Reviewer's report

Title: Long-Term Total Parenteral Nutrition Impairs Gut Immunity In Children With Short Bowel Syndrome: Part I, A Systematic Review

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Reviewer: David Sigalet

Reviewer's report:

Summary:

This article is a systematic review of the literature, investigating the relationship between total parenteral nutrition (TPN) in the immune system in short bowel syndrome patients.

The mesh terms used were total parenteral nutrition, bacterial translocation, immunity, infant, child, short bowel syndrome, short gut system, intestinal immunity.

The authors extracted 13 studies (1 unpublished) and from these conclude that long-term TPN promotes bacterial overgrowth, and impairs neutrophil functions, inhibits blood’s bactericidal, causes villus atrophy and can even lead to death.

The authors conclude that the studies reviewed suggest that there is little or no long-term benefit of long-term TPN when enteral feeding is withheld.

My recommendation is that this publication requires major revision prior to consideration for publication. The conclusions reached are not substantiated and cannot be substantiated from the articles reviewed.

Specific Comments:

The topic and methodology the author has chosen are very relevant. The question of the relationship between TPN or intravenous feedings and impaired immunity is an important problem in the care of short bowel syndrome patients. Moreover the methodology and mesh terms as well as the breadth of articles retrieved is good. The major criticism of this paper relates to the initial framework for the review of the studies, the categorization of the potential causes of infection related to TPN treatment, and then finally the conclusions reached from the data reviewed.

In the introduction the possibility that short bowel syndrome itself might increase intestinal permeability, or lead to bacterial overgrowth as a cause of recurrent sepsis it not discussed, and this is an important oversight.

The author sets out from the data reviewed to determine whether TPN causes or is associated with increased rates of infection or bacterial translocation. The results related to infection, septicemia and bacterial translocation were grouped under the incidence of bacterial growth and translocation.

Regarding the human outcome data the association of short bowel syndrome, TPN use, and episodes of sepsis is a well documented clinical problem.

However the association of these three problems is complicated. The author appears to lump these associations and draw the inference that TPN is causative. The opening line in the discussion is that
the descriptive systematic reviews show the benefit of enteral nutrition in reducing episodes of infection. This conclusion cannot be drawn. There are no randomized trials comparing TPN versus a specific enterally driven protocol.

The review documenting the impairment of immune function in in-vitro studies is stronger, and these conclusions are probably valid. Similarly the outline of mortality and the relationship between bowel length and TPN dependency is straightforward. The report of binds regarding use of a immuno acid formula in success rate in weaning infants from TPN is reviewed however the observations of multiple practitioners in the field who have tried to emulate these results since 1998 are not commented upon. Further the impact of associated food allergy on enteral tolerance in short bowel syndrome is not addressed.

Finally within the discussion the comparison of primitive TPN in the critical ill primarily adult trauma patients that has been well documented is discussed out of context. In adult trauma patients there are the possibilities of using either enteral or intravenous modes of nutrition for a relatively short term. In the pediatric patients with short bowel syndrome the lack of nutrient absorptive capacity from nutrients derived by the enteral route is fundamental. Therefore the conclusion that the risk of TPN is to great to consider as a first line solution for nutrition in SBS children is totally unsubstantiated.

In summary I would urge the author to review the results and use only conclusions that can be substantiated from the evidence reviewed. The projection of the results in fact weakens what is likely a valid conclusion.

There are several minor style and grammatical errors in the text.

Finally the title should be revised to more accurately reflect the level of evidence documented.

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