

28 May 2023

Jin-Lei Wang

Company Editor-in-Chief

Baishideng Publishing Group Inc

Dear Dr Wang and Reviewers,

Thank you for your kind comments. I have made the required changes as detailed below.

Sincerely,

Kay Choong See

National University Hospital, Singapore

Reviewer #1

Specific Comments to Authors: The authors conducted a comprehensive and systematic review on impact of inhaled and intranasal corticosteroids on glucose metabolism/diabetes mellitus. Overall, this is an informative and comprehensive review. There are several minor revisions that need to be made by the authors.

1. Since the manuscript not only elaborated on the impacts of ICS/INS on DM, but also on glucose metabolism with great length. Therefore, the title should be changed to "impact of inhaled and intranasal corticosteroids on glucose metabolism/diabetes mellitus".

Reply: Title has been changed from "Impact of inhaled and intranasal corticosteroids on diabetes mellitus: a mini review" to "Impact of inhaled and intranasal corticosteroids on glucose metabolism and diabetes mellitus: a mini review".

2. The authors should add references in Table 3 to support the methods reducing the impacts of ICS and INS on glucose metabolism and DM.

Reply: Supporting references have been added to each method.

Reviewer #2

Specific Comments to Authors: Congratulations to the authors, your efforts are highly appreciated.

Reply: Thank you for your review and kind comments.

Reviewer #3

Specific Comments to Authors: This review of the association between ICS/INS and DM Several large observational studies showing dose response are presented and the risk of DM is presented. The authors agree with the argument that we should avoid underestimating the adverse events associated with DM. I think this is a good paper for a correct assessment of the risks of ICS/INS since they are important drugs for the control of chronic respiratory diseases.

Reply: Thank you for your review and kind comments.

Reviewer #4

Specific Comments to Authors: The submitted manuscript evaluated the association between application of inhaled corticosteroids (ICS) and/or intranasal corticosteroids (INS) (such as Beclomethasone; Budesonide; Fluticasone)and the incidence of diabetes mellitus (DM). Authors used clinical data from human studies. The review is important and well-designed. However, there are several issues to address:

1. Introduction requires more substantial citation. For instance, the 1st paragraph in the section “EFFECT OF ICS AND INS ON GLUCOSE METABOLISM AND DM” (top of page 4) – has got only one citation ([5]) which is not acceptable. I suggest using some recent references-:

Li JX, Cummins CL. Fresh insights into glucocorticoid-induced diabetes mellitus and new therapeutic directions. Nat Rev Endocrinol. 2022 Sep;18(9):540-557. doi: 10.1038/s41574-022-00683-6. Epub 2022 May 18. PMID: 35585199; PMCID: PMC9116713.

Cui A, Fan H, Zhang Y, Zhang Y, Niu D, Liu S, Liu Q, Ma W, Shen Z, Shen L, Liu Y, Zhang H, Xue Y, Cui Y, Wang Q, Xiao X, Fang F, Yang J, Cui Q, Chang Y. Dexamethasone-induced Krüppel-like factor 9 expression promotes hepatic gluconeogenesis and hyperglycemia. J Clin Invest. 2019 Apr 29;129(6):2266-2278. doi: 10.1172/JCI66062. PMID: 31033478; PMCID: PMC6546458.

Kuo T, McQueen A, Chen TC, Wang JC. Regulation of Glucose Homeostasis by Glucocorticoids. Adv Exp Med Biol. 2015;872:99-126. doi: 10.1007/978-1-4939-2895-8_5. PMID: 26215992; PMCID: PMC6185996.

Reply: Thank you for your suggestions, which have been added to the introduction.

2. It would be good to draw a diagram to indicate how glucocorticoids are linked to hyperglycaemia (molecular signaling pathway). It would increase visual effect and attractiveness of this review.

Reply: Figure 1 showing the molecular signaling pathway of glucocorticoid-induced hyperglycaemia has been added.

3. Authors do not discuss application of natural compounds that can be used as glucocorticoids... here is an example : Wang Y, Gao J, Yu Y, Zhou L, Wang M, Xue W, Liu B, Wu X, Wu X, Gao H, Shen Y, Xu Q. A plant-derived glucocorticoid receptor modulator with potency to attenuate the side effects of glucocorticoid therapy. Br J Pharmacol. 2023 Jan;180(2):194-213. doi: 10.1111/bph.15957. Epub 2022 Oct 13. PMID: 36165414.

Reply: The suggested reference and further discussion have been added to the section on "Future Direction".

4. The indicated Conclusion (in the Abstract and at the end of the manuscript) "The following strategies for ICS/INS dose minimization can be considered: use of non-pharmacological measures (trigger avoidance, smoking cessation, vaccination to avoid infection), control of comorbid conditions, use of non-ICS-containing medications, intermittent rather than regular ICS dosing, and appropriate de-escalation of high ICS doses." – is relevant, although it can be specified and include application of natural compounds.

Reply: The suggested reference and further discussion have been added to the section on "Future Direction".

28 Jun 2023

Professor Md. Shahidul Islam
Editor-in-Chief
World Journal of Diabetes

Dear Professor Islam,

Thank you for your kind comments. I have made the required changes as detailed below.

Sincerely,

Kay Choong See
National University Hospital, Singapore

Comment 1

I have gone through the revised version of this manuscript. Although this manuscript is interesting and will add value to the scientific domain, the following revisions need to be done before reconsidering this manuscript for publication. 1) As suggested by reviewer 4 - Many paragraphs in the introduction section are still without necessary references e.g. paragraph 2 and 3. So citations must be used sufficiently and properly in the introduction section. Otherwise it seems like that the authors made their statements without citations, which is not acceptable.

[Reply: Six new references have been added to the Introduction.](#)

Comment 2

2) As suggested by same reviews or reviews 4 - The figure 1 must be presented as a drawn artwork using the picture of all organs and physiological components to show the mechanistic pathways but not how it is presented now as a flow chart. This is very important for a review article.

[Reply: Figure 1 has been changed from a flow chart into one with drawn artwork, using open-access clipart with acknowledgements.](#)

Comment 3

3) I noticed that although the title has been revised as per suggestion from a reviewer, the term "A mini review" at the end is missing. It is better add this term at the end of title since it is not a comprehensive review although it has scientific merit. Once all the above-mentioned revisions are done, please send the revised manuscript back with a point-by-point response letter for a final decision. Regards, Prof. Islam

[Reply: "A mini review" has been added to the title.](#)