Reviewer’s report

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

Version: 3 Date: 10 November 2010

Reviewer: Vijay Ganji

Reviewer’s report:

I looked at their revisions and found that they fail to address my comments. Their revisions were mostly cosmetic and hand waving at the best. Below are my comments in response to their revisions.

My initial review: 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.

Authors 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.

My Comment: They should clearly say that the compliance was not assessed and this is one of the limitations of this study.

My initial review 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.

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

My comment: I have no idea what the authors were trying to convey in the revision. My comment was not related to the "intent to treat analysis". My question was simply whether or not data associated with the drop of subjects were included in the data analysis. That needs to be explicitly stated. My take from reading it is that they did not include the data associated with drop out subjects. Table 1 should reflect actual sample size without drop out subjects. Who cares how many you started with, what people care is how many you actual end up with. The description on the drop out subjects is kind of "beating around the bush".

4) On page 11 (line # 197-200), they 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.

My comment: If there is more protein catabolism, protein gets excreted from the kidney? I doubt it. If at all if there is a more protein excretion it has to be in those subjects with high protein intake. Did they assess serum creatinine (or any other marker of renal function) to investigate whether subjects had any kidney dysfunction? Without this, this a major limitation and this should be explicitly indicated. Nonetheless this observation is very odd..

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.

My comment: Not sure how those two sentences are complimentary.

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.

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

My comment: I did not ask for evidence. The lack of change in blood lipids after 3 to 6 mo is more likely due to non-compliance by the subjects. Study results are good and until 3 to 6 months then all of a sudden you do not see anything happening. I am not sure what else is the explanation?

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 administering 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.

My comment: I see the rational but the protein recommendations are based on body weight as per the Institute of Medicine (0.8 g/kg body weight). My interpretation is that the amount of protein given in these two treatments is not that much based on the per kg body weight. If they do not want to give protein amount per kg body weight then they have to give a justification that the protein amount given is really high in protein for those participants. There is so much not so sound information is floating around, people might interpret this as a green signal to go and indulge in high protein diet.

Overall, the explanation was inadequate. There were several limitations in this study and they need to be explicitly explained. Given the limitations of the study, the conclusions were very strong.

**Level of interest:** Reject as not of sufficient priority to merit publishing in this journal

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

I declare that I have no competing interests.