Name of journal: World Journal of Hepatology

MANUSCRIPT NO: 75801

Title: Effect of probiotics on hemodynamic changes and complications associated with cirrhosis: A pilot randomized controlled trial

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 05351456

Position: Editorial Board

Academic degree: FACP, MBBS

Professional title: Assistant Professor

Reviewer’s Country/Territory: United States

Author’s Country/Territory: Russia

Manuscript submission date: 2022-02-15

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-02-18 16:55

Reviewer performed review: 2022-02-18 17:23

Review time: 1 Hour

Scientific quality

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[ ] Grade D: Fair  [ ] Grade E: Do not publish

Language quality

[ Y] Grade A: Priority publishing  [ ] 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
SPECIFIC COMMENTS TO AUTHORS
Authors present a pilot trial testing the utility of probiotics in cirrhosis patients. Major comments: Is there a preliminary data that authors have worked upon? Definitions: Authors need to define clearly about what do they mean by hyperdynamic circulation? If the patient is a presenting in the outpatient clinic in the assumption is that they are asymptomatic in which case the clinical relevance of “hyperdynamic circulation” comes into question. Follow-up: Of frequently with the patient followed up during the 3-month study time? How many visits did these patients have? Was there any attrition in the group of patients? Did any of the study patients need hospitalization during the study period? (related or unrelated to the study) What is the clinical equipoise? What is the significance of amelioration of hyperdynamic circulation? How is it clinically relevant? Authors should highlight the clinical relevance, just because something can be done does not mean that it needs to be done. Does this benefit the patients in long term? 12-month mortality difference or need for liver transplant? Based on the consort diagram the investigators screen 198 patients and were eventually successful in enrolling 40 patients cumulatively in both the arms. The overall accrual was less than 25% which questions the overall generalizability of the study. Table 3 is very busy and nearly impossible to interpret. The analysis plan and presentation needs to be improved. For example If they want to present the difference (or improvement) in BMI for before and after the study the analysis should be performed using differences in proportion etc. I would strongly recommend re-analysis for the entire table 3 with appropriate approach. In addition, in table 3, the authors are presenting the unadjusted analysis for the outcomes observed in the 2 groups, this needs to be adjusted for other variables that
could demonstrate a similar response. Adjust for age, disease severity etc. Title needs to be changed, I would recommend using “Pilot trial” to assess the safety and feasibility, based on such small numbers no inference can be drawn in terms of efficacy. Was there any power calculation for the trial? How did the author decide about the number of patients that need to be enrolled in the trial? A lot of information presented in table 3 is statistically significant but have very limited to no clinical relevance. Authors need to have a better discussion of the results and what do they propose based on this information. Was the trial registered at the Clinicaltrials.gov?
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Title: Effect of probiotics on hemodynamic changes and complications associated with cirrhosis: A pilot randomized controlled trial

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 05775860

Position: Editorial Board

Academic degree: PhD

Professional title: Assistant Professor

Reviewer’s Country/Territory: China

Author’s Country/Territory: Russia

Manuscript submission date: 2022-02-15

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-02-15 23:46

Reviewer performed review: 2022-02-20 01:01

Review time: 4 Days and 1 Hour

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SPECIFIC COMMENTS TO AUTHORS
The manuscript entitled “Effect of probiotics on hemodynamic changes and complications associated with cirrhosis: A randomized controlled trial” reports the effects of administration of a probiotic yeast, Saccharomyces boulardii, on clinical evaluation of patients with Child-Pugh class B and C cirrhosis. 24 patients received probiotics, while 16 patients received a placebo over the same period as the controls. The clinical evaluation results suggested that administration of S. boulardii was associated with a significant improvement in liver function of patients with cirrhosis. The study is interesting and may contribute to the filed. However, clinical evaluations at gene levels and relevant molecular mechanisms with novelty are lacking. The manuscript is more suitable for publication in a specialized journal.