

Our responses to the reviewers' comments for No: 26381

Title: A peptide-based enteral formula improves tolerance and clinical outcomes in abdominal surgery patients relative to a whole protein enteral formula.

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Reviewer 1

We thank the reviewer 1 for the critical comments which have helped us to improve the manuscript. We have addressed all comments as follows.

1. The selected patients were those who had serum albumin concentrations less than 3.0 g/dL. After treatment with WPF / PEF the level of serum albumin were still less than 3(2.70±0.30 and 2.89±0.27 g/dL, respectively. The significant decreased is not very impressive (p=0.01). Why?

Major surgery is followed by an significant metabolic stress response. The CRP levels correlate closely with the magnitude of surgery and are routinely assessed to monitor postoperative systemic inflammatory response. The serum albumin was strongly correlated with CRP levels, In hospitalized patients with high CRP levels bring up a decrease in albumin level during hospitalization. The CRP levels were high during the stay in the ICU and there were no significantly between the two groups . Therefore, the level of serum albumin were still less than 3.0 g/dL on POD-10, but It has gradually increase especially in PEF group.

2. Measurement of serum albumin, prealbumin, C-reactive protein (CRP) and total lymphocyte count (TLC) was performed at baseline, day 5, and day 10. The authors did not give the exact time and their measuring seemed to be different from the others which “absorption was evaluated by calculating the area under the curve of amino acid concentration in portal vein plasma of rats for 120 min after administration”. Please give the reason or discuss.

Yoshihara et al. studied the absorption patterns of each nitrogen source from portal vein plasma of rats for 120 min after administration. The portal vein is a blood duct that carry rich nutrients from the gastrointestinal tract to the liver, all blood proteins are synthesized in liver. Therefore, we measured serum albumin, prealbumin, CRP to confirm the results. We routine draw blood was at 7:00 am. with the glucose or blood lipid check.

3. What is POT ? Please define. It seems that PepT1 is involved in the absorption of di- and tri-peptides Is it possible to measure PepT1, to reconfirm the results of

serum albumin? The results showed that serum prealbumin has a trend to increase than serum albumin. Please discuss.

POT is an abbreviation for proton-coupled oligopeptide transporters, which has been mentioned in the introduction. PepT1 mRNA expression studies need gut-mucosal biopsy specimens for analysis. We did not execute the endoscope for each patient, but it can be considered in future. Prealbumin is a rapid-turnover protein (half-life <48 hours), which is a more sensitive indicator to assess the nutritional status than albumin (half-life 21 days). When patients' nutrition are improved that the serum prealbumin will increase rapidly.

4. Is it worth to give PEF instead of WPF ? 7 days with a peptide formula rather than whole-protein formula will cost roughly \$140 more and peptide formulas seem to shorten the average ICU stay by about one day. Please discuss.

The mean cost of intensive care unit was \$350 dollars per day in Taiwan. seven days of peptide formula can be shortened ICU stay by about one day is economic benefit.

5. Is it possible to increase the number of the patients?
We thank the reviewers' suggestions.

Reviewer 2: We thank the reviewer 1 for all comments.