

May 02, 2018

Science Editor, Professor Li-Jun Cui
World Journal of Diabetes

Dear Editor:

I, along with my coauthors, would like to thank you for considering our manuscript, 37699 entitled "Effects of glucagon-like peptide 1 analogs in combination with insulin on myocardial infarct size in rats with type 2 diabetes mellitus" for publication in the World Journal of Diabetes as a basic science article.

Please find the revised manuscript and our response to the comments made by the reviewers.

The changes made to the text have been highlighted. We hope that the present version is acceptable for publication in the International World Journal of Diabetes.

Thank you for your consideration. I look forward to hearing from you.

Sincerely,
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Response to the comments by Reviewer 1

We would like to thank the reviewer for the constructive comments on the manuscript.

Critique: The hypoglycemia and glycemic excursion data are of little consequence and should be removed.

Response: Although the data on hypoglycemia episodes are not directly related to the subject of the study, we feel that it might be important to keep them in the text because of their relevance to the regimen of insulin administration. Therefore, we would like to advocate this part of the "Results" section and present it in slightly modified form.

Critique: An hypothesis as to why insulin pretreatment reduced infarct size should be included.

Response: Our hypothesis on the putative infarct-limiting effect of insulin pretreatment was based on the data obtained in the study of Fuglestad et al. (2009) who showed mTOR-dependent reduction in infarct size after insulin administration in the Langendorff-perfused rat heart. There are, however, studies that have not confirmed this fact. Therefore, we thought to check if insulin is really cardioprotective when administered prior to ischemia. Please find respective changes in the text (p. 10-11).

Response to the comments by Reviewer 2

We would like to thank the reviewer for the constructive comments on the manuscript.

Critique: First paragraph is not related with the work performed. Erase it and maintain only the two last lines "These blood glucose targets are very difficult to achieve using insulin monotherapy, which has a high risk of hypoglycemia and glycemic variability that can increase the risk of complications in MI[11-13]" and rephrase it to fix to the second paragraph.

Response: The correction has been performed (see p. 4).

Critique: The end of the second paragraph repeated the aim that it expressed at the end of "Introduction". Mix both aims or erase one of them.

Response: The correction has been performed (see p. 5).

Critique: Design: How were compared discrete variables?

Response: Mann-Whitney test was used to evaluate the reliability of the differences between independent variables.

Critique: Discussion: Were are the conclusions? "The ratio of the myocardial ischemic zone to the necrotic zone was the worst in the rats treated with insulin before induction of ischemia, which confirmed the superior effectiveness of the existing protocols for managing patients with T2DM using insulin therapy during MI." What want the authors mind? I do not understand this conclusion.

Response: The correction has been done (p. 11). The conclusions have been added to the text (p. 11).