

Author's response to reviews

Title: Dietary patterns in clinical subtypes of multiple sclerosis: an exploratory study

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Nutrition Journal

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Lady Lake

Florida

United States

Groningen, May 22, 2009

Subject: electronic submission revised version of 'Dietary patterns in clinical subtypes of multiple sclerosis: an exploratory study',

Dear Dr. Gabriel,

Thank you for the opportunity to revise the manuscript according to the reviewers' comments. Please find as electronic file the revised version of 'Dietary patterns in clinical subtypes of multiple sclerosis: an exploratory study'. The reviewers' comments are addressed as follows:

Reviewer K.M. Spach

1. Magnesium, calcium and iron levels are lowest in SPMS, and intermediate in benign MS and highest in PPMS. How does this fit the fact that benign MS is not the intermediate disease type.

It is a misconception to classify the subgroups of MS as 'worse' (PPMS), 'intermediate' (SPMS), and 'good' (benign MS). Because the pathophysiological bases of the different disease courses is still not clear, we do not know the

meaning of the 'intermediate' value of magnesium and calcium in the benign group. Furthermore, the primary progressive patients are thought to have a possible different pathophysiological mechanism than the secondary progressive MS patients. For example, a patient with a slow progression of the primary progressive form may be better off than a secondary progressive patient with early onset of the disease. Benign disease can be viewed as a secondary progressive form in which the secondary progressive state is postponed for at least 10 years.

Are differenced biologically different since serum levels did not differ?

Serum levels of several vitamins and elements are maintained in a homeostasis to a certain degree, even if there is a shortage in the body or an excess. For example; magnesium is mobilised from bone if necessary to maintain a steady serum level. This implicates that, although serum levels are within normal range, the metabolism at tissue level may be altered in disease and may possibly lead to biological relevant effects.

2. Folic acid may be the most important item to discuss. This item is now discussed separately in the discussion and a reference to another study of our group is highlighted.

3. Difference what is reported in table 2. and that what is reported in the text (calcium intake). Indeed this was a mistake. It is corrected.

4. Suggestion to determine which foods are the major sources of magnesium, protein, MUFA, copper and folic acid in the MS patients group as compared it to the general population.

Unfortunately, this comparison was not possible since we had no data on specific food sources for the general population. Furthermore, we decided to focus on the nutrient intake, and not specific on which foods were eaten, because a specific nutrient may be linked more easily to a certain biological effect. To provide the reader with more information, however, we inserted more information in the discussion on which foods contain magnesium, protein, MUFA, copper and folic acid.

5. Conclusion 'dietary counselling seems necessary to find and treat nutritional deficiencies in MS patients' is a strong recommendation with little supportive data. We agree with the reviewer and weakened this conclusion.

6. Hypothesize that present diet would affect disease subtypes? Yes, we assumed that this would happen, based on the assumption that their present day diet reflects their diet over the past years.

7. Differences and similarities between subtypes must be explained more in detail. This was done.

Rationale for comparing subtypes? For MS patients disease modifying drugs, such as beta interferons, are used in an attempt to modify the disease course. These medications are prone for side effects, and should be used cautiously.

Patients may be treated unnecessary while there is a prospect of a benign course. If dietary intake can be related to disease course severity, it might be a way to influence the course of MS as an alternative or complementary strategy.

8. Table 2. Consider using kcal for better comparison of protein, SAFA, MUFA, PUFA, total fat, linoleic acid, carbohydrate. This was done (see table 2.) Total kcal would be useful. This was calculated and inserted in the Table.

9. Discuss why serum levels did not correlate with intake. See above.

10. Verify chemical names of vitamins are correct. This was verified.

11. Carbon hydrate = carbohydrate? Yes, this was corrected.

12. Abbreviation of magnesium (mg) is not consistently used. This was corrected.

13. Paper should be checked for spelling errors. This was done.

Reviewer S. Schwarz

1. Problematic group selection. Relapsing- remitting patients without a 'benign' course were not included.

We decide not to include this group, because this group contains patients with a disease duration of less than 10 years. It may be that these patients switch to a secondary progressive state and need to be included in the SPMS group; it may also be that these patients after ten years show minimal disability and should be included in the 'benign' group. Since we cannot determine this, the data of their dietary habits could not be used for this study.

Control group of age and sex matched were not included. We used matched controls from our data of the Dutch population.

Small group size with regard to variability of dietary habits. Indeed the groups are not very large, but are similar to other studies on dietary habits in MS patients. We decided to measure dietary intake over a relative long period (14 days) to be sure that our intake data would be more accurate. Furthermore, we did find significant differences, even after the statistical Bonferroni correction, making our results interesting and important despite the small group size.

2. Method how food diary was structured and analysed is not well explained. This is now explained in the materials and methods section.

Computerized analysis were performed based on a validated Dutch nutrient database. Is this procedure generally accepted? Yes it is validated, kept up to date, and generally accepted and used by health care workers in The Netherlands such as dietary counsellors and software providers.

3. Did authors analyse food supplements? Yes we did, but we could not correlate the use of supplements to a certain disease course. Per group, only a few patients used them and were mostly herbal-based products. This information is now entered in the article.

4. Co-morbidity as factor? We analysed if co-morbidity was a factor but we could not relate dietary intake to the presence of co-morbidity. This information is now in the manuscript.

5. BMI is a problematic parameter of nutrition. We agree with the reviewer, we used the BMI only to assess the incidence of over- or underweight.

6. Explanation why serum levels did not differ and intake did. See above (reviewer Spach).

7. Secondary progressive MS patients have higher rate of disability and this may explain the results. As can be observed in table 1, the disability as measured by the EDSS does not differ between the SPMS group and the PPMS group. It seems unlikely that this absence of difference would explain the significant differences found in nutritional intake.

8. Authors should make more clear that relations between MS and dietary factors are still hypothetical. This is made more clear in the article (introduction).

We feel that the quality of the revised paper has improved and hope it will be suitable for publication.

Please let me know if you need any more information,

Awaiting your reply, I remain,

Sincerely,

Dr. G. Ramsaransing

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