Author’s response to reviews

Title: Obese adolescents exhibit a constant ratio of GH isoforms after whole body vibration and maximal voluntary contractions

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Author’s response to reviews:

Dear Prof. Gutiérrez-Juárez,

We thank you and the Referees for the careful evaluation and appreciation of our manuscript entitled: “Obese adolescents exhibit a constant ratio of GH isoforms after whole body vibration and maximal voluntary contractions” by Rigamonti et al. (BEND-D-18-00323R1).

All the suggestions raised by the Referees aimed to improve the quality of the manuscript have been taken care of and the necessary amendments have been incorporated into the revised version.
Here enclosed please find the revised version of the manuscript together with a report containing the responses to the comments.

We are confident that the manuscript may be now suitable for publication in BMC Endocrine Disorders.

Sincerely yours

Antonello Rigamonti

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Manuel H Aguiar-Oliveira (Reviewer #1)

We thank the Referee for the evaluation and appreciation of our manuscript.

Q1. I still suggest a language review. I doubt if the sentence "and only 22kDa-GH peak after MVC+WBV than MVC ", is the best writing, and so on.

A1. The manuscript has been revised by an English teacher. The paragraph indicated by the Referee has been reworded (pag. 7 – lines 55-59; pag. 8 – lines 1-2).

Q2. Line 51 of introduction. I prefer the word hyperglycemic than diabetogenic. The reference 30 could be anticipated to this sentence.

A2. We have replaced "diabetogenic" with "hyperglycemic" in two points of the text (pag. 3 – line 53; pag. 9 – line 37).

As suggested, Ref. 30 has been anticipated in the Introduction (now Ref. 15).

Q3. Lines 57 and 58 of discussion "circulating levels of some GH isoforms, particularly 22kDa- and 20kDa-GH, are increased after acute exercise" may be replaced with: " circulating levels of 22kDa- and 20kDa-GH isoforms are increased after acute exercise", to be more precise.

A3. We have now reported the sentence suggested by the Referee (pag. 8 – lines 20-22).

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Nigel Glynn (Reviewer #2)

We thank the Referee for the comments we have used to improve our manuscript.
Q1. The results are interesting; however, I believe the authors need to be more guarded about their conclusions particularly in view of the highly selected small cohort studied.

A1. Taking into account the limited number of the subjects recruited in the study, we have toned down the conclusions in the Abstract and in the final part of the Discussion. Please, note that this limitation of our study had been pointed out in the Discussion (pag. 10 – lines 22-24).

Q2. The Methods section should provide greater explanation and justification for the selection of this patient cohort.

Why were only male subjects recruited - was this a pre-specified inclusion criterion or did it occur during open, unselected recruitment?

Why were adolescents chosen as the research group as opposed to adults?

A2. We have originally determined to select only male subjects as a pre-specified criterion of inclusion due to the well-known effects of female sex steroids on GH secretion and the difficulty to perform the three exercise protocols in the same phase of the menstrual cycle. This aspect has been now clearly stated in the Methods (pag. 4 – lines 46-51).

We have recruited adolescent subjects since they are usually more responsive to pharmacological and physiological GH stimuli than adults. This aspect has been now stated in the manuscript (pag. 8 – lines 18-20).

Q3. The authors claim that the results will be applicable to doping test for GH in athletes who have a high BMI. However, it would seem that a sedentary obese teenager is very different to any athlete, regardless of BMI. Can the authors provide any further justification for these claims?

A3. We agree with the Referee: obese "sedentary" adolescents cannot be equated to obese "athlete" adolescents. Consequently, we have better circumstantiated our proposal to use the results of the present study in an antidoping setting. In particular, we have stated that the results are preliminary and that a more appropriate cohort of obese athlete subjects should be recruited in future studies (pag. 10 – lines 47-51).

Q4. Furthermore, the methods mention that the subjects were undergoing an "integrated body weight reduction program".

What does this program involve? Were the subjects restricting calories?

A4. We apologize for not having specified that the present study was carried out before starting the integrated body weight reduction program for which the obese subjects were hospitalised. This (important) aspect has been now specified in the Methods (pag. 4 – lines 31-37). So, any
carry-over effect of a potential weight loss or modifications in diet and physical activity is excluded a priori.

Q5. Were they confirmed to be euthyroid and eugonadal? If so, this data should be provided.

Did any have diabetes or glucose intolerance? Did any have Prader-Willi syndrome?

A5. Thyroidal (TSH and free T4 levels) and gonadal functions (LH, FSH, testosterone levels) were normal in all the subjects (data not shown).

Diabetes mellitus, including glucose intolerance, was excluded by a 75 g oral glucose load, while Prader-Willi syndrome was excluded by clinical history, physical examination and FISH detection of chromosome 15 deletions. See pag. 4 – lines 42-46.

Q6. The authors could expand the discussion regarding the phenomenon of low serum GH concentration in obesity.

A6. As requested, we have expanded the part of the Discussion regarding the hyposomatotropism in obesity. Being constant the ratio of GH isoforms in circulation, obese state causes a “quantitative” rather than a “qualitative” alteration of GH secretion. See pag. 8 – lines 49-57.

Q7. Page 4, line 53: Should be "per diem"

A7. We apologize for the misprint, which has been corrected.

Q8. The authors use the term "Anyway.." at the beginning of many sentences throughout the text. This should be reworded.

A8. As requested, we have limited the use of the term "anyway" throughout the text.