

June 10th, 2022

Dr. Jin-Lei Wang,

World Journal of Clinical Cases.

Dear Dr. Wang,

Re: 77099-Sulfonylurea therapy increase serum free fatty acid in diabetic patients: a systematic review and meta-analysis

Thank you for considering our paper and encouraging a revision. After reviewing both reviewer's comments, we have improved the content in accordance with the reviewers' comments and have revised our manuscript accordingly. We confirm that all of the authors have approved the changes to the revised manuscript. We would be grateful if the revised manuscript could be further considered for publication in *World journal of Clinical Cases*, and we look forward to hearing from you soon.

Yours sincerely,

Ping Yang, MD, PhD,

China-Japan Union Hospital of Jilin University,

Email: pyang@jlu.edu.cn.

Response to technical Comments:

Editor Comments:

(1) Science editor:

Please revise the paper according to the comments.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade C (Good)

Res: Thank you for helping us with our manuscript 77099. After revision, we will follow the journal's recommended retouching agency to retouch the article.

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Clinical Cases, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Before final acceptance, uniform presentation should be used for figures showing the same or similar contents; for example, "Figure 1 Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...". Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor. In order to respect and protect the author's intellectual property rights and prevent others from misappropriating figures without the author's authorization or abusing figures without indicating the source, we will indicate the author's copyright for figures originally generated by the author, and if the author has used a figure published elsewhere or that is copyrighted, the author needs to be authorized by the previous publisher or the copyright holder and/or indicate the reference source and

copyrights. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2022. Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content. Please upload the approved grant application form(s) or funding agency copy of any approval document(s). Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the RCA. RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: <https://www.referencecitationanalysis.com/>.

Res: Thank you for the positive and valuable comment. We have optimized figures in a single PowerPoint, and organized Tables in a single Word.

Also, we totally agree that it is necessary to supplement the highlights of the latest cutting-edge research results.

ARTICLE HIGHLIGHTS

Research background

Previous studies suggested that FFA concentration was potentially associated with anti-diabetic drugs of SU. The results were inconsistent. We assess the effects of SU on the level of FFA concentration in diabetic patients.

Research motivation

SU are one of the most commonly used anti-diabetic medications. Several studies reported that SU treatment increases the risk of cardiovascular death and stroke in diabetic patients. Despite the reason for this result is unclear, but may be related to the effect of SU on FFA and blood lipids.

Research objectives

The primary objective was to perform a meta-analysis of diabetic patients treated with SU and analyze changes in FFA concentration.

Research methods

We reviewed PubMed, EMBASE, Cochrane Library, and Web of Science databases to identify studies using SU for diabetic patients. The after-before FFA value change was measured. A random-effect model or fixed-effect model was used according to the test of heterogeneity, and I^2 index was used to assess the heterogeneity.

Research results

We included 13 observational studies comprising 16 treatment arms in the meta-analysis. FFA concentration was increased after the treatment of SU in diabetic patients. When combined with other antidiabetics, the effects of SU treatment on FFA concentration were more pronounced. There was no significant different effect of FFA concentration when treatment with Glimepiride or Glibenclamide.

Research conclusions

Sulfonylurea drugs increase serum free fatty acid in diabetic patients.

Research perspectives

The association between FFA concentration and SU treatment requires more studies and longer follow-up. Page 13, line 9-Page 14, line 22

Response to Reviewer 1

1. Comments: The review study of this subject is very important. According to Table 1, the levels of FFA is lower than control on subjecting gliclazide as a drug. Therefore, the authors have to modify the title of the manuscript to be "Some sulfonylurea drugs increase serum free fatty acid in diabetic patients: a systematic review and meta-analysis". Moreover, in Table 1, no levels of TG, TC, LDL, and HDL as shown in the table legend. TG is the abbreviation of triglycerides and TC is the abbreviation of total cholesterol. These abbreviation were reversed in the legend. The authors have to rewrite some sentences such as in page 6 (lines 7-10) and lines 21-24). The numbers in page 8 (lines 21-23) have to be changed to a word. The number in page 8 (line 28) is 61.5. The sentence "To comprehensively analyze the effects of SU on plasma FFA, we also conducted a series of subgroup analyses (Table 2)" in page 9 (lines 16-18) should be corrected or rewritten. Also, the sentence at the end of page 10 should be rewritten. In page 11 (line 8), duration but not durations. In the page (line 14), "RCT, which" but not "RCT, that".

Res: We are grateful for the valuable suggestions. We agree with the point and modify the title of the manuscript to be "*Certain sulfonylurea drugs increase serum free fatty acid in diabetic patients: A systematic review and meta-analysis*" (Page 1, line 5-6)

For consistency, we delete TG, TC, LDL, and HDL in the table legend.

Thank you for underlining these deficiencies. We rewrote some sentences such as literature search, selection criteria, extraction criteria, the sentence in page 9 (line16-18), and the sentence at the end of page 10. Detailed as follows: Page 6, line 19-22; Page 7, line 2-9; Page 10, line 4; Page 11, line 3-7

Also, we totally agree that "the number in page 8 (lines 21-23)" is better changed to a word.

Moreover, some words and clerical error were revised and modified according to the information suggested by the reviewer.

Response to Reviewer 2

1. Comments: Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (High priority)

Specific Comments to Authors: 1 Title. Appropriate 2 Abstract. Appropriate 3 Key words. Appropriate 4 Background. Appropriate 5 Methods. Appropriate 6 Results. Appropriate 7 Discussion. Appropriate 8 Illustrations and tables. Appropriate 9 Biostatistics. Appropriate 10 Units. Appropriate 11 References. Appropriate 12 Quality of manuscript organization and presentation. Appropriate 13 Research methods and reporting. Appropriate 14 Ethics statements. Appropriate

Res: I want to thank the reviewer for the valuable comments. We will make further comprehensive revisions to the manuscript, once the manuscript is completed, we will follow the journal's recommended retouching agency to retouch the article.