

Editor,

World Journal of Diabetes

Re: Management of Critically Ill patients with Daibetes

ID #: 29789

Dear Sir/Madam

Attached please find the revised manuscript based on the reviewers comments. I hope your readership will find this interesting and educational. We like to thank the reviewers and editorial staff in advance for their time and patience.

Warm regards

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Response to Reviewers Comments

Reviewer 1:

Authors: This article shows the relevance of the variation in glucose control in critically ill patients, emphasizing the effect of hypoglycemia in mortality. The control must be done in a suitable form to the clinical status of the patient, where moderate glucose strips should be kept to a better prognosis. In several states there is still no consensus on the range of glucose for critically ill patients, but that it can be concluded is that there is a consensus that hypoglycemic conditions is more harmful than hyperglycemia per se. So, they consider that further randomized control studies are suggested to further evaluate the variability in the target blood glucose level among different conditions. This study has a relevance in search of appropriate guidelines for glycemic variation in various clinical states in both diabetics and non-diabetics

Response 1: We appreciate the reviewer's comments. We have added a section in the conclusion that states the current status of evidence and guidelines as well as the need for further randomized control studies.

Reviewer 2:

The authors have given an overview about the importance of diabetes in critically ill patients. The manuscript requires certain important modifications as suggested below: 2) Abstract: The recommendation to maintain blood glucose above 200 in patients with A1c above 7% is not as per the standard guidelines on the subject. This is rather incorrect as it may lead to worse outcomes.

Response: We appreciate the reviewers' vigilance in this regard. That typo has been modified and corrected. Abstract has been modified to reflect those changes in the text.

Core tip: The term looser glycemic control is inappropriate. The optimum range of glucose is mentioned correctly. Please modify the sentence.

Response: We appreciate the reviewer comment. We have modified as suggested in the document from looser to moderate.

Introduction: You focused mostly on the stress hyperglycemia which is a minor component of the problem or the purview of your title. "Management of critically ill with diabetes" involves the pathophysiological alterations, dietary modifications, effects of the drugs and insulin, glycemic variability etc. Please modify accordingly.

Response: We agree with the reviewer comment and introduction has been modified to reflect those changes.

Epidemiology: OK

Response: Thanks

Pathophysiology: Please give a table about the factors leading to hyperglycemia and also hypoglycemia in critically ill patients.

Response: We appreciate the reviewer input. We have added a table pertaining to the factors, leading to hyperglycemia and hypoglycemia.

Stress induced hyperglycemia: Use either HgA1c or HbA1c throughout the manuscript. The second follow up study from the Belgium group was in medical ICU and not in the surgical ICU as mentioned.

Response: We appreciate reviewers' attention to detail. We agree with the reviewer. We have formatted in consistent manner in the manuscript and also have change to medical ICU as it was a typo error.

Glycemic variability: The importance of this entity as a standalone marker is not very clear in clinical practice. It is better to suggest that the same is being evaluated further. The conclusion at the end of this section is inappropriate in the absence of grade A, level 1 evidence.

Response: We appreciate the reviewer input. We have adjusted the conclusion in the section of *Glycemic Variability and Hypoglycemia* to reflect the lack of evidence in respect to glycemic variability. We have modified the manuscript to reflect those changes.

Guideline recommendations: The entire section is irrelevant as the topic is management of diabetes patients in critically ill and not vice-versa. Keep the table as a summary and remove the other portions

Response: We appreciate the reviewer liking the table. Since the summary in text is very short. We as an authors' feel that keeping in the manuscript will keep the flow and readability of the manuscript better.

10) Glycemic control therapy: OK

Response: Thanks

Conclusion: The abstract and the conclusion differ about the targets. Please reconcile.

Response: We appreciate the reviewer's suggestion and abstract has been modified to be in consistent with the manuscript and conclusion.

Reviewer 3:

The review is well written presenting the current data about the glucose management in critically ill patients. A paragraph mentioned about the real-time continuous measurement of blood glucose in these patients could be added to the manuscript (literature: PLoS One. 2016 Mar 10;11(3), Diabetes Technol Ther. 2015 Dec;17(12):889-98)

Response 3: We appreciate the reviewers' comment and have added to the section on continuous glucose monitoring as well as the article suggested.