Reviewer's report

Title: Positive regulatory effects of perioperative probiotic treatment on postoperative liver complications after colorectal liver metastases surgery: a double-center and double-blind randomized clinical trial

Version: 2
Date: 19 December 2014

Reviewer: Luca Gianotti

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Positive regulatory effects of perioperative probiotic treatment on postoperative liver complications after colorectal liver metastases surgery: a double-center and double-blind randomized clinical trial, by Zhihua Liu et al.

This is a potentially interesting study. Although there are several potential flaws and the paper needs to be reorganized deeply.

1. In the abstract, as well in the material section is not clear at all with type of surgery the patients received. It appears intuitive to think that they underwent synchronous colo-rectal and liver resection but there is no mentioning of the extent and type of hepatectomy.

2. There are a multitude of endpoints. It is not clear which is the primary one and the secondary one.

3. The introduction is too long and full of redundant information and sometimes also real commonplaces (such as epidemiology and role of surgery)

4. Statistical methods are unclear, especially the sample size calculation (12 pts/group) and 134 patients were enrolled (great confusion!!)

5. It may be that most of the finding are related to pringle manoeuvre !. There is not data on how many patients received pringle and the time of pringle.

6. A mean of three hours for a combined colorectal resection and hepatic resection seems not believable at all.

7. The description of inclusion and exclusion criteria are repetitive

8. Which stain of probiotic bacteria were used ?? (BL-88, LA-11, LP ??). An international coding for probiotic should be used otherwise no one may reproduce the study design

9. Are these probiotics dried or alive ?

10. Which is the definition of septicaemia ?. Positive blood cultures ? or simple SIRS ?

11. Bowel preparation may affect deeply the survival of probiotic. Did the authors test for viability
12. I am always quite doubtful when I see zero surgical complications in such an extensive surgery. 134 simultaneous colorectal resection and liver resection with no surgical-related morbidity is very uncommon to find in the international literature. I have looked at the same group previous publications and it seems that in none of their trials there is one anastomotic leak, fistula, or bleeding in hundreds of cases.

13. It is unclear why only 117 /134 completed the study.

14. Are there patients receiving TPN or enteral feeding?

15. The authors state that some infections such as central line and pneumonia are not correlated with intestinal infection. Which is the rational for this statement?

16. Diarrhea is not an infectious complication unless pathogens are proven in the stools.

17. There is overlapping period of patients enrollement with their previous publications about RCTs. How is it possible?

18. In the present study they could not reproduce the effect of probiotic on intestinal permeability (as measured by L/M ratio) found their previous publications. Why?

19. In the discussion is too long and there are multiple repetitions of the results and prosaic sentences (liver get a dual blood supply, etc)

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

No conflict