

Institute of Endocrinology, Diabetes and Metabolism

October 16, 2021

Re: Revision of "Hypoglycemia in Diabetes" (Manuscript NO: 71309, Minireviews)

Lian-Sheng Ma, Science Editor, Company Editor-in-Chief, Editorial Office Baishideng Publishing Group Inc 7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA E-mail: l.s.ma@wjgnet.com

Dear Editor-in-Chief,

Enclosed please find our manuscript entitled "Hypoglycemia in Diabetes" that was submitted to World Journal of Diabetes.

First, we would like to thank the reviewers for their valuable comments, we feel taking them into account greatly improves our article. Below are your review comments and our responses.

REVIEWERS COMMENTS

1. Scientific Comments (reviewers and science editor comments)

Comment #1

The paper is a mini-review examining the treatment and prevention of hypoglycemia in type 1 and type 2 diabetes patients. The novelty of contents is scarce, and there are some concerns to be addressed. A comprehensive analysis of the most recent and representative papers addressing the management of hypoglycemia in type 1 and type 2 diabetes patients is lacking. Only 25% of cited papers represent publications from the recent 5 years. It should be more than 50%.

Response to comment #1

We have made a comprehensive analysis of the most relevant papers addressing the management of hypoglycemia in type 1 and type 2 diabetes patients. The review content has now been updated to include more publications from the recent five years comprising >50% of the cited papers.





Institute of Endocrinology, Diabetes and Metabolism

Comment #2

The content of hypoglycemia caused by oral drugs is suggested to be added in the introduction.

Response to comment #2

We have added the content of hypoglycemia caused by oral medications to the introduction. The changes in the manuscript are highlighted in red.

Comment #3

Does concentration also appear in neuroglycopenic symptoms? For example, some patients will repeat the same action.

Response to comment #3

Neuroglycopenic symptoms are the result of brain neuronal glucose deprivation. The glycemic threshold for neuroglycopenic symptoms is typically around 54 mg/dL [reference 13]. Unlike autonomic symptoms, the onset of neuroglycopenic symptoms usually is not affected by the counter-regulatory hormonal failure or by previous episodes of hypoglycemia [reference 14]. This paragraph was added to the manuscript. The changes in the manuscript are highlighted in red.

Comment #3

A recent systematic review and meta-analysis show that the use of artificial pancreas technology is effective and safe for patients with type 1 diabetes and leads to improved diabetes control and hypoglycemic episodes. This is a welcome system, and authors should elaborate on this system in detail.

Response to comment #3

The artificial pancreas system has been elaborated in more detail as follows. In recent years, much effort has been invested in building an "artificial pancreas"- a closed-loop system combining a real-time CGM and CSII using glucose control and safety algorithms that manage insulin delivery in a glucose-responsive manner. The use of an artificial pancreas can reduce the burden on patients by automatically adjusting the delivery of insulin based on sensor glucose levels. Both single-hormone (insulin-only) and dual-hormone (insulin and glucagon) systems have been developed. In the dual-hormone system glucagon is also delivered in a similar glucose responsive manner.





Institute of Endocrinology, Diabetes and Metabolism

In a recent systematic review and meta-analysis, it was shown that the use of the "artificial pancreas" technology constitutes effective and safe treatment for patients with type 1 diabetes and leads to improved diabetes control, and reduced time in hypoglycemia [reference 64]. However, current evidence for artificial pancreas systems is limited by inconsistent reporting of outcomes and short follow-up time [references 64-67].

This paragraph was added to the manuscript. The changes in the manuscript are highlighted in red.

2. Language Quality

A native-English speaker medical editor reviewed the manuscript, and a new language certificate is provided.

3. Abbreviations

Article Highlights were prepared with abbreviations defined upon first appearance. The abbreviations used in the figures and tables are defined below the figure titles and separated by semicolons.

4. Editorial Office's Comments

- (1) The science editor comments were addressed in detail above.
- (2) The manuscript has been revised according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.
- (3) The original figure files are prepared and arranged using PowerPoint as requested. A decomposable table is provided as requested.
- (5) The reference list has been revised according to the format for references guidelines.
- (4) The signed Conflict-of-Interest Disclosure Form and Copyright License Agreement are provided.

Sincerely Yours,

Afif Nakhleh, MD

Institute of Endocrinology, Diabetes and Metabolism, Rambam Health Care Campus,





Institute of Endocrinology, Diabetes and Metabolism HaAliya HaShniya Street 8, Haifa 3109601, Israel.

E-mail address: anakhleh@gmail.com

