Author's response to reviews

Title: Intake of partially defatted Brazil nut flour reduces serum cholesterol in hypercholesterolemic patients- a randomized controlled trial

Authors:

Roberta F de Carvalho (beta_franca_carvalho@yahoo.com.br)
Grazielle VB Huguenin (grazielle.huguenin@gmail.com)
Ronir R Luiz (ronir@iesc.ufri.br)
Annie SB Moreira (anniebello@gmail.com)
Glaucia MM Oliveira (glauciamoraesoliveira@gmail.com)
Glorimar Rosa (glorimar@nutricao.ufrj.br)

Version: 2
Date: 7 March 2015

Author's response to reviews: see over
 Rio de Janeiro, March 6th, 2015

Dear Dr. Hiromichi Kumagai

The Nutrition Journal Editorial Team

MS: 3604681181277040

Manuscript title: Intake of partially defatted Brazil nut flour reduces serum cholesterol in hypercholesterolemic patients- a randomized controlled trial

We have received the editorial requirements and the reviewers’ comments and thank them for their suggestions to improve the manuscript, which considers the fact that the main issue is current and clinically important because it addresses a We do hope that our responses are considered appropriate and allow the acceptance of our manuscript at the Nutrition Journal. The editorial requirements and the reviewers’ comments are in italics, and our responses are below.

Please contact us if further explanation is needed.

Sincerely,

Glorimar Rosa
Answers to the referee’s comments

Reviewer 1: Shridhar Sathe

No further comments.

Reviewer 2: Alejandro Fernández Montero

Major Compulsory Revisions

1) Inclusion criteria should be better described. Hypertensive patients are included, but hypertension criteria are not well defined. (Study patients, Paragraph one)

The patients had referred diagnoses of hypertension and dyslipidemia, and we checked their drug histories for hypertension, hypercholesterolemia and hypertriglyceridemia. All patients were using drug therapy for both hypertension and hypercholesterolemia or hypertriglyceridemia. In addition, all patients were followed by a multidisciplinary team at the Atherosclerosis and Cardiovascular Prevention Clinic at the National Institute of Cardiology when they were recruited for the present study.

We reviewed the sentence on the inclusion criteria (page 4, lines 92 - 94).

2) The estimation of sample size was based on the detection of significant increase in T3 levels in previous studies, but the main variable of this study is serum lipids levels, not T3 levels, therefore this should be better explained. (Statistical Analyses in paragraph one)

We agree with the reviewer; however, one of the main objectives of this study was to investigate the effect of a personalized healthy diet with defatted Brazil nut flour on thyroid hormones as we mentioned at the last paragraph of the introduction.

We reviewed paragraph one of the Statistical Analyses (page 7, line 170).

Minor Essential Revisions

1) The placebo (Cassava flour) should be better defined (nutritional composition, antioxidants, vitamins, or other substances that could affect the results…) (Experimental design, Paragraph one)

The nutritional composition of the placebo was added to the manuscript (page 6, line 133). Cassava, is also called by Yuca or Manioc, is a tuberous root with a major source of carbohydrates, however the amount given to the subjects was small, and we believe that it worked as a good placebo. We calculated the nutritional composition using the Food Composition Table of USDA for selenium content and a Brazilian Food Composition Table for the other parameters.
2) Results are not clear enough. When describing table 4, the lack of any statistically significant difference in the studied variables (serum lipoprotein levels and blood pressure) between the placebo and the Brazil-nut group is not well described. This is the main result of the study, and data are not given. It is a negative result but it should be better detailed. Only the differences found intragroup are described. We performed the repeated measurement ANOVA, but it did not change the results about the significance intragroup and between the groups.

3) Table 3 is incorrectly referred as table “2”. (Results, paragraph 5) We reviewed the sentence (page 9, line 210)

4) English use should be reviewed. Language corrections should be done before publishing. We reviewed the English language.

5) Spelling: “dropouthe” study: ?? (First paragraph of Results) “thatevaluate” glutathione peroxidase levels: ?? (Last paragraph of Discussion) We corrected the sentences.

Reviewer 3: Alfredo Gea

Major Compulsory Revisions:

1) In this study, "there were no differences between Brazil nut and placebo group throughout the study". Therefore, any effect between baseline and the end of the study may not be attributed to the intervention. Some of the effects may be due to the diet itself and no due to the supplementation. Therefore, authors should discuss why there were no differences between groups instead of discussing the possible mechanisms underlying the effects of selenium. Because, as I mentioned before, we cannot distinguish which of the factors is causing the effect found in the intervention group. And the same happens with attributing the effects of the flour to the nut. (discussion: "Finally, our results indicate that Brazil nut in association with a healthy diet did not promotes weight gain...")

We agree with the reviewer and reviewed the discussion.

2) Therefore, the title have to change in accordance to that.
We reviewed the title: “Effects of a personalized balanced diet with defatted Brazil nut flour on the lipid levels and thyroid hormones of dyslipidemic and hypertensive patients.”

3) If authors collected data not only at baseline and at the end of the study, but also in some intermediate points, I would use repeated measurement ANOVA or any other equivalent methods in order to take advantage of these data.

We agree with the revisor and performed the repeated measurement ANOVA, but it did not change the results about the significance intragroup and between the groups.

4) I think table 4 is more interesting than any of the figures and should be in the main text and not as a supplemental file.

We agree with the reviewer and added this table to the main text.

Minor Essential Revisions:

There are some questions that author should consider responding on the main text:
5) Why do you use partially defatted Brazil nut flour and not Brazil nuts? Fat from nuts has been proposed as beneficial for some health outcomes.

We have chosen to use the partially defatted granulated Brazil nut in this study instead of Brazil nut because the granulated Brazil nut allowed us to blind the study and is already commercialized. Partially defatted Brazil nut flour is made via the mechanical cold extraction of the nut’s extra-virgin oil at atmosphere temperature. We had already compared the centesimal composition of partially defatted granulated Brazil nut with the Brazil nut composition in the USDA table, and we found a total fat decrease of 35%, 24% fewer calories, and similar Se content (227.50 µg vs. 249.21 µg, respectively). These data were submitted to Food Research International, and we are awaiting a response from the journal.

We reviewed the Methods at page 6, line 137.

6) Why do you use block randomization instead of individual randomization?

We used the block randomization to have the same number of subjects starting in each group of the study.

7) Why the quantity of flour per day is different in both the placebo and the intervention group?

According to the total volume of the opaque flask used to store the supplements, we could not give the same volume of Brazil as placebo, since placebo is less dense and it requires a higher volume and more flasks. So it could difficult the double blinding of the study.

We reviewed this point at page 6, line 133.
8) When describing the estimation of sample size, it is written "Thus, 70 patients would be required for a statistical power of 80% or more". It should say "more than 80%" or just "80%".

We reviewed the first paragraph of Statistical analysis at page 8, line 179.

9) It might be adequate to clearly include a strength and limitation section.

We agree with the reviewer and we reviewed the last paragraph of the discussion highlighting the section Strengths and limitations at page 11, line 271.

10) Between some words words there is no space. It happens throughout the manuscript.

We apologize about this; there was an error in the editor software during the writing of the manuscript. We reviewed all the text and hope it is not a problem anymore.

11) Although I am not a native English, I think English should be revised.

We reviewed the English language.

Editorial comments

Acknowledgements

Please include an acknowledgement section at the end of the manuscript before the reference list. Please acknowledge anyone who contributed towards the study by making substantial contributions to conception, design, acquisition of data, or analysis and interpretation of data, or who was involved in drafting the manuscript or revising it critically for important intellectual content, but who does not meet the criteria for authorship. Please also include the source(s) of funding for all authors. Authors should obtain permission to acknowledge from all those mentioned in the Acknowledgements.

We included the Competing interests, Authors’ contributions and Acknowledgements at page 12.