Round-1

March 19, 2021

Lian-Sheng Ma
Section Editor
World Journal of Gastrointestinal Pharmacology and Therapeutics

Dear Editor:

We would like to thank you for your response and for giving us the opportunity to improve and resubmit the paper (63216) entitled "**Castor Oil as Booster for Colon Capsule Endoscopy Preparation Reduction: A Prospective Pilot Study and Patient Questionnaire**."

We are hereby resubmitting a revised manuscript conforming to all of the reviewers' comments. We have addressed all the reviewers' comments in a point-by-point manner, and revisions are indicated in red font in the revised paper. We hope that the revised manuscript is now suitable for publication in your journal.

Thank you for your consideration. I look forward to hearing from you.

Sincerely,
Yoriaki Komeda, MD, PhD
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Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (High priority)

Specific Comments to Authors: 1. It is a well carried out study. It showed that the castor oil-based regimen can reduce bowel preparation dose and improve CCE compliance. 2. Manuscript is well written. 3. It can change the pre procedure protocols of CCE.

Response: We would like to thank the reviewer for the positive evaluation of our work.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: With great interest I read the paper „Castor Oil as Booster for Colon Capsule Endoscopy Preparation Reduction: A Prospective Pilot Study and Patient Questionnaire“ by Takashima et al. In their study they investigated the impact of castor oil on capsule endoscopy. The work is clear, however there are some points which should be addressed by the authors:

Response: We thank the reviewer for his/her constructive critique to improve the manuscript. We have made every effort to address the issues raised and to respond to all comments. The revisions are indicated in red font in the revised manuscript. Below is a detailed, point-by-point response to the reviewer's comments.

MAJOR: - Despite being an interventional and prospective study, it lacks a control arm (of patients not receiving castor oil). With an appropriate control arm, this study would win much importance and impact! Would the authors be able to add (at least a historic) control?

Response: We thank the reviewer for evaluating our manuscript and for his/her comment. Please note that we have added the data of the historical control group in which the participants did not use castor oil and the following part to the revised manuscript (Page 7, Lines 22-27): “Nakaji et al showed that in their historical control group, in which patients did not receive castor oil (total liquid laxatives, 4.1 L; n=82), the capsule excretion rate (total large intestine observation) was 83% [20], the average colon transit time was 259 min, the bowel cleaning level (excellent/good) was 82% and the colorectal polyp detection rate was 49%. Interestingly, no adverse events were observed.”
Moreover, we have added reference number 20 to complement this text.

- Figure 1: representative images of the cleansing levels would be helpful to illustrate your gradings.

Response: We thank the reviewer for the comment. Please note that we have attached an image of the Aronchick bowel preparation scale as Figure 1.

- Table 4: The sensitivity and specificity (and probably also diagnostic accuracy) percentages for “detection of adenoma <5mm” seem to be wrong - or at least do not fit to the numbers presented in this table. - Please also check the respective passage in the methods (In fact, the sensitivity, specificity, and diagnostic accuracy in detecting adenoma ≤5 mm were 50.0%, 100.0%, and 88.2%, respectively).

Response: We thank the reviewer for the comment. We apologize for the description error. The sensitivity, specificity, and diagnostic accuracy rates for detecting adenomas ≤5 mm were 50.0%, 66.7%, and 55.6%, respectively (Table 4). Please note that we have corrected this in Table 4 of the revised manuscript.

MINOR: - Capsule transit time and diagnostic accuracy correlate indirectly. It might be interesting to test this in a subgroup of quick transit time vs. slow transit time in your cohort, but I acknowledge that the number of patients might be too low for significant results. However, it might be worthwhile discussing this point. –

Response: We thank the reviewer for the comment. In five cases that were found in the group with an early transit time of ≤60 min, the findings were consistent in 4/5 (80%) cases. In contrast, in four cases, which were found in the group with a slow transit time of ≥300 min, the findings were consistent in 3/4 (75%) of cases. However, we did not obtain any significant results because of the limited data.

"The diagnosis of colorectal disease obtained by CCE was verified by subsequent colonoscopy in our university hospital" - I think the inherent limitation, that capsule endoscopy cannot sample tissue should be mentioned in the discussion.

Response: We thank the reviewer for their comment. We agree with this comment. Please note that we have added a description of this limitation to the Discussion section as follows (Page 9, Lines 20-22): "Despite a relatively small number of cases and no sampling the tissue for capsule endoscopy as inherent limitation, we evaluated the diagnostic performance of colorectal polyps."

- Is the i.v. administration of metoclopramide 10mg after swallowing the capsule a standard in Japan or just performed at the Kindai Hospital? –

Response: We would like to thank the reviewer for their question. Please note that the administration of 10 mg of metoclopramide is included in the standard Japanese regimen. It is also included in the added historical control regimen.

-Figure 2: Pie charts are prone for biased interpretation. Box plots would be the recommended way of showing this data.

Response: We thank the reviewer for pointing out that the pie chart is prone to biased interpretation. We have added the box plots in Figure 3 accordingly.

Round-2

May 7, 2021

Lian-Sheng Ma

Section Editor

World Journal of Gastrointestinal Pharmacology and Therapeutics

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Thank you for your consideration.

I look forward to hearing from you.

Sincerely,

Yoriaki Komeda, MD, PhD

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Tel.: +81-72-366-0221 E-mail: y-komme@mvb.biglobe.ne.jp

Reviewer #1:

Specific Comments to Authors: Thank you for revising the manuscript. There are two minor points remaining: 1) The relatively poor detection rates of adenomas <5 mm should be highlighted in the discussion section as a potential limitation. 2) There are some formatting issues with the greater sign. Sometimes it is illustrated as ³6mm instead of >6 mm

Response: Thank you for important comments. we inserted the relatively poor detection rates of adenomas <5mm as a potential limitation in the discussion section. Also, thank you for your careful review. Accordingly, we have revised the formatting issues of ³6mm.