Author's response to reviews

Title: Circulating adiponectin levels are lower in Latino versus non-Latino white patients at risk for cardiovascular disease, independent of adiposity measures

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Version: 2 Date: 10 May 2011

Author's response to reviews: see over
May 10, 2011

Tim Shipley, PhD
Executive Editor
BMC-series Journals
BioMed Central

RE: MS 7775176915006402

Dear Dr. Shipley,

Please find attached our revised manuscript originally entitled “Circulating adiponectin levels are lower in Latino versus non-Latino white patients independent of adiposity measures: a cross-sectional study”. We appreciate the reviewers’ comments and have made the following changes in response:

Reviewer 1

1. The cohort needs to be stratified according to gender. The cohort has now been stratified according to gender and the ethnic-specific differences in total adiponectin remain significant. Clinical characteristics in the cohort stratified by gender and ethnicity are presented in revised Table 1. As presented in the original manuscript, the multivariate analyses controlling for gender demonstrate that the lower levels of adiponectin observed among Latinos are not due to a greater representation of males in this group.

2. If the cohort is separated by gender, include a sample size calculation in the data analysis part. We are a bit unclear about this request. Ours is a post-hoc analysis, and therefore our initial sample size calculation was based on a CVD outcome and not on adiponectin. In response to the reviewer’s request, we were able to find two previously published reports comparing total adiponectin in Hispanics and non-Hispanic whites and used these to do the following sample size calculations for our study. A Diabetes Prevention Program analysis by Mather et al. (Diabetes 2008, 57(4):980-6) reports adiponectin levels in individuals with pre-diabetes. Doing a sample size calculation using the natural log of reported adiponectin values, we calculated that we would have needed 2666 males and 1902 females in our study to have 80% power to detect a similar difference, with an alpha error of 0.05. A second published comparison of pre-menopausal females (where the Hispanic females had significantly higher BMI than the non-Hispanic females) showed a larger difference in adiponectin levels. We would have needed 4 females in our study to observe a similar difference between the two groups. A sample size calculation based on our own adiponectin measurements did not seem to make
sense given that our sample size was large enough to observe a significant
difference between the groups. We have not included this additional data in the
manuscript, but would welcome any further guidance from the reviewer regarding
this point.

3. **Revise the title as the cohort is not representative of the population.** The title of
the manuscript has now been changed to “Circulating adiponectin levels are lower
in Latino versus non-Latino white patients at risk for cardiovascular disease,
independent of adiposity measures” to more accurately reflect the population
studied.

Reviewer 2

1. **Show adiponectin levels in males and females separately, for example, in Figures
2 and 3.** We now include Supplemental Figures 2a and 3a with data for males and
females in each ethnic group presented separately. Due to the small number of
subjects in each group (especially the male groups) when the data are presented in
this way, the regression lines shown may be less informative. With this caveat in
mind, when the data are separated by gender, it becomes evident that our
observation of an expected inverse relationship between adiponectin and waist
circumference in the non-Latino group but not the Latino group is driven by the
men (Supplemental Figure 2a). Whereas the expected relationship between the
two variables are observed in the females in both ethnic groups. This additional
finding has been added to the Results and Discussion sections. Looking at
adiponectin plotted by BMI, our observation of decreased adiponectin in Latinos
versus non-Latinos at any given BMI holds true, except at the higher BMIs in the
men, where men in both ethnic groups have low adiponectin (Supplemental
Figure 3a).

Reviewer 3

1. **The results of this study would bear much more weight if healthy control groups
were included.** If it is impossible to include data from healthy/lean controls, then
the conclusion should be changed to: “We report decreased adiponectin levels in
Latinos at increased risk of cardiovascular disease, when compared to non-Latino
whites, independent of adiposity measures”. We are unfortunately unable to
include healthy control groups. The recommended wording change has been made
in the conclusion section.

2. **The obesity variance in both Latino and non-Latino groups were perhaps too
small to truly investigate the association between e.g. BMI or WC and
adiponectin.** It is quite strange that no significant association between BMI and
adiponectin were found in any group, which may make one doubt the data a bit.
However, it is perhaps the fact that both groups were quite obese. This should be
addressed in the Discussion. No significant association was found between
adiponectin and BMI on univariatate analysis. However, when included in the
multivariate analyses, BMI (per 5 kg/m$^2$) **was** significantly associated with both total and HMW adiponectin. We believe that the lack of association between adiponectin and BMI on univariate analysis is likely due to the very heterogenous population studied. In other words, a number of variables other than BMI influence adiponectin, and these need to be taken into account in order to measure the isolated association of BMI and adiponectin. When we control for these variables in the multivariate analyses, the expected association between BMI and adiponectin is apparent. This observation has now been added to the Discussion.

Reviewer 3 Discretionary Revisions- The following additional changes have been made as recommended by Reviewer 3.

1. The Introduction section has been shortened and the last paragraph of the original Introduction section has been removed.

2. Abbreviation legends have been added to the bottom of tables.

3. Figure 1- p-values have been added. Y-axis label has been changed to “Total Adiponectin”.

4. Figure 3- icons have been changed to better distinguish between the two ethnic groups.

We greatly appreciate the reviewer’s comments and suggestions and believe the recommended changes have significantly improved our manuscript. We thank all individuals involved for their time and effort.

Sincerely,

Rocio I. Pereira, MD
And Co-authors