Name of journal: World Journal of Clinical Cases

Manuscript NO: 66499

Title: The gut-liver axis in cirrhosis: Are hemodynamic changes a missing link?

Reviewer's code: 05355546

Position: Peer Reviewer

Academic degree: MD

Professional title: Associate Chief Physician

Reviewer's Country/Territory: China

Author's Country/Territory: Russia

Manuscript submission date: 2021-03-29

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-03-30 05:44

Reviewer performed review: 2021-04-11 14:42

Review time: 12 Days and 8 Hours

Scientific quality

| [ ] Grade A: Excellent | [ ] Grade B: Very good | [ Y] Grade C: Good |
| [ ] Grade D: Fair | [ ] Grade E: Do not publish |

Language quality

| [ ] Grade A: Priority publishing | [ Y] Grade B: Minor language polishing |
| [ ] Grade C: A great deal of language polishing | [ ] Grade D: Rejection |

Conclusion

| [ ] Accept (High priority) | [ ] Accept (General priority) |
| [ ] Minor revision | [ Y] Major revision | [ ] Rejection |

Re-review

| [ Y] Yes | [ ] No |

Peer-reviewer statements

Peer-Review: [ Y] Anonymous | [ ] Onymous

Conflicts-of-Interest: [ ] Yes | [ Y] No
SPECIFIC COMMENTS TO AUTHORs

This is a frontier article, authors discussed the evidence of the gut–liver axis in cirrhosis: gut dysbiosis, small intestinal bacterial overgrowth, and intestinal barrier alteration, bacterial translocation, systemic inflammation, vasodilation, arterial hypotension, and hyperdynamic circulation, and then the development of cirrhosis, then authors proposed a model of the gut–liver axis. In general, authors lists many research results, but the summary and analysis are not enough. Some of the articles need to be revised.

1. “Normally, bacterial translocation inhibits the predominance of strict anaerobes (Clostridia and Bacteroidetes) and bacteria without LPS (Firmicutes) or with low-activity LPS (Bacteroidetes) in the gut microbiome as well as low permeability of the intestinal barrier”. It is hard to understand.

2. “short-chain fatty acids (SCFA) produced by the gut microbiota, especially butyrate, play an important role in maintaining the intestinal barrier”. authors may need to discuss how short-chain fatty acids (SCFA) act in maintaining the intestinal barrier.

3. “The intestinal mucosal mitotic count was significantly lower in patients with cirrhosis than in the controls, and a trend toward increased apoptosis was recorded. Lipid peroxidation in the intestinal cells increased in decompensated cirrhosis but not in compensated cirrhosis”. authors did not explain the correlation between intestinal mucosal mitotic count, lipid peroxidation in the intestinal cells and intestinal barrier dysfunction.

4. “Patients with cirrhosis had a diminished expression of antibacterial peptides defensins 5 and 6 at the intestinal crypts compared with healthy controls, and this was negatively correlated with the blood LPS levels. In addition, the content of intraepithelial lymphocytes in the duodenal biopsy specimen was lower in patients with decompensated cirrhosis than in healthy controls” authors did not explain the correlation between antibacterial peptides defensins 5 and 6 at the intestinal crypts, intraepithelial lymphocytes in the duodenal biopsy specimen and intestinal barrier dysfunction.

5. BACTERIAL TRANSLOCATION IN CIRRHOSIS
authors discussed a number of evidence of Bacterial translocation in cirrhosis, But the author may need to make a summary of the passage to help the reader understand it better .

6. SYSTEMIC INFLAMMATION IN CIRRHOSIS authors discussed pro-inflammatory cytokine TNF-a, blood CRP level, anti-inflammatory cytokine, pro-inflammatory cytokine, systemic immune activation biomarkers in cirrhosis, but the author may need to summarize and analyze the evidence.

7. HEMODYNAMIC CHANGES IN CIRRHOSIS authors discussed the evidence of association between NO and pro-inflammatory cytokines, may still need to discuss the evidence of other molecules, including carbon monoxide. The organization of this passage is not so good.

8. authors may need to discuss the mechanism of pro-inflammatory cytokines promote the release of NO from the vascular wall?
RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Manuscript submission date: 2021-03-29

Reviewer chosen by: Yun-Xiaojian Wu

Reviewer accepted review: 2021-06-15 14:04

Reviewer performed review: 2021-06-15 14:24

Review time: 1 Hour

<table>
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<th>Scientific quality</th>
<th>[ ] Grade A: Excellent</th>
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<th>[ ] Grade D: Fair</th>
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SPECIFIC COMMENTS TO AUTHORS

The paper gets better, and I think the scientific quality, language quality, and ethical documents of the revised manuscript meet the publishing requirements.