Author's response to reviews

Title: Effects of Protein-Enriched Meal in a Weight Loss Program on Liver, Kidney or Bone: a Randomized Controlled Trial

Authors:

Zhaoping Li (zli@mednet.ucla.edu)
Leo Treyzon (ltreyzon@hotmail.com)
Steve Chen (steve.chen@amylin.com)
Eric Yan (ericyanmd@yahoo.com)
Gail Thames (gthames@mednet.ucla.edu)
Catherine Carpenter (ccarpenter@mednet.ucla.edu)

Version: 3 Date: 9 November 2010

Author's response to reviews: see over
Reviewer's report
Title: Effects of Protein-Enriched Meal in a Weight Loss Program on Liver, Kidney or Bone: a Randomized Controlled Trial
Version: 2 Date: 25 August 2010

Reviewer: Frank f Greenway
Reviewer's report:
There are some spelling mistakes and grammar corrections needed in the modifications make in track changes. There are also a couple of references that remain after a sentence was removed.

Response: Revised as recommended.

Reviewer: Vijay Ganji
Reviewer's report:
Authors have some addresses some but not all. Some of my concerns remain.
1) Although they mentioned the procedures for compliance, they failed to mention the level of compliance that the investigators are looking for. Was it 70%, or 80% or 90% compliance with the MR? If they did not measure that should be mentioned the limitation section.

Response: Face-to-face counseling sessions by our dietary staff were provided to promote compliance to MR. Biochemical compliance was not determined. We changed the statement in the methods section and added limitation statement in discussion.

2) There was no mention of "fasting". Whether or not blood was collected after overnight fast?

Response: Blood-based parameters were collected after a >10-hour fast. Line 109

3) I see they have included the drop out data in the revised manuscript. It was not clear, whether the data associated with the drop out subjects were eliminated in the final analysis? This needs to mentioned in the "statistical analysis" section.

Response: Statement was added to methods section. We did not perform intention to treat analysis.

4) On page 11 (line # 197-200), there is a mention of increased protein excretion SP but no in the HP group. I wish they had commented about this in the discussion. This definitely may not be due to the MR administration. This is an odd observation. Any mix up of samples or mislabeling of specimen?

Response: Human studies are not consistent sometimes. We do not know why protein excretion was higher in SP but not in the HP group. Perhaps the SP group underwent more protein catabolism from their muscle mass while the muscle mass in the HP group, because they were consuming more protein, was spared. Results from our earlier study support this.

5) I am little confused with "weight loss". On page 14, line #261-262 you said " the expected effects of increased weight loss resulting from a high protein diet were not seen in this study". At the bottom of the same page, under conclusion you said ".....HP and Sp diets resulted in the
expected weight loss typical of an MR diet plan at 12 months”. Can make these 2 statements a bit more clearer. It appears those two statements contradict.

Response: The two statements in question are complementary. The first statement refers to the lack of difference in weight loss experienced by the HP group. Second statement says that both HP and SP lost weight, which was typical of a MR diet plan after one year.

6) It is interesting to see there is some beneficial effects with the MR in lipid profile at 3 or 6 month level depending on the type of lipid. Authors should comment on this. Perhaps it may be due to the fact that participants did not adhere to the diet plan after first 3 or 6 months. Studies have shown after 3 to 6 months the compliance with the study procedures goes down. This is a possibility but not sure how likely in your study. This may also likely explanation for lack of effect on other biochemical parameters. This should be mentioned in the discussion and put under limitation.

Response: We mentioned that biochemical compliance was not determined and therefore we have no evidence to confirm what the reviewer is suggesting.

7) What is the grams of protein per kg of body weight. This should also be given in addition to the intake per kg of lean body mass. I would expect the protein in MR per kg body weight would be much less. My guess is that the protein content in the HP group would be around 1.6-1.8 g/kg body weight. If this is correct and this is not a very high protein diet by any means. Then the the biochemical markers would not be affected that much because our body can easily adjust to fluctuations in macronutrient intake on a daily basis.

Response: Our MR treatment consisted of administrating protein according to Kg of lean body mass (HP: 2.2 grams protein per Kg; SP: 1.1 gms per Kg of lean body mass). We did not consider total weight because of variation in body fat mass. Our population was obese by definition and most likely the protein administered per Kg would be low because of excess body fat in our population.

Minor points:
1) First time when abbreviation is used, it should be spelled out. For example MR, GFR, and ANOVA.

Response: revised as recommended.

2) Line 14. "no difference between..." mean no difference between "end point weights of two treatments".

Response: revised as recommended.

3) Line 23: "secretion". You mean excretion?

Response: revised as recommended.

4) Line 19: You mean "alkaline phosphatase".
Response: revised as recommended.

5) Line 52: Please spell out MR first time.
Response: revised as recommended.

6) Line 109: week 0? I thought the weights were done every 3 months.
Response: Weight was measured at each visit but height was only measured at week 0.

7) Methods: I see the explanation was given for measurement of lipids. This is more than I was looking for. How about other biochemicals such as AST, bilirubin. There is no need to give a very elaborate methodology but in 1 or 2 statements, very briefly state the methodology for the rest.
Response: revised as recommended.

8) Line 149: Spell out ANOVA first itme.
Response: revised as recommended.

9) Line 174: Please add p-value.
Response: revised as recommended.

10) Line 181: Please change level to concentration not only here but also other places. "Concentration" is a better choice than the "level".
Response: revised as recommended.

11) Line 198: Please change "secretion: to "excretion".
Response: revised as recommended.

12) Line 251: Please add reference (after metabolic syndrome).
Response: revised as recommended.

13) Table 1: Table shows that there were 100 subjects infact study had only 35 in each group. This table should only have the data for subjects who completed the study. The table is more meaningful this way.
Response: We have included all 100 subjects to provide information on overall study population and randomization.

14) The protein diet was based on LBM. In the table 1, there is no LBM for those two groups.
Response: The meal plan was individualized based on estimated resting metabolic rate. The group average LBM would not be helpful.
15) Please change "triglycerides" to "triacylglycerol".

Response: revised as recommended.

**Reviewer:** Jennifer Keogh  
**Reviewer's report:**  
I recommended reject for this paper in my original review.

Response: There has been both scientific concern and public concern that high protein diets are unsafe. In particular studies have shown that long-term use of high protein diets may damage the liver, kidney and adversely influence bone metabolism. The American Heart Association's 2006 guidelines suggest a sustained high protein diet may have adverse effects on renal function among individuals with chronic kidney disease (ref), however not many studies have been conducted to evaluate whether high protein diets affect healthy populations. Results from our study are therefore important because we demonstrated that high protein diets sustained up to one year had no adverse impact on bone metabolism, renal, or liver function at one year. Our study population was obese but otherwise healthy.

Reference: