

35260 Response to the reviewers

To reviewer code 03656594

Reviewers comment:

The case description in the article is very detailed, the analysis is also very thorough. The article has a good clinical significance. Suggested publication.

Response by the author:

Thank you for your comments and accepting our article.

To reviewer code 00159305

Reviewers comment:

In the group of 8 patients with conditions other than rCDI, FMT treatment was “experimental”. Please, make it clear in Methods section that you had the approval for such therapy. For the reader is not clear if FIMEA approved FMT therapy in such patients. 2. Please, mention the strength and limitations of your study in the Discussion section. 3. In the Conclusion, indications for FMT in patients not having rCDI should be drawn more precisely, based on your study

Response by the author:

Thank you of good and constructive comments, here is how we modified the text:

1. The Finnish drug authority Fimea stated that stool is not a drug and therefore they did not find a reason to regulate FMT studies regardless of the indication. According to Fimea their approval is not needed for FMT studies. To make this more clear for the reader, we added the following sentence: **“In Finland FMT studies do not require approval of the drug authority Fimea.”**
2. The strengths and limitations are mentioned in the Discussion. To make this more evident, we added the following **bolded** text: **“The 21 patients reviewed were a heterogenous group with many comorbidities. This sets a limitation to our study; profound conclusions cannot be drawn of the patients as a group. The strength of our study is that we review real life patients, who are often excluded from studies due to their comorbidities.”**
3. To clarify the indications of FMT, we added the following: **“FMT is only indicated for rCDI; for other indications, FMT should still be performed only in a clinical trial setting. “**

To reviewer code 03317125

Reviewers comment:

This article gives a clear description of 21 cases and reasonable discussion, and I believe it can provide a good reference in the daily performance of FMT. But I still have some small advices: 1. The front part is about FMT treatments of patients with different co-morbidities, mainly focus on the immunocompromised patients, but there is no selection criteria or exclusion criteria mentioned, it's better to add. 2. Sufficient samples are crucial to drawing a statistically convincing conclusion. The sample with only 13 patients may be not enough to confirm the safety in FMT treatment for patients with significant co-morbidities. 3. There are some confusing and irrelevant statements in the article, such as the problem of "DIY FMT" doesn't seem to have much relation with the cases, it could be modified (or removed). 4. The language use of the article should be more careful, Page 18 Line 6 "effecs" should revise to "effects".

Response by the author:

Thank you of good and constructive comments, here is how we modified the text:

1. To clarify our patient selection, we added the following **"We included dialysis patients and patients with known immune deficiencies in the rCDI group; HIV, organ transplant or hematologic disease. "**
2. To address the impact of the sample size, we added the following bolded parts " In conclusion, **in our cohort**, FMT appeared to be a safe and effective treatment for rCDI for patients with significant comorbidities, **although further conclusions cannot be drawn due to the small sample size.**"
3. We removed the following as irrelevant " According to internet chat sites, risky DIY FMT's are currently being done for various conditions. To prevent this kind of self-medication from expanding, the health professionals should provide objective information on FMT. Hence,"
4. Revised to "...suggested by the positive effects of metronidazole followed..."

Other:

1. The text was edited according to the instructions by the editor. A throughout language editing was made by an official language editing office who also provided us with a language certificate.
2. The author list was revised since we unfortunately had forgotten an important contributor from the list. Professor Seppo Salminen was added to the list of authors since he significantly contributed in planning the treatment of some of the patients.

On behalf of all the authors,

Perttu Lahtinen
the 18th August