

Re: Manuscript ID: 37096

Dear Editor-in-Chief:

Please find enclosed our re-revised paper entitled “*Enteral nutrition combined with glutamine promotes recovery after ileal pouch-anal anastomosis in rats*”. We greatly appreciate the opportunity to improve our article, and have revised the text based on the reviewers’ comments and suggestions. We have provided a Word file of the revised manuscript with the relevant changes indicated in red font, and a file containing publication-quality figures. We thank the reviewers for their constructive comments, and hope that our revisions have resulted in a manuscript that is now satisfactory for publication in *World Journal of Gastroenterology*.

Please find our point-by-point replies to the reviewers’ comments below.

Answers to Reviewer #1’s comments:

Xu et al present their interesting and relevant findings on the efficacy of enteral nutrition and glutamine in improving nutritional status after an ileal pouch-anal anastomosis procedure in male Sprague-Dawley rats.

Question 1: The title notes that enteral nutrition and glutamine “promotes recovery FROM ileal pouch-anal anastomosis”. It probably meant "recovery AFTER ileal pouch-anal anastomosis".

Answer: We thank the reviewer for pointing this out and have amended the title accordingly.

Question 2: Please provide some quantitative results in the Abstract. The Abstract should specify the “Histopathological score” used. The Abstract would benefit from some information about the weight changes across the 3 treatment arms. Using total protein, albumin, prealbumin, and transferrin as surrogate markers of nutritional status is considered inaccurate by nutrition experts. The changes in weight are more convincing markers of the nutritional benefits of EN and IN, although the current presentation is fine as is. The clinical significance of the laboratory differences (TP, ALB, PA, TF) is unclear.

Answer: We apologize for our lack of clarity. We have added some quantitative results, including information on the histopathological score and body weight changes, in the revised Abstract, in addition to the results for the serum protein indicators of nutritional status. We recognize the importance of weight change in terms of nutrition, and we have therefore also reported on this in the Methods and Results sections. We believe that the combination of changes in serum protein levels and body weight make our results more convincing.

Question 3: Are there any data from other studies to demonstrate that the small variations in these measures confer any clinically meaningful changes in outcomes? If not, then it may be premature to state that glutamine supplementation should necessarily be done for UC patients undergoing an IPAA. So, instead of saying that the “results provide experimental evidence to support glutamine supplementation”, it may be better to say that it “suggests a benefit of glutamine supplementation” (or something similar). It is also too strong to say that “EN combined with glutamine can effectively improve the nutritional status”. This language should be slightly attenuated.

Answer: We thank the reviewer for this helpful comment. We have amended the Conclusions in the revised manuscript accordingly.

Answers to Reviewer #2’s comments:

First of all, need to congratulate you for carrying out this research with a good design. While reviewing this article, it was fun though; my job is to find the deficiencies before it is presented to readers, so to make it more appealing and authentic. So here they are,

Question 1: There are many grammatical mistakes, please rectify them all. There are also places where two words are not separated by space, please check them all.

Answer: We apologize for any grammatical or typographical errors. The revised manuscript has been edited by a native English speaker from a professional editing company. Besides, we checked the whole article word for word and the situation that “two words are not separated by space” was extinguish.

Question 2: Provide full names of abbreviations used for first time i.e., PBS (Phosphate Buffered Solution) etc.

Answer: Thank you for pointing this out. We have provided the full terms for most abbreviations.

Question 3: Use word 'anaesthesia' instead of 'anaesthetic' while mentioning how tissue was acquired from rats for histology.

Answer: Thank you for this suggestion. We have corrected this in the revised manuscript.

Question 4: Use word 'anal canal or anus' instead of 'anal' in discussion part.

Answer: Thank you for this suggestion. We have corrected this in the revised manuscript.

Question 5: Give details of composition of standard rat chow used in this research, and if possible give glutamine content too.

Answer: We appreciate the reviewer's comment. We have included information on the composition of standard rat chow.

Question 6: In methods, please explain how the sample size was counted and how you decided the number 8 for each group.

Answer: We apologize for this omission. The sample size and the number of rats in each group were reference previous experience (Shebani KO, Stucchi AF, Fruin B, et al. Pouchitis in a rat model of ileal J pouch-anal anastomosis. *INFLAMM BOWEL DIS.* 2002;8:23-34) and our previous experimental results: (Yan-Yan Xu, Ying-Ying Zhang, An-Qi He, Kai-Yu Li, Sen-Yang Gao, Gang Liu. Lactobacillus acidophilus alleviates pouchitis after ileal pouch-anal anastomosis in rats. 2017; 14; 23(26): 4735-4743.) and (Kaiyu Li, Jianlin Wang, Yanyan Xu, Senyang Gao, Yingying Zhang, Anqi He, Gang Liu. Intestinal barrier disruption in ileal pouchitis after ileal pouch-anal anastomosis in a rat model. *Inflamm Bowel Dis.* 2017;23(6):923-931.).

Question 7: Mention when the rat chow was started in control group, as EN and IN group intake was started on day 3.

Answer: We apologize for the confusion. The rat chow in the control group was also started on the third day post-operation. We have added this information in the revised Methods in the Abstract and main text.

Question 8: In results section, use different sentences to show significant difference between two groups, stating results for all three of them in single sentence may create some confusion while reading.

Answer: Thank you for this suggestion. We have revised the Results section to make it clearer.

Question 9: In my opinion, rather than directly stating that ‘Our results provide experimental evidence to support glutamine supplementation of EN for UC patients undergoing IPAA.’, provide basic evidence and simultaneously suggest for human studies by stating ‘our results provide some evidence for usefulness of glutamine enriched enteral nutrition in patients undergoing IPAA; though human studies for same are recommended.’ Thank you very much.

Answer: We appreciate the reviewer’s helpful comment, and have modified the Conclusions accordingly.

We greatly appreciate the reviewers’ comments and constructive suggestions, which we believe have enabled us to improve our manuscript significantly. We hope that you will reconsider our revised manuscript for publication in *World Journal of Gastroenterology*.

Sincerely,

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