Author's response to reviews

Title: A prospective, randomized, controlled study of omega-3 fish oil fat emulsion-based parenteral nutrition for patients following surgical resection of gastric tumors

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Author's response to reviews:

Thank you for your letter and for the reviewers' comments concerning our manuscript. Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. Revised portion are marked in red in the paper. The main corrections in the paper and the responds to the reviewer's comments are as flowing:

Responds to the reviewer's comments:

Referee 1:
Reviewer's report
Title: A prospective, randomized, controlled study of omega-3 fish oil fat emulsion-based parenteral nutrition for patients following surgical resection of gastric tumors
Version: 2
Date: 18 December 2013
Reviewer: Philip Calder

Reviewer's report:
This is the revised version of this manuscript which reports data from a RCT of ivfish oil in post surgery patients. This is a topic of interest. The revisions have greatly improved the manuscript and I thank the authors for their efforts. However there are still a number of issues that require attention:

Answer: Thank you for taking the time to review our paper and also thanks for
the helpful critical comments.

1. Abstract, Results, line 2. Strictly speaking authors did not measure "inflammatory reaction" but the "concentrations of inflammatory markers". 

Answer: it has been revised to “the levels of inflammatory markers were significantly decreased.”

2. Abstract, Conclusion, lines 1 and 2. There is a conclusion "promotes the recovery of the immune function" but a) there is nothing in the Results section of the Abstract about "immune function" and b) authors did not assess immune function. 

Answer: it has been revied to “#-3 fish oil fat emulsion-based parenteral nutrition alleviates the inflammatory reaction and reduces the rate of inflammatory complications.”

3. Introduction is still inadequate. There are three key issues to be addressed here:

a) there needs to be better referencing. how can a reader find about the calimed effects of EPA and DHA on growth, apoptosis, immune function, SIRS if the authors do not provide references to support these statements;

Answer: We have provided 6 additional references for these statements.

b) The new section does not provide any rationale for doing the study. There are many studies of iv fish oil in surgical patients and several meta-analyses (in my last report I mentioned those of Chen and of Wei both published in 2010). What do these studies show? Why is it necessary to do more studies?

Answer: We have provided additional information of iv fish oil in surgical patients including a recent meta analysis (2012).

c) No clear rationale or hypothesis for this study is provided.

Answer: We have provided the following hypothesis in Introduction: “The above findings prompted us to speculate that f #-3 fish oil fat emulsion-supplemented PN could be beneficial to the overall functional recovery of gastric tumor patients. Here, we designed a prospective, randomized, single-blinded control clinical trial to investigate the effect of #-3 fish oil fat emulsion-supplemented PN on nutritional state, immune function, inflammatory reaction, expression of tumor factors and complication incidence in patients after surgery of gastric tumors.”

4. References are presented in several different formats. Please unify these.

Answer: We have streamlined the references in the revised manuscript.

Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I have received speaking honoraria from Fresenius Kabi, the producers of the fish oil emulsion used in this study

Referee 2:

Reviewer's report

Title: A prospective, randomized, controlled study of omega-3 fish oil fat emulsion-based parenteral nutrition for patients following surgical resection of gastric tumors

Version: 2Date: 18 December 2013

Reviewer: Sigrun Friesecke

Reviewer's report:

The revision has improved the manuscript substantially.

Answer: Thank you for reviewing our paper and also thanks for the helpful critical comments.

There are some problems remaining:

1. the deprivation of early enteral feeding for the study patients. Early enteral feeding after elective and cancer gastrointestinal surgery reduces complication rate and duration of hospital stay (Bozzetti, Lancet 2001). So the authors may have deprived their patients of this advantage. I miss a justification for this management.

Answer: We agree with the reviewer that deprivation of early enteral feeding may deny the patients of reduced complication rates and hospital stay length. However, most hospitals in mainland China still follow or require the traditional practice of preoperative fasting.

2. The simple change in indicated duration of antibiotics from version I to version II seems not convincing (first version 7 days, now changed to 3-4 days). There should be a trustable explanation for this difference.

Answer: the antibiotics were used about 7 days in early experiment. But later, we found that in patients with body temperature and white blood cells restored normal after 3-4 days postoperative, it suggested that patient don't need to use antibiotics. So the antibiotics in later patients were used for about 3 to 4 days.

Furthermore, duration of antibiotic prophylaxis does not exceed 24 h, otherwise it is therapy. If it is therapy, which infection is treated? Nosocomial infections are selected as an outcome parameter. Should we assume break through infections
under ongoing antibiotic therapy? This should be clarified.

Answer: This group information of patient are some of early surgery patients in our hospital, and we admit that antibiotics are used in a non-standard manner at that time and antibiotics were used for a prolonged period time, so some patients may be controlled by antibiotics with mild infection and only 7 patients showed evidence of infection.

Minor essential revisions

Methods

- Nutrition: kJ/kg/d of calories.../ liquid instead of liquid support/

Answer: The errors are corrected.

- The randomisation procedure should be explained in this section

Answer: it has been done as suggested.

- Why a fixed ratio of insulin and glucose? metabolism and glucose tolerance is highly variable between patients.

Answer: Usually we use a fixed ratio of insulin and glucose, but we monitor finger blood sugar every 4-6 hours, if blood sugar is high, we use insulin to control it. This information is incorporated in Methods in the revised manuscript.

Results

adverse effects of parenteral nutrition... my question did not address different adverse effects of PN, instead I would like to know which of them you analysed to contend that there were no adverse effects. Please clarify. I’m sure, not only PNALD was analysed.

Answer: Parenteral nutrition-associated liver disease (PNALD), infection, phlebitis, and glucose intolerance were assessed.

Discussion

section: “fish oil is made up ...” The pathophysiology is described much more detailed now. The effect of omega-3-fatty acids replacing omega-6-fatty acids, and being precursors of eicosanoids with less pro-inflammatory effects should be explained more clearly. There are still some important statements without any reference: "release of antibodies and..of macrophages are ..enhanced."

"inhibiting the release of proinflammatory cytokines.."; "increases the release of antiinflammatory cytokines,,"

Answer: The references have been updated.

"The mortality of patients was therefore decreased.." Which patients in which context?
Answer: The study by Heller et al. included 255 patients after major abdominal surgery, 276 with peritonitis and abdominal sepsis, 16 with nonabdominal sepsis, 59 after multiple trauma, 18 with severe head injury, and 37 with other diagnoses, and the authors found that administration of omega-3 fatty acid reduce mortality of these patients. The following has been added “The mortality of patients was therefore decreased and the prognosis of patients improved after major abdominal surgery, and in patients with peritonitis and abdominal sepsis and other conditions”

. I’m not sure what is meant with "...most likely due to the post-surgery nutritional status of the patients." Do you mean, the substitution of omega-3-fatty acids decreases creatinine? Why should this happen? The consideration regarding bilirubin is a totally different point and should explained in a new sentence.

Answer: The sentence is removed. “Total bilirubin and serum creatinine were significantly decreased, most likely due to the post-surgery nutritional status of the patients.

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

Answer: We have asked Dr. Cui at Department of Surgery, Duke University Medical Center to proofread the manuscript.

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I have no competing interests.