Author's response to reviews

Title: Increased Vertebral Morphometric Fracture in Patients with Postsurgical Hypoparathyroidism Despite Normal Bone Mineral Density

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Version: 2 Date: 30 November 2012

Author's response to reviews: see over
Ms Babyllynne Barretto  
The BioMed Central Editorial Team Editor  
Clinics  
RE: BMC Endocrine Disorders MS: 1059320223789255

Dear Ms Barretto,

Thank you for your message related to the above mentioned manuscript. We appreciate the opportunity of submitting a revised version of the manuscript that has incorporated the constructive comments of the expert reviewers.

Reviewer #1

1. **The title does not well reflect the indeed very new and spectacular result that despite normal or high BMD at the spine, the incidence of vertebral fractures is higher in PhPT.**

   - Thanks for your comment related to our study. We accepted the suggestion and in the current version of the MS the title is: “Increased Vertebral Morphometric Fracture in Patients with Postsurgical Hypoparathyroidism Despite Normal Bone Mineral Density.

2. **“Primary hypoparathyroidism” should be replaced as it may be misleading and interpreted as idiopathic hypoparathyroidism while all included patients have postsurgical permanent hypoparathyroidism.**

   - We carefully revised the text of the manuscript and changed Primary hypoparathyroidism to Postsurgical hypoparathyroidism in the Short title and Key words and in: p. 11; l. 7; p.13, first paragraph, p. 17 ls.17, 21 and 23)

3. **Discussion “while osteoporosis is rare” needs to be clarified further because the presence of vertebral fractures imply osteoporosis. The authors mean “T-Score > 2.5” or “low BMD”**

   - We agree with the reviewer and we have reformulated the sentence as follows: The present study demonstrated that patients with PhPT have marked heterogeneity in lumbar spine BMD, usually exhibiting high or normal bone mass, while densitometric osteoporosis is uncommon (p. 13, ls 12-14).

4. **It is a limitation that all patients showed normal serum 25(OH)D levels without treatment because this is possibly not the case in other countries than Brazil.**

   - We agree with the reviewer. Thus, we added a comment regarding this particular point (p. 17, ls. 5-9): In agreement with these results, we did not observed a high frequency of hypovitaminosis D in this region of the state of São Paulo, Brazil, in previous studies [34,35]. As vitamin D deficiency is associated with worse bone outcome, it is likely that our groups were in advantageous conditions compared to other populations with a higher incidence of vitamin D deficiency [36].
5. Have the authors also data on clinically evident fractures since the patients became hypoparathyroid?

One individual from the hypoparathyroidism group had a fracture in the proximal humerus. This information was added to the manuscript (p.13, first paragraph of the discussion section): A previous nonvertebral fracture was present in one patient of the PhPT group, while no individual of the control group sustained clinical fracture.

6. Is there a correlation between duration of PhPT and vertebral fractures?

No, there was no correlation between these parameters (p=0.70). We added this result to the text (p.13, ls.2 and 3): However, there was no correlation between the duration of postsurgical hypoparathyroidism and vertebral fracture.

Minor
1. Fig 2: could you give R2 and the extrapolated line?
   -As requested, we added this information to figure 2 (extrapolated line) and to its legend (R2).

2. “and no woman had premature ovarian failure.” Is redundant in the Results Section.
   The suggestion was accepted. The redundant information was deleted from p.11, l.4.

3. The given duration of primary hypoparathyroidism does not exactly match between Results and Methods section.
   -Thanks for your detailed revision; we corrected the duration of postsurgical hypoparathyroidism in the Results section (p. 11, l. 7)

4. Is it really true that the much larger absolute difference in BMD of the lumbar spine (CG = 0.970 ± 0.153 vs PhPTG = 1.088 ± 0.250 g/cm) is not significant while the one at the radius is (CG = 0.630 ± 0.07 vs PhPTG = 0.570 ± 0.09, P < 0.05)? Also, is in both cases SD given? (such a difference!?).
   -We agree with the reviewer that these results call the attention of the reader. This aspect motivated us to show the results of BMD measurement in a scatter plot graph (Figure 1). The Figure shows a greater variation in lumbar spine BMD in comparison to the 1/3 radius. Yes, in both cases the results are expressed as mean ± SD.
Reviewer #2

1: **Obviously patients and controls were not matched for L-thyroxine intake. Have the authors taken into account the serum TSH levels and included this in the regression analysis? Do they consider this could have added to the altered Morphometry.**

Thanks for calling attention to this relevant point. We added the data about TSH in PhPT group and analyzed its influence on the regression analysis (P.11; first paragraph of the results section).

There were no differences in the results after adjustment for serum TSH levels.

2- **What is the reason of comparable serum 25(OH)D to the extent of normal values in both control and postsurgical hypoparathyroidism. I presume patients were on oral elemental calcium. Does the oral calcium contained vitamin D in their country. Often calcium tablets have some vitamin D in the formulation.**

The patients had prescription of calcium carbonate without vitamin D. In previous studies we had not observed vitamin D deficiency even in patients harboring diseases such as leprosy (Am J Med Sci. 2007 Nov;334(5):322-6). Since this is a very important subject, we added the following comment to the Discussion section (p. 17; ls. 7-11): In agreement with these results, we did not observed a high frequency of hypovitaminosis D in this region of the state of São Paulo, Brazil, in previous studies [34,35]. As vitamin D deficiency is associated with worse bone outcome, it is likely that our groups were in advantageous conditions compared to other populations with a higher incidence of vitamin D deficiency [36].

3: **The authors should include into the discussion the clinical significance of their findings in terms for the advise to the medical community while following patients with postsurgical hypoparathyroidism.**

-We agree with the reviewer. A comment about this topic was added to the first paragraph of the discussion section: These results are of a great significance in the clinical setting since these data correspond to the first evidence of increased risk of fractures in postsurgical hypoparathyroidism. Therefore, these preliminary results encourage further investigation of the etiopathogenesis and prevalence of this condition and a more appropriate approach to the management of this particular group of patients.

4: **Some assessment of power calculation of the study sample size is warranted.**

As requested, we added the following comment (p.10, last paragraph): Considering the method described by Hsieh et al. [22] for determining the sample size required for the estimation of a correlation coefficient and for linear regression models, a sample of size 16 is sufficient for estimating a correlation coefficient equal to 0.65, with a level of significance of 0.05 and a power of 0.20. Thus, it was established that the sample size in each group should be at least 16.
Thanks for your constructive comment.

We trust that the above-mentioned changes will make the manuscript suitable for publication in BMC Endocrine Disorders. Should you have any additional question, please do not hesitate to contact us.

Yours sincerely,

For the authors,

Maira L. Mendonça