

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 65913

Title: Novel frontiers of agents for bowel cleansing for colonoscopy

Reviewer's code: 05083825

Position: Peer Reviewer

Academic degree:

Professional title:

Reviewer's Country/Territory: Portugal

Author's Country/Territory: Italy

Manuscript submission date:2021-03-17

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-03-19 18:22

Reviewer performed review:2021-03-24 20:10

Review time:5 Days and 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent[<input checked="" type="checkbox"/> Y] Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	[<input checked="" type="checkbox"/> Y] Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	[<input checked="" type="checkbox"/> Y] Accept (High priority) <input type="checkbox"/> Accept(General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes [<input checked="" type="checkbox"/> Y] No
Peer-reviewer statements	Peer-Review:[<input checked="" type="checkbox"/> Y]Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes[<input checked="" type="checkbox"/> Y] No

SPECIFIC COMMENTS TO AUTHORS

I read with great interest the manuscript presented, addressing the extremely important thematic of bowel cleansing in colonoscopy, and reviewing the most controversial topics. I would like to congratulate the authors, this revision paper is very well executed and organized, clearly written and easy to understand and up-to-date, approaching essential clinical issues and displaying the solutions the scientific evidence has to offer. I merely have a few questions regarding the topic:

1) Was this a systematic revision? Was there any methodology in the selection of the papers to include?

This manuscript is not a systematic revision. We tried to include the most important and /or the most recent papers regarding the topics. We stated in the introduction that the paper is a review aimed to describe current literature.

2) The manuscript addresses the bowel preparation for colonoscopy. If in a conventional colonoscopy washing and sucking are possible and advisable to improve an adequate bowel cleansing (BBPS is considered after this interventions), for colon capsule an initial optimal bowel cleansing is paramount. Did the authors find dome information regarding this topic?

We thank the reviewer for this interesting comment. However, the aim of our manuscript was to focus on bowel cleansing only for colonoscopy, therefore we did not explore bowel cleansing in colon capsule endoscopy.

3) Specifically addressing bubbles scale, did the authors find clinical benefit in addressing bubbles subs-cores separately from the overall classifications, wouldn't it only bring complexity to the final cleansing classification?

An accurate description of bowel preparation quality considering liquid/stool and bubble has a paramount importance if the procedure needs to be repeated. In case of inadequate bowel

preparation due to bubbles, oral simethicone could be considered, while in case of inadequate bowel preparation due to stool, an alternative agent cleaning should be considered.

Is really through the scope simethicone so unsafe to endoscope working channels?

ESGE guideline advised against the use of simethicone due to evidence it may contribute to biofilm formation in the endoscope channel. In clinical practice, we use small amount of simethicone if needed, and after that we immediately wash with water the endoscope working channel.

4) Several risk factors are described to predict inadequate bowel cleansing. An anecdotal experience leads me to think that, inflammatory bowel disease patients present overall higher rates of inadequate bowel cleansings. Did the authors find some information regarding this topic?

In our experience, we have the same feeling. However, we did not found any data to support the hypothesis that rate of inadequate bowel preparation is increased in patients with inflammatory bowel disease (IBD). On contrary, in the meta-analysis of Mahmood S et al. (Predictors of inadequate bowel preparation for colonoscopy: a systematic review and meta-analysis. European Journal of Gastroenterology & Hepatology. 2018. doi: 10.1097/MEG.0000000000001175), IBD is one of the factors which did not significantly affect the quality of bowel preparation.

5) Regarding the subset of patients with low gastrointestinal bleeding, recent evidence points out against the benefit for early colonoscopy (<24h). Would this imply any alteration in cleansing protocols?

We thank the reviewer for pointing out this interesting aspect. Considering that, even in case of lower bleeding, an immediate colonoscopy does not have any benefit, as standard cleansing protocol in order to plan the exam as soon as possible is advised. Therefore, the cleansing protocols

did not changed. We added the latest guideline in the manuscript.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 65913

Title: Novel frontiers of agents for bowel cleansing for colonoscopy

Reviewer's code:03725492

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Assistant Professor, Attending Doctor

Reviewer's Country/Territory: South Korea

Author's Country/Territory: Italy

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Reviewer accepted review: 2021-03-18 01:21

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Review time:10 Days and 11 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This review article includes a lot of information regarding bowel cleansing. Although there is no limitation of review article there are a lot of page in this article, which might interfere with understanding the manuscript.

The abbreviations should be totally edited, especially CRC, ADR.

We explained all the abbreviations when they were used to the first time in the manuscript.

Page 10 Cleansing agents for bowel preparation

These isosmotic solutions provide rates of adequate bowel preparation >70% -> Recently published articles reported that bowel cleansing efficacy of PEG based solution > 90% (Dis Colon Rectum. 2019 Dec;62(12):1518-1527, Am J Gastroenterol 2020;115:2068–2076) Although some studies reported unfavorable bowel cleansing efficacy than the guidelines, bowel cleansing efficacy was over 85-90% in most studies. I recommend you to edit this point.

Thanks for the correction. We modified accordingly.

Diet before colonoscopy (page 13-17)

This topic is too long. I recommend you to shorten this topic up to 2 pages. Furthermore, I recommend you to suggest strategy regarding diet plan at the end of this topic.

We shortened the paragraph underlining the results of meta-analysis. Moreover, we added a table describing the foods that should be avoided and ones allowed the day before the procedure.

Simethicone (page 18)

The last meta-analysis by Moolla et al. [27] aimed to determine the effect that simethicone has on bowel cleanliness, ADR and tolerability, and included 16 RCT (5630 patients) using PEG for bowel agent cleaning. Authors found an increase rate of adequate bowel preparation in PEG cohort considering all 16 RCT (OR 1.48)

-> It seems that this part does not contain the effect of simethicone.

We corrected the mistake.

Chronic kidney disease and hemodialysis (Page 25)

Only the British consensus guidelines suggest the administration of PEG -based solutions or sodium picosulphate plus magnesium salts in this setting, although the statement is graded as weak recommendation based on very low quality evidence. -> British guideline the same reference you suggested recommend the use of picosulfate cautiously in patients with CKD or hemodialysis as below. I recommend you to revise this part. Picosulfate is rarely used in CKD or hemodialysis patients. Sodium picosulphate preparations should be used with caution in patients at risk of, or suffering from, hypovolaemia, including those patients taking high-dose diuretics, those with congestive cardiac failure and advanced cirrhosis, and those with chronic kidney disease (evidence: grade 1C).

Thank you for pointing put this inconsistency. We deleted the sentence that could be misleading.

Inpatients (page 27-28)

The multicenter observational study of Fuccio L. et al. [1 52] identified the factors associated with a more proper colon cleansing (Physicians' meetings to optimize bowel preparation, written and oral instructions to patients, admission to gastroenterology unit, split-dose regimens, a 1-liter polyethylene glycol-based bowel purge, and 75% or more intake of bowel preparation) and to increase risk of inadequate bowel preparation -> I cannot understanding what you meant. The last part (and to increase ~~~) looks useless. Other factors significantly reduced odds of inadequate colon cleansing (bedridden status, constipation, diabetes mellitus, use of anti-psychotic drugs, and 7 or more

days of hospitalization -> The factors can increase odds of inadequate colon cleansing ???

We corrected the mistakes.

Patients with constipation (Page 30 – 34)

This topic should be shortened. Some part of this topic looks wrong. I recommend you to totally revise this topic.

We agree with this comment. We shortened this part and totally revised its content

Bowel preparation and post-colonoscopy syndrome.

You should suggest the reference of post colonoscopy syndrome. Mild abdominal pain is most common minor complication after colonoscopy. I think you overestimate abdominal pain after colonoscopy.

Post-colonoscopy syndrome is an umbrella term that we herein used to define persistent pain or bloating after colonoscopy, therefore a single literature reference is not available in this case. To describe the incidence of such condition, we referred to the paper by Ko et al (ref. 168). We agree with the referee that such symptoms are quite common after a colonoscopy, therefore the term "syndrome" may be misleading, but it is the only one may summarize this condition. Therefore, in the revised manuscript, we precised that persistent symptoms are usually mild and self limiting.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 65913

Title:Novel frontiers of agents for bowel cleansing for colonoscopy

Reviewer's code:03475142

Position:Peer Reviewer

Academic degree:MD, PhD

Professional title:Assistant Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory:Italy

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Verygood[<input checked="" type="checkbox"/>] Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing[<input checked="" type="checkbox"/>] Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept(General priority) [<input checked="" type="checkbox"/>]Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	[<input checked="" type="checkbox"/>] Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review:[<input checked="" type="checkbox"/>]Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes[<input checked="" type="checkbox"/>] No

SPECIFIC COMMENTS TO AUTHORS

The manuscript was reviewed for publication in the journal. The review manuscript was designed to summarize the current strategy to increase bowel cleansing before colonoscopy. It is the reviewer's opinion that the review is quite interesting and that the manuscript is easy to follow for the readers. However, it appears that there are a couple of concerns in the manuscript.

1) There are several review papers regarding bowel cleansing (Gastroenterol Hepatol. 2019;42:326-338, Gastroenterol Res Pract. 2019;5147208, Curr Treat Options Gastroenterol. 2018;16:165-181, etc). Authors should explain/discuss what are new in this review compared to previous similar reviews.

We updated the bibliography to 2021 and we tried to extensive explain all parts of bowel preparations and all special categories of patients. We added a sentence in Introduction to discuss why we wrote this paper.

2) This review does not include any table or figure. In order to enhance the readers' understanding of this review, authors should add the table or figure.

We added one table to explain low fiber diet. We hope that this correction may make the paper more appealing for the readers.

3) To show the literatures in the manuscript, authors should fix the format (space before [brackets]). There were no spaces before brackets in many places. Also, authors should rearrange the literature in a new order. For example, Page 9, line 15-16, [30] was shown before [29]. Page 10, line 3-4, [38] was shown before [37]. Page21, line 9-11, [122] was shown before [121].

We corrected the format of bibliography. Instead, the order was correct, because the references were previously cited.

4) Authors should use abbreviations after explaining. For example, page 11, line 9: adenoma detection rates.

We explained all the abbreviations when they were used to the first time.

5) Grammar corrections: Page 4, line 5: aimed to summarized may be summarize Page 7, line 25: BBPS > 5, higher no space before higher Page 8, line 3: a correlation with PDR What is PDR? Page 35, line 23: overall, Authors authors

We corrected all the grammar mistakes that have been reported.