

10th November

World Journal of Gastroenterology

Re: Response to Letter to the Editor Reviewers Comments

"Role of exercise in preventing and restoring gut dysbiosis in patients with inflammatory bowel disease: A letter to the editor"

Dear Reviewers,

We thank you for your time and comments on our Letter to the Editor, Manuscript NO: 71582. Please see our response to your comments below.

Yours sincerely,

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Reviewer#1 comments:

1. However, there is one question that needs to be answered. The authors suggest that an exercise programme of at least 12 weeks is required to restore intestinal ecological dysregulation and mention that "the positive effects of a more prolonged programme may extend to inflammatory mediation through regulation of immunometabolism" in the manuscript.

Response: We refer to the duration of the programme over time rather than short bursts of multiple sessions over a limited period of time whereby positive changes revert back to normal when exercise patterns aren't sustained.

From the review article presented, positive alterations in the microbiome were not seen in studies of short duration and therefore, we suggest that exercise programmes of longer duration may be required to restore intestinal ecological dysregulation. Two studies presented in the review demonstrated changes in the gut microbiome composition, diversity and functionality and both were of 12 week duration, however did not involve IBD patients [1, 2]. Therefore, we acknowledge that further studies of longer duration (at least 12 weeks or more) are required to demonstrate changes in the gut microbiome in IBD patients.

2. What is the exact definition of prolonged exercise suggested by the authors, given that one paper suggests that excessive exercise is harmful to health [Complementary and Alternative Medicines Used by Patients With Inflammatory Bowel Diseases]?

- Our comment relates to sustaining the physical activity at the recommended level over a longer period of time i.e. at least 12 weeks duration and not to promote excessive harmful exercise activities.
- We suggest that excessive exercise that is harmful is related to type and intensity and not to the cumulative time of the programme that will lead to the adaptation of healthy exercise behaviours.
- A range of exercise activities including moderate aerobic exercise, resistance training and high intensity interval training have previously been shown to be safe in IBD patients [3-5].
- The recommended physical activity for individuals aged 18-65 years is moderate-intensity aerobic exercise for a minimum of 30 minutes 5 days each week [6-8].

3. Does this contradict the above literature?

As described above, we recommend adhering to the recommended physical activity guidelines and exercise programmes that have previously been shown to be safe in IBD patients, however, we advise that programmes in future studies are designed

to continue over a longer period of time- 12 weeks at minimum, to promote disease-altering changes in the microbiome and sustained physical activity behaviours.

1. Quiroga, R., et al., *Exercise training modulates the gut microbiota profile and impairs inflammatory signaling pathways in obese children*. Exp Mol Med, 2020. **52**(7): p. 1048-1061.
2. Morita, E., et al., *Aerobic Exercise Training with Brisk Walking Increases Intestinal Bacteroides in Healthy Elderly Women*. Nutrients, 2019. **11**(4).
3. Cronin, O., et al., *Moderate-intensity aerobic and resistance exercise is safe and favorably influences body composition in patients with quiescent Inflammatory Bowel Disease: a randomized controlled cross-over trial*. BMC Gastroenterol, 2019. **19**(1): p. 29.
4. Klare, P., et al., *The impact of a ten-week physical exercise program on health-related quality of life in patients with inflammatory bowel disease: a prospective randomized controlled trial*. Digestion, 2015. **91**(3): p. 239-47.
5. Jones, P.D., et al., *Exercise decreases risk of future active disease in patients with inflammatory bowel disease in remission*. Inflamm Bowel Dis, 2015. **21**(5): p. 1063-71.
6. Haskell, W.L., et al., *Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association*. Med Sci Sports Exerc, 2007. **39**(8): p. 1423-34.
7. Ball, E., *Exercise guidelines for patients with inflammatory bowel disease*. Gastroenterol Nurs, 1998. **21**(3): p. 108-11.
8. Bull, F.C., et al., *World Health Organization 2020 guidelines on physical activity and sedentary behaviour*. Br J Sports Med, 2020. **54**(24): p. 1451-1462.

Reviewer#2 comments:

I think this will be a good addition to the review.

Thanks for your comments.