OPEN PEER REVIEW

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Peer Review Report for "Comparison of the Effects of Two Different Intensities of Combined Training on Irisin, Betatrophin, and Insulin Levels in Women with Type 2 Diabetes"

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Review Timeline:

Submit Date: 27 Mar 2018
Revised Date: 18 Mar 2019
Accepted Date: 31 Mar 2019

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (0)

29 Sep 2018

Dear AE,

- General comment (originality, scientific accuracy, strengths and/or weaknesses): In this work, authors tried to compare the effects of two different intensities of combined exercises on the level of three hormones related to obesity and its comorbidity. What the authors reported is not yet well known, so high level of novelty. However, the manner in which this manuscript was presented, and some other reservations, does not allow us to advance a definitive judgment regarding its publication in The Asian Journal of Sports Medicine. Thereby, authors are invited to provide more effort in the preparation of their manuscript and to provide all necessary information to make it clear and readable by persons who are specialist or non-specialist in sports medicine.

Major comments:

- The introduction is too long. It should be rewritten in a way that emphasizes the importance of such study and advance the problematic in a clear way.
- A native English-speaking person must go over the manuscript in order to re-write some sentences and correct some grammatical errors.
- The "Patients and Methods" section should be structured as follows: Subjects, Study

Design, Outcomes and assessments, Interventions, and Statistics.

- Authors compared the initial and final concentrations of Irisin, Betatrophin and Insulin. In my view, this is not very expressive, and comparisons should be made on modifications expressed in percentage.
- The methods used to measure Irisin and Betatrophin should be summarized.
- Training protocol is too long and needs some clarifications.
- Several references are missing.
- The discussion needs to be shortened, it is far too long and it needs to be more focused on the important aspects of the paper.
- References should be presented in the text and at the end of the manuscript according to The Asian journal of Sports Medicine recommendations.

Thanks,

REFEREE: Reviewer | **Revision** (0) 6 Dec 2018

Dear AE,

Thanks to the authors for this research in the field of exercise in diabetic patients. The physical activity and structured exercise program have an important role in the prevention and management of DM.

However, in the methodology of the trial- in exercise prescription section- some errors are seen. - According to the ACSM's guideline, the intensity of exercise has been defined as low intensity: lower than 40% HRR (or lower than 64% MHR), moderate intensity: between 40-60% HRR (or between 64-76% MHR) and high intensity: upper than 60%HRR (or upper than 76% MHR). Therefore, in the present trial, the prescribed exercise in the two groups was low intensity and high intensity. Consequently, the related terms through the manuscript need to be revised.

- According to the existing evidence, low-intensity aerobic exercise has little effect on diabetic status. On the other hand, the high-intensity exercise prescription needs doing maximal exercise test for patient safety before non-supervised or even supervised exercise program. In sum, it seems that the exercise prescription and methodology have some faults.

Some minor comments are added in the following:

- The preparation of the manuscript needs revision according to the journal guideline.
- Frequently, the mistakes in the use of terms are seen in the manuscript, for example: "Endurance trainings were performed using an elastic band during 2 days/week for 8 weeks- in page 8", in general, the definition of training with elastic band is a resistance training. Another example in page 12: "In sum, the results of the present research showed that combined exercises can lead to the elevated irisin hormone level (P<0/05) that is 88.4% in high-intensity exercises and 367% in moderate intensity exercises", please check the presented numbers.
- The heart rate monitoring is not a good choice for calculating exercise intensity, especially in diabetic patients.
- The first paragraph of the summary is a section of introduction. Please delete the mentioned paragraph.
- Paper massage is not relevant to the primary and secondary outcomes

Thanks.

REFEREE: Associate Editor | **Revision** (0) 3 Jan 2019

Dear EIC,
This manuscript was reviewed by our reviewers. The reviewers have raised concerns regarding the manuscript, and therefore, the paper is not acceptable for publication in this format. However since the reviewers do find some merit in the paper, I would be willing to reconsider if the authors wish to undertake major revisions and re-submit, addressing the referees' concerns.
Thanks.

REFEREE: EIC | **Revision** (0) 3 Jan 2019

Dear Author,
Thank you for submitting your manuscript to Asian J Sports Med. I now have the reports of the Referees, which suggest that your manuscript might be suitable for publication following a number of revisions. I attach some reviewer comments and invite you to submit a revised version of your manuscript addressing the points made.
Thanks.

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

We would like to thank Reviewers #1 and #2 for completing the review of our manuscript. We believe that the extensive changes that have been made to the manuscript in response to these comments have improved it considerably. In order to clarify how we have responded to the reviewers' comments, we have cut-and-pasted each of their comments below and have then responded to each one, explaining how the comment has been addressed in the revised manuscript.

Reviewer 1:

General comment (originality, scientific accuracy, strengths and/or weaknesses): In this work, authors tried to compare the effects of two different intensities of combined exercises on the level of three hormones related to obesity and its comorbidity. What the authors reported is not yet well known, so high level of novelty. However, the manner in which this manuscript was presented, and some other reservations, does not allow us to advance a definitive judgment regarding its publication in The Asian Journal of Sports Medicine. Thereby, authors are invited to provide more effort in the preparation of their manuscript and to provide all necessary information to make it clear and readable by persons who are specialist or non-specialist in sports medicine.

Major comments:

- The introduction is too long. It should be rewritten in a way that emphasizes the importance of such study and advance the problematic in a clear way.

>> Thank you very much for your comment. We tried to address your comments and introduction was summarized thorough the manuscript.

- A native English-speaking person must go over the manuscript in order to re-write some sentences and correct some grammatical errors.

>> Many thanks for your attention; the manuscript was edited with native edition by iranvirayeshcenter

- The "Patients and Methods" section should be structured as follows: Subjects, Study Design, Outcomes and assessments, Interventions, and Statistics.

>>Methodology was revised and corrected.

- Authors compared the initial and final concentrations of Irisin, Betatrophin and Insulin. In my view, this is not very expressive, and comparisons should be made on modifications expressed in percentage.

>> The comparison of concentrations of Irisin, Betatrophin and Insulin was expressed in percentage.in discussion section as " In sum, the results of the present research showed that combined aerobic and resistance training led to elevated irisin hormone levels ($P < 0.05$): by 88.4% in the high-intensity training group and by 36.7% in the moderate-

intensity training group. Additionally, combined training resulted in a rise in the betatrophin hormone level ($P < 0.05$). The serum level of the betatrophin hormone rose by 67.3% in the high-intensity training group and by 1.6% in the moderate-intensity training group. The level of insulin was also increased as a result of combined training in our 2 training groups ($P < 0.05$): by 100.2% in the high-intensity training group and by 56.7% in the moderate-intensity training group.

>> measuring Irisin and Betatrophin was summarized.

- Training protocol is too long and needs some clarifications.

>>Thank you very much for your comment. Training protocol was summarized.

- Several references are missing.

>>all references were corrected.

- The discussion needs to be shortened, it is far too long and it needs to be more focused on the important aspects of the paper.

>> The discussion was shortened.

- References should be presented in the text and at the end of the manuscript according to The Asian journal of Sports Medicine recommendations.

>>>>all references were corrected.

Reviewer 2:

Dear authors, thank you for your research in the field of exercise in diabetic patients. The physical activity and structured exercise program have an important role in the prevention and management of DM.

However, in the methodology of the trial- in exercise prescription section- some errors are seen. According to the ACSM's guideline, the intensity of exercise has been defined as low intensity: lower than 40%HRR (or lower than 64% MHR), moderate intensity: between 40-60% HRR (or between 64-76% MHR) and high intensity: upper than 60%HRR (or upper than 76% MHR). Therefore, in the present trial, the prescribed exercise in the two groups was low intensity and high intensity. Consequently, the related terms through the manuscript need to be revised.

According to the existing evidence, low-intensity aerobic exercise has little effect on diabetic status. On the other hand, the high-intensity exercise prescription needs doing maximal exercise test for patient safety before non-supervised or even supervised exercise program. In sum, it seems that the exercise prescription and methodology have some faults.

>> Thank you for your remark. At first, all patients were given permission to practice. Also During the training, all diabetic patients were under the supervision of a physician and the physician reduced the dose of insulin injections. Furthermore According to previous studies by McGarrah RW et al (2016) and Hordern MD et al (2012), The combined moderate-intensity training group performed aerobic exercises, comprised of walking at 55% to 69% of the maximum heart rate (HRmax) over the 8-week. These exercises were performed at 12 to 13 ratings of perceived exertion (RPEs) for 150 minutes per week, each session for 30 minutes. Resistance training was performed using colored resistance bands 2 days per week for 8 weeks. The subjects were recommended to take 10 to 15 g of carbohydrate before training to prevent hypoglycemia. The combined high-intensity training group performed aerobic exercises, comprised of walking or running fast at 70% to 89% HRmax and at 14 to 16 RPEs for 75 minutes for 5 days. In each training session, the aerobic exercises lasted for 15 minutes. Resistance training was performed using colored resistance bands for 2 days per week for 8 weeks (10, 11).

10. McGarrah RW, Slentz CA, Kraus WE. The effect of vigorous-versus moderate-intensity aerobic exercise on insulin action. Current cardiology reports. 2016;18(12):117.
11. Hordern MD, Dunstan DW, Prins JB, Baker MK, Singh MAF, Coombes JS. Exercise prescription for patients with type 2 diabetes and pre-diabetes: a position statement from Exercise and Sport Science Australia. Journal of Science and Medicine in Sport. 2012;15(1):25-31. Some minor comments are added in the following:

-The preparation of the manuscript needs revision according to the journal guideline.

Thank you very much for your comment. We tried to address your comments and manuscript was revised according to the journal guideline.

-Frequently, the mistakes in the use of terms are seen in the manuscript, for example: “Endurance trainings were performed using an elastic band during 2 days/week for 8 weeks-in page 8”, in general, the definition of training with elastic band is a resistance training. Another example in page 12: “In sum, the results of the present research showed that combined exercises can lead to the elevated irisin hormone level (P<0/05) that is 88.4% in high-intensity exercises and 367% in moderate intensity exercises”, please check the presented numbers.

>> Apologize, it was corrected and now reads as: "Resistance training was performed using colored resistance bands for 2 days per week for 8 weeks" And " In sum, the results of the present research showed that combined aerobic and resistance training led to elevated irisin hormone

levels ($P < 0.05$): by 88.4% in the high-intensity training group and by 36.7% in the moderate-intensity training group"

-The heart rate monitoring is not a good choice for calculating exercise intensity, especially in diabetic patients.

>> Thank you for your remark. According to the ACSM's guideline, and The American Diabetes Association and previous studies by McGarrah RW et al (2016) and Hordern MD et al (2012), we use MHR and RPE to monitor exercise intensity.

-The first paragraph of the summary is a section of introduction. Please delete the mentioned paragraph.

Thank you very much for your comment. The mentioned paragraph were deleted.

OPEN PEER REVIEW

Revision (1)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Associate Editor | **Revision** (1) 15 Mar 2019

Dear EIC,
Please rearrange references number. References should be cited in the text consecutively. (reference 8, 9, 10 before references 6 and 7). Please recheck all references again.
Thanks.

REFEREE: EIC | **Revision** (1) 15 Mar 2019

Dear Author,
The second round of peer review of your manuscript is completed. I now have the reports of the Referees, which suggest that your manuscript needs more correction.
Thanks.

OPEN PEER REVIEW

Revision (2)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

We would like to thank Reviewers for completing the review of our manuscript.

- **Associate Editor's Comments:**

  Associate Editor 1:
  Please rearrange references number. References should be cited in the text consecutively. (reference 8, 9, 10 before references 6 and 7). Please recheck all references again.

Reply: all references were rearranged.

OPEN PEER REVIEW

Revision (2)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: EIC | **Revision** (2) 31 Mar 2019

Dear Author,
The third round of peer review of your manuscript has been completed, and I am pleased to inform you that your manuscript has now been accepted for publication in our journal.
Thanks.