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: khursheed Jeejeebhoy

Reviewer’s report:

Duran Beyhan has examined the literature for the effects of “Long-term Total Parenteral Nutrition on Gut immunity in children. A descriptive review has been performed of 13 papers and concluded that: “One must be, however, cautious and knowledgeable of the potential adverse changes TPN can induce in the mucosal immunity of gastrointestinal tract, which leads to bacterial translocation, dysfunction neutrophil, cytokine, macrophage killing activity, and intestinal immune deficiency in children following bowel resection when luminal or enteral feeding is withheld. Clinical significance of the changes of mucosal immunity induced by longterm TPN is great and one should be aware of the importance of oral or enteral feeding from immunological standpoint. Therefore, TPN should not be seen as a panacea for children with SBS. The risk of infection, possible death and/or a life with TPN is too great to consider it as the first solution for nutrition in SBS children”.

COMMENT:
1. There were 5 retrospective or case studies, 3 in vitro studies all by the same authors, three cohort studies of which two were by the same authors. One experimental study and one prospective study. The paper is very uncritical about the poor quality of data provided by these studies which are largely retrospective, in vitro (how does it translate to the whole person?) and the fact that Okada and Pierro may be multiple studies of the same patients making them really 2 instead of 5 studies. The one properly conducted experimental study by Rossi et al. showed clearly that even after long term TPN intestinal atrophy was mild. There was no atrophy after 1 month of TPN. This well done study was not commented upon as being against the dogma that TPN induces gut atrophy. This is true in rats [48] but not in humans. The statement “Although numerous experimental studies suggest that long-term TPN alters the morphologic structure of intestinal mucosa, there is limited clinical evidence in the literature [48]. This is mostly because, for ethical reasons, obtaining tissues from sick infants or children might be difficult [49]” is incorrectly quoted as there are many human studies showing no atrophy or mild atrophy even after very prolonged TPN.

The paper would have been strengthened by providing critically analyzing the data on villus atrophy.

2. In vitro studies in which blood from patients (Okada et al) or TPN added to blood is used to show abnormal immunity is unreliable because it is well known that high glucose levels inhibits the immune function of a variety of cells. When TPN is infused or added to blood simply increasing glycemia will alter the response. A recent study by Van Den Bergh et al. N Engl J Med 2001;345:1359-67 clearly showed that with TPN or EN in the ICU mortality can be halved by rigid control of blood glucose levels and there was no difference between patients fed TPN or EN. Again a critical review of these facts would strengthen the paper. Did Okada et al account for glycemia?

3. Dahlstrom unpublished study shows that despite food by mouth patients had low lymphocytes and
some died. Here despite enteral nourishment and gut stimulation patients had reduced lymphocytes. This may have no relation to TPN but to loss of lymphoid tissue in the bowel as pointed out in the review.

4. The review does not point out the difficulty of distinguishing between TPN and the underlying disease as cause of morbidity and mortality. The review places the entire list of complications as being TPN driven which is certainly not proven from the data provided. There is no true control enteral feeding, data about glycemic control which has a major impact on mortality as shown in the paper by Van den Berghe which studied in excess of 1500 patients in a randomized trial.

5. In summary a descriptive study is useful if critically appraised and not described without an appraisal of quality, controls, nature of study and emphasis on the stronger studies. This review needs considerable modification with critical review to be useful.

What next?: Accept after minor essential revisions

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