

Department of Gastroenterology
Shengjing Hospital of China Medical University
No.36. Sanhao Street, Heping District
110004 Shenyang,
People's Republic of China
Tel:024-96615-27111
Fax: 024-96615-27112
Email: sanglixuan2008@163.com
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Dear Jin-Lei Wang:

We would like to thank the editor and the reviewers for their conscientious reviews, insightful comments and suggestions to improve our manuscript entitled "**Fecal microbiota transplantation as potential first-line treatment for patients with *Clostridioides difficile* infection and prior appendectomy.**" (Manuscript NO.81628, Letter to the Editor). All the comments are valued, professional and helpful for revising and improving our paper, as well as the important guiding significance to our researches. In the response below, we have addressed all the concerns raised by the editor and the reviewers. We hope our paper could achieve the academic standards of your magazine and be published finally. Thank you very much.

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: The authors have picked a relevant topic and discussed FMT in case of CDI. A brief summary of this novel treatment option is provided in a concise way. 1. The authors have mentioned about probiotics. It will be interesting to elaborate on which bacteria have been found to be most beneficial. 2. Any geographical differences observed on the outcome of treatment. 3. Long term benefits of therapy / they can discuss some long term follow up studies.

Response: Thank you very much for your careful reading of the manuscript, and thank you for your valuable comments for our manuscript. According to the comments, we carefully read relevant literature and processed the content of the article based on the experience of FMT application in our department. We hope to be able to meet the

requirements for publication, if you are not satisfied with the revised manuscript, we will make a second revision.

Question 1: The authors have mentioned about probiotics. It will be interesting to elaborate on which bacteria have been found to be most beneficial.

Response: We gratefully appreciate for your valuable suggestion and we add some probiotic strains with potential protective effects on CDI in this paper. We will continue to follow potential probiotics on CDI with interest and write high-quality articles.

Question 2: Any geographical differences observed on the outcome of treatment

Response: Thank you for your valuable comments for our manuscript. Based on literature review, we find that there are significant geographical differences in the intestinal microbial composition of the population, and the researches on FMT are also unevenly distributed in various regions of the world. But there was still no report indicating that there were significant geographical differences observed on the outcome of treatment.

Question3: Long term benefits of therapy / they can discuss some long term follow up studies.

Response: We appreciate your valuable suggestion. We carefully read relevant literature and we add the discussion of the related long-term follow-up researches in the last paragraph of this paper.

Reviewer #3:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: The authors provide the letter to the editor to the paper that has been published in 2021. Title needs revision as it does not reflect the message of the letter to the editor: FMT as potential first-line treatment for patients with The authors should apply the newest nomenclature: *Clostridioides difficile*. This needs to be written in cursive. The authors state that the cited work studied “the impact” of appendectomy, however, this is not correct as the authors in the cited work evaluated an association between appendectomy and severity of CDI infection. The authors state that there is limited evidence for the better outcome after FMT with a reference 7. This is only partially true while some groups have indeed shown substantial improvement of outcome (randomized trials and particularly this work Cammarota et al. Ann Intern Med 2015). Final message/sentence of the letter is kind of too broad and with a borderline message.

Response: Thank you very much for your careful reading of the manuscript and thank you for your valuable comments for our manuscript. According to your comments, we made a point-to-point response, we hope to be able to meet the requirements for publication, if you are not satisfied with the revised manuscript, we will make a second

revision.

Question 1: The authors provide the letter to the editor to the paper that has been published in 2021. Title needs revision as it does not reflect the message of the letter to the editor: FMT as potential first-line treatment for patients with

Response: We gratefully thanks for your careful reading and change our title into Fecal microbiota transplantation as potential first-line treatment for patients with *Clostridioides difficile* infection and prior appendectomy.

Question 2: The authors should apply the newest nomenclature: *Clostridioides difficile*. This needs to be written in cursive.

Response: Thank you very much for pointing out the problems. We have revised the article and made the changes accordingly.

Question 3: The authors state that the cited work studied “the impact” of appendectomy, however, this is not correct as the authors in the cited work evaluated an association between appendectomy and severity of CDI infection.

Response: Thank you very much for your careful reading of the manuscript. “Impact” surely cannot express the original intention of the cited well and we change the word into “association” to express the original intention of the author.

Question 4: The authors state that there is limited evidence for the better outcome after FMT with a reference 7. This is only partially true while some groups have indeed shown substantial improvement of outcome (randomized trials and particularly this work Cammarota et al. Ann Intern Med 2015).

Response: Thank you for your careful reading and we apologize for our incomplete literature search. We realized that different studies have made substantial progress after a more comprehensive literature review. We improved the expression of our manuscript.

Question 5: Final message/sentence of the letter is kind of too broad and with a borderline message.

Response: Thank you very much for pointing out this problem and we change the sentence into “For patients who have undergone prior appendectomy, preventive improvement of intestinal flora is the key to avoid worse outcomes.”

The Editorial Office’s comments and suggestions are listed below:

(1) Science editor:

The manuscript has been peer-reviewed, and it's ready for the first decision. Language

Quality: Grade B (Minor language polishing)

Scientific Quality: Grade C (Good)

Response: Thank you for your affirmation of our manuscript. In the future, we will continue to study and write other articles that meet the requirements of your magazine. Thanks again.

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Gastrointestinal Surgery, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the RCA.

Response: Thank you for your valuable advice. We have revised and submitted the article in accordance with the comments of the reviewers and the requirements of the magazine. I hope it can reach the publication level of your magazine. Thank you again.