cause of endoscopy. 2. It would be better for the authors to give more details about the methods of patients collecting and randomizing. 3. In table 2, the result showed simethicone premedication did not significantly improve mucosal visibility score of the esophagus, since esophagus is an essential site for gastroscopy examination, it would be better to give some explanation and solutions for this phenomenon. 4. In the result, since the authors had calculate mean score of each region, it would be nice to give more data about volume of additional water flushed required and time of examination for each of them, this could enrich the result and give readers more information.

Reply to reviewer 2979057:

Thank you for the suggestions.

For point (1), we checked through the medical records of the database and added the necessary information for the indication of gastroscopy.

For point (2), we added additional descriptive information about patient collection and randomisation:

"This study was conducted in Changi General Hospital in Singapore, from 14th August 2015 to 19th November 2015, *at the outpatient gastroenterology clinics. All patients who were planned for gastroscopy as part of their management plan were asked by their respective clinic attending if they would permit a research coordinator to speak to them. If they agreed, the research coordinator would find the patient at the endoscopy listing room to obtain informed consent from the patient to participate in the study.* Patients who were at least 21 years old, mentally competent to give informed consent, and scheduled for outpatient elective diagnostic gastroscopy were enrolled. Patients who were incarcerated; had prior history of surgical resection of the esophagus, stomach, or duodenum; had known hypersensitivity to simethicone; or required gastroscopy for urgent indications such as suspected gastrointestinal bleeding were all excluded from the study. This was a randomized, placebo-controlled, endoscopist-blinded study which was approved by the SingHealth Centralized Institutional Review Board (Ref: 2015/2519) and registered under clinicaltrials.gov (NCT02555228). The randomisation sequence (in blocks of 6) was computer generated by a statistician at Changi General Hospital's Clinical Trials and Research Unit (CTRU). *The allocation sequence was written on separate cards as number codes and each card was placed inside a sealed opaque envelope. After a study participant registered for the elective gastroscopy, the research coordinator would open an opaque envelope outside the endoscopy suites and the patient would be allocated to either the simethicone group (100mg of liquid simethicone added to 5 ml of water) or the placebo group (5 ml of water) based on the number written on a card."*

For point (3), we have elaborated why the mucosal visibility score of the esophagus was low and had no significant improvement with simethicone:

"This resulted in significant improvement of TMVS compared to placebo (Fig. 5, Fig. 6). *Although the improvement in mucosal visibility scores was not significant for the esophageal area, the mean scores for the esophageal area were already very low to begin with (1.48 ± 0.57 in*

the simethicone group and 1.59 ± 0.57 in the placebo group). We postulated that this was because of the tubular structure of the esophagus as well as the peristaltic movements of the esophagus allowing mucus and secretions to flow down into the stomach. In additional, our study population is made up of healthy patients who were predominantly undergoing gastroscopy for dyspepsia; only 1 patient had dysphagia and 9 patients had reflux symptoms. This may result in the study population having a better mucosal visibility score in the esophageal area at baseline and explain why low volume simethicone solution did not make much of a difference. There was also significantly lower volume of additional flushes required during gastroscopy if simethicone was given."

For point (4), we apologize that this aspect of the procedure time for mucosal inspection and the volume of additional flush used per specific area was not possible for us to measure accurately during the study. This was because the mucosal inspection time was generally less than 5 minutes and our sole research coordinator's reaction time would have introduced significant human reaction error on different start and stop times, and different volumes of water flushed in each area. To overcome this, we would have required two or three research coordinators following each patient's gastroscopy so that the specific areas are divided among them – but this was logistically impossible.