

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 65913

Title: Novel frontiers of agents for bowel cleansing for colonoscopy

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05083825

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

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"/> 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 Grade E: Do not publish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"/> 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"/> 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"/> No
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous

statements

Conflicts-of-Interest: [] Yes [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 uptodate, 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? 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? 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? Is really through the scope simethicone so unsafe to endoscope working channels? 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? 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?

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Peer-review model: Single blind

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

Manuscript submission date: 2021-03-17

Reviewer chosen by: AI Technique

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

Reviewer performed review: 2021-03-28 12:41

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
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Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous

statements

Conflicts-of-Interest: [] Yes [Y] 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. 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. 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. 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. 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). Inpatients (page 27-28) The multicenter observational study of Fuccio L. et al. [152] 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 ??? 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. 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.

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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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Reviewer chosen by: AI Technique

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Review time: 16 Days and 9 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <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	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous

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.
- 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.
- 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]. Page 21, line 9-11, [122] was shown before [121].
- 4) Authors should use abbreviations after explaining. For example, page 11, line 9: adenoma detection rates.
- 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

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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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

Manuscript submission date: 2021-03-17

Reviewer chosen by: Man Liu

Reviewer accepted review: 2021-04-27 12:44

Reviewer performed review: 2021-05-13 03:10

Review time: 15 Days and 14 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> 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"/> 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 checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
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



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SPECIFIC COMMENTS TO AUTHORS

This article still contains a lot of pages which should be cut. There are a lot of errors for abbreviations which should be totally checked. ASGE and ESGE guidelines were frequently referred. You used European guideline and ESGE guideline. You used ASGE, American, and US guideline for ASGE guideline. I recommend you to unify the term. Abbreviation 1. The abbreviations should be totally edited, especially 4L PEG, 4l PEG 4-liter PEG. 2. Do you want to use BP (bowel preparation) ? BP and Bowel preparation were simultaneously used. Page 16 Table 1 was not introduced in the manuscript. Page 22 Although colonoscopy has several ~ but serious complications. [111] □ This paragraph does not need in this manuscript. I recommend you to delete this paragraph. Page 27 Inpatient I recommend you to delete the paragraph of inpatient. It does not give us additional information. There are some factors for poor bowel preparation such as diabetes and inpatients. You don't have to review all subgroup. Patients who are high risk for poor bowel preparation, some standard manner such as split dose, diet restriction, and high volume PEG might be sufficient. Page 30-31 Although constipation is important factor for bowel preparation, the section of Patients with constipation was poorly written. The contents were mixed up. You should totally revise them. Sodium phosphate is not recommended for purgative anymore. The contents regarding sodium phosphate should be deleted. Bowel preparation and post-colonoscopy syndrome The relationship of post-colonoscopy syndrome and microbiota change should be suggested cautiously. I don't think post-colonoscopy syndrome is related to microbiota change. Rather, post colonoscopy syndrome is more related to mechanical effect during 'colonoscopy' This paragraph should be shortened and revised.