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

Authors:

Beyhan Duran (beyhan.duran@uconn.edu)

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Author's response to reviews: see over
Author’s response to reviewers

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Author: 
Beyhan Duran (Beyhan.duran@uconn.edu)

Version: 2 Date: 28 July 04
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.

All revised sections have been written in blue font. I have revised the result section in the abstract.

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
   - I have included new information on hyperglycemia, insulin’s effects on immune system including following papers
     - van-den-Berghe (2001), NEJM, 345 (19) 1359-67
     - Campbell (2004), Clinical Diabetes, 22(2), 81-88
   - 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
   - I have compared enteral versus parenteral nutrition
   - I have included additional studies (positive and negative results) on immunosuppressive effect of lipid components of TPN
   - 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.
   - In Sample section, I have included a new paragraph explaining why I have included retrospective and cohort studies instead of PRCT.
   - At the end, briefly I have discussed implications for nursing practice
   - 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!