

July 6, 2020

Dear Drs. Ghosh and Tarnawski,

Thank you for reviewing our manuscript " **Pediatric Bowel Preparation: Sodium Picosulfate, Magnesium Oxide, Citric Acid vs Polyethylene Glycol- A Randomized Trial**" for publication in *World Journal of Gastroenterology* (manuscript ID 56995). We appreciate the feedback and have revised the manuscript accordingly.

Below please find our response to each review comment in blue. The revisions in the manuscript are highlighted with red text.

Please let me know if you have any further comments or questions. I look forward to receiving your decision.

Sincerely,

Carmen Cuffari, MD

Department of Pediatrics
The Johns Hopkins University School of Medicine
410-955-8769
ccuffari@jmhi.edu

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: This is a randomized clinical trial that adds to the growing literature on bowel preparation in children. The authors concluded that the efficacy and safety of SPMC bowel preparation were comparable to PEG due to a lower volume of bowel preparation to ingest. The overall presentation is logical, the data is well illustrated. I have the following minor comments:

Question 1: Please mention the P value for the comparison between the groups.

Thank you for taking the time to review our manuscript and for the comment. The objective of this study was to describe the efficacy, safety, and tolerability of SPMC bowel preparation in children, and therefore, the study was not designed or powered to

perform statistical comparisons between the SPMC and PEG groups. The PEG group was included as a reference only, and therefore, the primary efficacy results were descriptively presented using the 90% confidence intervals within groups.

Question 2: The authors mentioned different medical history of constipation rate between two groups. Does it influence the comparison result?

Thank you for your question. Upon reviewing the manuscript in light of your question, we realized there was an error in the data (numbers were swapped for the SPMC group). We have corrected the data in the manuscript to reflect the correct data 19% (9/48) baseline constipation. Of those patients with baseline constipation, 6/9 (66.7%) in the any SPMC group and 9/9 (100%) in the PEG group were responders. Of those patients without baseline constipation, responder rates were 29/39 (74.4%) and 16/21 (76.2%), respectively. Given the small sample size, it may be difficult to assess any effect but, overall, there doesn't appear to be a trend in responder rate with constipation history.

Question 3: Sleep disturbance partly depends on the time point of administration. But the time point of participants receiving PEG is not clarified.

Thank you for your comment. The PEG administration protocol was determined at each study site and was not prescribed by the study protocol. Data on PEG dosing regimen was available for 22/27 participants, all of whom used a day-before regimen; we have added this new text to the manuscript. However, the exact time of administration for the PEG protocol was not available in our study database, making it difficult to comment on the likelihood of sleep disturbance in each treatment arm.

Question 4: Question "How easy was it to drink the bowel cleanout regimen?" is quite subjective. Would it be better use objective items to evaluate ie. the times of discontinuing drinking?

Thank you for your comment. The tolerability questions were pre-specified in the protocol and were adapted from the standard Mayo Clinic Bowel Preparation Questionnaire. In future studies, it would be important to expand the tolerability measures to include objective measures and we will keep this point in mind when designing study protocols.

Question 5: Achieving compliance with administration in children remains challenging. Children usually need parents' instructions when take medications. Will the educational level of caregivers influence the efficacy of bowl preparation?

Thank you for your comment. We agree that children, especially in the 9-12 yr age range, would need some assistance from caregivers on how and when to take

medications, including bowel preparation agents. Some literature shows that health literacy, which could be related to educational level, is a predictor of poor quality bowel preparation in adults (Nguyen DL, Wieland M. *J Gastrointest Liver Dis.* 2010;19(4):369-372.) This study did not document the educational level of the caregiver so, unfortunately, we cannot report on any link between caregiver education and bowel cleansing efficacy.

Step 6: Editorial Office's comments

The author must revise the manuscript according to the Editorial Office's comments and suggestions, which listed below:

(1) Science Editor: 1 Scientific quality: This is a clinical trials study of the pediatric bowel preparation. The topic is within the scope of the WJG. (1) Classification: Grade B; (2) Summary of the Peer-Review Report: This is a randomized clinical trial that adds to the growing literature on bowel preparation in children. The overall presentation is logical, the data is well illustrated. The authors need to mention the P value for the comparison between the groups and different medical history of constipation rate between two groups. The time point of participants receiving PEG is not clarified. The authors should use objective items to evaluate the bowel cleanout regimen and discuss the influence of educational level to the efficacy of bowel preparation. The questions raised by the reviewers should be answered;

Thank you for your comment. We have made a point-by-point response to the reviewer's comments and added new information to the manuscript where possible.

and (3) Format: There are 2 tables and 3 figures. A total of 19 references are cited, including 3 references published in the last 3 years. There are no self-citations. 2 Language evaluation: Classification: Grade A. 3 Academic norms and rules: The authors provided the Biostatistics Review Certificate, the Conflict-of-Interest Disclosure Form, the Institutional Review Board Approval Form, the Informed Consent Form, Clinical Trial Registration Statement and the CONSORT 2010 Statement. The authors need to provide the Copyright License Agreement signed by all authors.

We have uploaded the agreement with the revision.

No academic misconduct was found in the CrossCheck detection and Bing search. 4 Supplementary comments: This is an unsolicited manuscript. The study was supported by Ferring Pharmaceuticals Inc. The topic has not previously been published in the WJG. The corresponding author has not published articles in the BPG. 5 Issues raised: (1) I found the authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s);

The funding for the study was internal, there were no grants given/received to conduct the study.

(2) I found the authors did not provide the original figures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;

We have uploaded original figure files with the revision.

(3) I found the authors did not add the PMID and DOI in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout;

We have added PMID and DOI numbers throughout the reference list.

(4) I found the authors did not write the “article highlight” section. Please write the “article highlights” section at the end of the main text; and

We have added the Article Highlights section in the revised manuscript.

(5) the author should number the references in Arabic numerals according to the citation order in the text. The reference numbers will be superscripted in square brackets at the end of the sentence with the citation content or after the cited author’s name, with no spaces.

We have reformatted the in-text citations as requested.

6 Re-Review: Required. 7 Recommendation: Conditionally accepted. (Man Liu)