

May 29, 2019

Editorial Office

*World Journal of Gastrointestinal Endoscopy*

Re: "Randomized, Double-Blinded, Placebo-Controlled Trial Evaluating Simethicone Pretreatment with Bowel Preparation during Colonoscopy"

Dear editor,

Thank you for inviting our manuscript for publication in *World Journal of Gastrointestinal Endoscopy*.

We appreciate the reviewer comments and suggestions on our manuscript. We have revised the manuscript according to the comments. The revised parts have been marked in highlighted text and quoted below.

#### **Reviewer comments**

Comment 1:

"Shell, we understand that after the extra Simethicone irrigation during colonoscopy, a level of bowel cleansing was similar in both groups? In my personal opinion – cleansing the bowel during colonoscopy with water (what is very common to improve bowel prep removing residual stool from the colon) and irrigation with Simethicone, which is able drastically remove bubbles) are really very important approaches during colonoscopy (30% of colonoscopies has significant bubbles) - I do not remove the endoscope until no bubbles in the colon or I cannot improve a quality of bowel prep with water irrigation. Therefore, the authors' statement if the endoscope was removed from the colon even when extra irrigation with Simethicone did not remove bubbles totally from the colon is crucial to assess the value of the study and understand Simethicone impact on ADR."

Response

Thank you for insightful comment. We agree with the reviewer in such that withdrawing colonoscope until the visual field is completely clear of bubbles and mucosa is clear of residual stool is vital to the adequacy of the procedure. Clear visualization was obtained in all procedures even if it required extra irrigation. We apologize for not making this clear. To clarify this we have added a sentence in the discussion portion (Page 15, lines 25-27) of the revised manuscript.

"Complete mucosal visibility was achieved prior to withdrawing colonoscope even if extra irrigation was required."

#### Comment 2

It's unclear for me why the authors did not assess the caecum – bubbles there can be a real problem without irrigation without Simethicone during colonoscopy

#### Response

Thank you for your comment. Caecum was assessed in all colonoscopies and incomplete procedures were not analyzed. To clarify, we have added a sentence in the revised methods portion (Page 10, Line 1-2). We apologize for not making this clear.

“The primary outcome measure was bubble reduction during the withdrawal phase starting from the cecum.”

#### Comment 3

The authors did not mention if more adenomas were discovered in the whole colon or in the right colon.

#### Response

Thank you for this thoughtful comment. We agree with your astute observation and data addition including polyp localization has been added to the manuscript. In our analysis, there was no significant difference between polyps detected in the right vs. left colon. Adenoma differentiation between right and left colon was not reported on all pathologies and therefore this variable was not analyzed upon revision.

Please note Table 3 on Pages 26-28 of the revised manuscript.

Right sided polyps [Mean ±SD]	1.23±1.95	0.98±0.96	P=0.429
Left sided polyps [Mean ±SD]	1.53±1.56	1.18±1.19	P=0.228

#### Comment 4

“the authors assessment regarding bubbles did not concern the sigmoid and the rectum”

Response

We are grateful for your observation. We agree that differentiation of Intraluminal Bubbles Scale between right and left colon would have provided more insight into this issue. However, this variable was not recorded according to laterality. This has been added to the discussion portion of the manuscript as a limitation. Please see revised manuscript Page 18 Lines 7-8.

“This study was not designed to calculate ADR and adenoma localization was not performed.”

Comment 5

“If it concerned flat polyps or tiny polyps or small and/or large polyps”

Response

Thank you for your suggestion. We agree that including polyp size is important as it contributes to assigned surveillance intervals for colonoscopies. As per your request, we have revised our manuscript to add polyp details including size. This has been added to Table 3 on Pages 26-28 of the manuscript. According to our analysis, there was no significant difference in small or large polyp detection between the simethicone and placebo groups.

Large polyps (>5mm) [Mean ±SD]	1.13±1.71	1.16±1.27	P=0.937
Small polyps (1mm-4mm) [Mean ±SD]	1.56±1.92	1.00±1.14	P=0.093

Comment 6

“The authors did not randomize gastroenterologists between two groups (with Simethicone and without it. The question stands whether they had similar ADR before the study”

Response

Thank you for the thoughtful comment. All gastroenterologists were blinded to patient assignment during the procedure. Individual endoscopist ADR was not

cofactored in the study and gastroenterologist randomization with respect to simethicone and placebo groups was not performed due to the following reasons; a combination of screening, surveillance, and diagnostic colonoscopies were performed instead of screening colonoscopies alone. Furthermore, since the ADR is a quality measure of the proportion of screening colonoscopy patients who are found to have atleast one adenoma, the measurement of ADR does not account an endoscopist's ability to identify multiple adenomatous polyps in a patient. It is for these reasons a formal ADR was not calculated in this study. However we agree that gastroenterologist randomization is an important factor for evaluation for ADR between groups and this has been mentioned in the limitations portion of discussion on Page 18 Line 9. We hope to see further research in the future with simethicone infused bowel preparation utilizing large sample sizes of screening colonopies for the purposes of ADR calculation.

**"Gastroenterologists were not randomized between the two study arms."**

#### **Editor Comments**

Thank you for your suggestions.

The revised manuscript has been submitted in word format as requested.

Author contributions have been provided in the title page as recommended.

As requested, Background has been removed from the abstract and replaced by Aim.

Article Highlights have been added as requested.

References have been checked for duplicates.

Figure 1 has been submitted as an editable word document.

We hope that the revised version of our paper is now suitable for publication in the *World Journal of Gastrointestinal Endoscopy*. We look forward to hearing from you soon.

Sincerely,

Mohit Rishi MD