

Reviewer's code: 00503587

Specific Comments:

1. The Methods of the Abstract contains information that would typically be found in the Results section, suggest to move this.

Answer: Thank you very much for the comment. The results from Methods have been now moved to the Results section in the abstract. Please see the abstract.

2. It would've been more helpful if all patients were in remission, with objective info to confirm this. One would not expect a reduction in inflammatory scores.

Answer. Agree with this important comment - it can confuse the picture with the different disease status. Most of the patients from this study were in remission 65 (83%) and only a small sample size 13 (17%) had mild-to-moderate disease activity (minus bloody stools). The results of IBS-SSS in different subgroups, including disease activity in this study have been performed, confirming efficacy of the LFD in patients with remission. Furthermore, inflammatory markers (CRP and FC) measured in this study are reassuring that majority of patients were in remission. Please see results chapter.

3. In the Introduction, there is only one irritable bowel syndrome (not many).

Answer: It has been corrected in the text.

4. The point in the first [paragraph of the Intro is that patients with IBD may have only symptoms (similar to those seen in IBS alone) that reflect coincident IBS in these patients. This text could be more clear.

Answer. The suggested text has been clarified.

5. The authors refer to two studies (17 and 18) prior to establishing the aim of their work. It could be more clearly stated why this study adds to the other two reports.

Answer. There has so far only been published two articles regarding the low FODMAP diet and IBD. One retrospective study from 2009 and one prospectively 2016. Diet low in FODMAPs has shown to be effective in reducing symptoms in patients with irritable bowel syndrome (IBS). Furthermore, the low FODMAP diet has also been shown to be beneficial for patients suffering from inflammatory bowel disease (IBD) in one retrospective and one prospective study, however, no randomized controlled trial (RCT) has ever substantiated the beneficial effect of the diet for IBD. Our study supports their results. Please see introduction, references 18 and 19, page 6.

6. The first part of the RESULTS does not have a subheading.

Answer. The subheading of the first part of the Results has been added. Please see manuscript Results "Patient flow and baseline characteristics".

7. The authors note in the discussion that the LFD did not lead to any increase in objective inflammatory markers. They should also state that the dietary intervention did not improve inflammation either.

Answer: The suggested have now been added to the manuscript, introduction, page 16.

8. The Table headings could be enhanced to be more clear. Table 4 for example is incomplete and vague.

Answer: The table headings have been enhanced.

9. There are many figures and tables. some showing negative data could be excluded and/or made as supplementary figures. Do all need to be included?

Answer: Figure 4 and Table 4 have now been removed as supplemental material. Figure 5 has also been excluded due to negative data that are well demonstrated in table 2.

Reviewer's code: 00068090

The author showed in their study that Low-FODMAP Diet Reduces Irritable Bowel Symptoms in Patients with Inflammatory Bowel Disease in remission while the question of the efficacious role of LFD in patients with mild-to-moderate-activity remains inconclusive,

MAJOR COMMENTS: 1) The authors should have shown the possible changes in inflammatory cytokines, microbiota profile, and SCFAs, which may have consequences for gut health with the low FODMAP diet.

Answer: Your comment is very relevant! Halmos et al 2015 in GUT showed the relevance of measuring microbiota and SCFA in IBS patients which actually led to the recommendation of only using the diet until symptom control because the Low FODMAP diet increased the dysbiosis. Furthermore, at an oral presentation at UEGW in Vienna 2016: LOW FODMAP DIET ALTERS SYMPTOMS, MICROBIOTA, SHORT-CHAIN FATTY ACIDS AND CYTOKINE PROFILES IN PATIENTS WITH IBS: A RANDOMIZED CONTROLLED TRIAL also showed that patients became more dysbiotic during the low FODMAP diet, however pro-inflammatory Il6 and Il8 seemed to decrease during the low FODMAP diet. In order to evaluate the diet for IBD with IBS like symptoms further studies are indeed need in order evaluate the microbiome and



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metabolites but also nutritional adequacy as you pointed out in your last comment (4). Due to economic restrictions, we have chosen only to measure inflammatory marker CRP and FC. We have added the word metabolites in the discussion section.

2) The authors should consider the patient's adherent to the diet. High adherence was associated with longer duration of dietary treatment. It is important to consider if the majority of patients were satisfied with the dietary treatment and did not quit the dietary course before planned. The probability of patients discontinuing dietary management increases with duration of dietary course, as motivation tends to dwindle.

Answer: In this RCT adherence to the diet have been evaluated by a self-constructed food frequency questionnaire (FFQ) at baseline and at week 6. Patients' FFQ was used to calculate the total quantity of FODMAP (g/day) intake for each patient. FODMAPs (g/day) were significantly reduced in the low FODMAP group, indicating that the majority of the patients were adherent to the diet. However, being adherent is different from being satisfied with the diet. A follow up study evaluating effect and the satisfactory of the Low FODMAP diet was published in WJG in 2016, Maagaard et al, however, only 49 of the 89 IBD patients participating in this study replied. Only 11 percent did not have any effect of the diet and the majority was satisfied.

3) While beneficial for symptom reduction, there is evidence suggesting that a low FODMAP diet also has negative effects on microbiota. This was first suggested in a trial where a dietitian-taught low FODMAP diet reduced relative abundance of fecal Bifidobacteria spp in IBS subjects. For this reason, evaluation of gut microbiome composition and, perhaps more importantly the microbiome's metabolic byproducts, may help further elucidate the mechanism of the low FODMAP diet and its potential biological implications.



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Answer: We do agree, that the microbiome and metabolites are essential, and should be recommended to be included in future studies for evaluation the diet- see also answer to your first comment (1).

4) Other indications for this more gentle restriction include patients at risk of nutritional inadequacy or who have other dietary restrictions, which may again encompass the IBD population. Because of the complex and individual nature of an FODMAP restriction, implementation should be done in guidance with a dietitian well versed in IBD. In addition to appropriate FODMAP manipulation, a dietitian will assess and closely monitor nutritional adequacy with dietary restriction and manage as appropriate, including patients in whom nutrient absorption is impaired or dietary intake is altered.

Answer: A dietician is very essential both for the success of implementing the diet and therefore also the effect one might expect to receive from it. The dietician individualizes the diet and finds matchable food substitutions and will insure relative nutritional adequacy during the diet. We have therefore added to the conclusion 'with guidance from a dietician'.