Author's response to reviews

Title: The Effects of Long-Term Total Parenteral Nutrition on Gut Mucosal Immunity in Children with Short Bowel Syndrome: A Systematic Review

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Author's response to reviews: see over
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Title: The Effects of Long-Term Total Parenteral Nutrition on Gut Mucosal Immunity in Children with Short Bowel Syndrome: A Systematic Review

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I would like to thank both my reviewers and editors at BMC for their valuable comments. I am really sorry that this revision is longer than the previous version. Please, advise me if I need to cut any part. Thank you.

**Responses to Reviewers’ Comments**

**Dr. Sigalet**

1. I have changed the title to reflect the content of the article and the evidence documented.
2. New key words included: epithelial permeability, hyperglycemia, immunonutrition
3. I have revised entire introduction section
4. In the introduction, I have included and discussed individually mucosal permeability, bacterial overgrowth, and the most important ongoing complications of SBS.
5. In the results section, I have changed “incidents of bacterial growth and bacterial translocation” to “Sepsis” to make it simple.
6. I have included additional information on surveillance culture from Pierro’s[17] studies
7. I have included metabolic and inflammatory responses to trauma and surgical illness.
8. I have included anatomy and physiology of small intestine and mucosal immune system to help reader understand the content of the paper. Please, let me know if I need to remove this part.
9. I have included and discussed amino acid containing nutrition “immunonutrition.” Although there are many papers available on glutamine and arginine, I could not include all of them because of the length of this paper.
10. After reading the bulk of literature on adult patients from different disciplines and countries, I am convinced that long-term TPN has no negative effect on human. I have also changed my conclusion.

**Dr. Jeejeebhoy**

1. First of all I would like to thank you for taking the time and providing me the references!
2. I have revised entire discussion section. I have included the following papers:
• I have included all studies on villous atrophy:
  • Pironi (1994) JPEN, 18: 351-54
  • Guedon (1986), Gastroenterology, 90: 373-8
  • Sedman (1995), Br J Surg, 82: 1663-7
  • Groos (1996), J Submicros Cyto Patho, 28: 61-74
  • Buchman (1995), JPEN, 19 (6), 453-60
  • Lipman, TO (1997) JPEN, 22(3), 167-82

3. I have included new information on hyperglycemia, insulin’s effects on immune system including following papers
  • van-den-Bergh-e (2001), NEJM, 345 (19) 1359-67
  • Campbell (2004), Clinical Diabetes, 22(2), 81-88
  • Montori, V. M. (2002), JAMA, 288(17) 2167-9

4. I have also included the topic of immunonutrition and new formulas, IMPACT and Immune-Aid, including the following papers:
  • Heyland (2001), JAMA 286(8), 944-53
  • Daly et al. (1992) Surgery, 112:56-67

5. I have compared enteral versus parenteral nutrition
6. I have included additional studies (positive and negative results) on immunosuppressive effect of lipid components of TPN
7. In the Sample section of Methods, I have changed the total number of participants from 398 to 414, because in my original paper, I missed counting the control in one study.
8. In Sample section, I have included a new paragraph explaining why I have included retrospective and cohort studies instead of PRCT.
9. At the end, briefly I have discussed implications for nursing practice
10. After reading vast majority of PRCTs and critical reviews, I have changed my conclusion.

***Please, advise me if I need to cut any parts or move sections somewhere else in the paper.

Thank you!