Author's response to reviews

Title: Fibroblast growth factor-23 and calcium phosphate product in young chronic kidney disease patients: A cross-sectional study

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Version: 4 Date: 7 February 2013

Author's response to reviews: see over
Dear Dr. Henderson,

Re: MS: 8033286026865782

Thank you for reviewing our manuscript and for the editor's and reviewers’ comments. Please find our comments and responses to the concerns below. For added clarity about the point-to-point reply, we have first repeated the requests then added our comments in *italics*, and changes to the manuscript were indicated in [highlighted text](#). We hope that the edited manuscript is now acceptable for publication and wish to resubmit.

**Reviewer(s)' Comments to Author:**

Reviewer: 1

1. Please specify whether the children analyzed in the present work have been recruited from earlier cohort studies (such as Wong H: Prevalence of complications in children with chronic kidney disease according to KDOQI. *Kidney Int* 2006, 70:585-590), or whether they specifically recruited for the present analyses?
We would like to thank the reviewer for the careful review of our manuscript and its agreement with the new statistical results. This cohort of patients was recruited in another center in London, Ontario, while the previous one in the mentioned study was recruited in Ottawa, Ontario. While both populations seem similar, in fact, they are totally different patient cohorts. We did not perceive a change in the manuscript was necessary for this question. Please advise if you see otherwise.

2. The statements "As the presence of vascular calcifications was an exclusion criterion, our data would suggest that FGF-23 is associated with calcium phosphate metabolism disorders, and not with aortic calcifications." needs revision. First, we do not know whether patients were free of calcification (as hopefully not all patients underwent X-ray examination). Moreover, any association of FGF-23 with calcium phosphate will not exclude an association of FGF-23 with calcification.

We agree with the reviewer, and in fact, only 32 patients had an x-ray of the chest to assess for vascular calcification. We verified that none of the patients included in the study had any calcifications. We added this information to the results section. It reads:

X-rays were performed in 32 of the patients, with 100% of patients in the two highest stages of CKD. None showed calcifications.

We also changed the comments in the discussion. They now read:

Our data would suggest that FGF-23 is associated with calcium phosphate metabolism disorders, and not necessarily with aortic calcifications, although we have to acknowledge the limitation that only 32 patients had a chest x-ray. With this limitation, our data would support the interpretation by Kojima et al. [9].

3. "Therefore, FGF-23 levels may provide a reliable marker of calcium and phosphate imbalance. It may be easier to measure a single biomarker, and its association with endothelial dysfunction and cardiovascular outcome [13] make it an attractive marker." should be deleted. The authors found some correlation between FGF-23 and calcium-phosphate balance. They did not test whether FGF-23 is a valid indicator of CKD-MBD imbalance. Such statement would require much more solid data, including testing for sensitivity and specificity. Finally, FGF-23 measurement is much more expensive than calcium and phosphate measurement. Why should it be "easier" to determine FGF-23 than conventional lab values such as Ca / phosphate?

We agree that in fact FGF-23 measurement is much more complicated than the simple calcium phosphate product. We have recently experienced the difficulties in getting measurements in Ontario for clinical reasons in a family with autosomal dominant hypophosphataemic rickets. However, we don't agree with completely deleting the two sentences. We changed the two sentences into one sentence that now reads:
FGF-23 levels may provide an additional marker of the morbidity and mortality of Ca*P as it is associated with endothelial dysfunction and cardiovascular outcome [13].

4. Calcium, phosphate, vitamin D, PTH and FGF-23 should be labeled CKD-MBD parameters rather than "markers of renal osteodystrophy".

We would like to thank the reviewer for his suggestion and change in the manuscript has been done accordingly. The following changes have been made to the manuscript as follows:

- The second line of page 11 now reads:
  A prospective, longitudinal study is required to further delineate the relationship between GFR and CKD-MBD parameters.

- The first line of the conclusion paragraph on page 12 now reads:
  In conclusion, the current study describes FGF-23 in relationship to other CKD-MBD parameters in 81 CKD patients (the first line in the conclusion paragraph, page 12).

Reviewer: 2

Table 3 in the title says patients <13 years of age and >13 years of age but in the table says <12 or >12

We would like to thank the reviewer for turning our attention to this typo. We apologize for this mistake. The groups of patients were in fact two, the first one up to but not including the age of 13 and the second one age 13 and older. As such, corrections have been made to the table and it reads <13 and >13

Sincerely

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