

REBUTTAL LETTER

09 December 2022

Prof. Lian-Sheng Ma,
Editorial Office Director,
Company Editor-in-Chief, Editorial Office, Baishideng Publishing Group Inc

RE: Manuscript Ref. No: 80355 entitled: Inter-relationships between gastric emptying and glycaemia: Implications for clinical practice.

Dear Professor Lian-Sheng Ma,

On behalf of my co-authors, we thank the reviewers and the Editorial Team for their comments. A rebuttal letter, which provides our responses, is appended. We hope that the revised manuscript will prove acceptable for publication.

Kind regards,

Dr. Tejaswini Arunachala Murthy
(On behalf of co-authors)

POINT-BY-POINT REBUTTAL

Please find below the responses to each of the specific issues raised by the reviewers. The page numbers and paragraphs have been updated from the **clean version of the manuscript**.

Reviewer #1:

Specific Comments to Authors: I am really grateful to review this manuscript. As this study reports, gastric emptying is a major determinant of postprandial glycaemia in health, diabetes and critical illness. Acute hyperglycaemia slows gastric emptying while insulin-induced hypoglycaemia accelerates it. Gastroparesis is frequent in diabetes and critical illness with a weak correlation between gastrointestinal symptoms and gastric emptying/motility. Accordingly, the diagnosis of gastroparesis should ideally be made only after measuring gastric emptying with an optimal technique. GLP-1 receptor agonists, commonly used in the treatment of type 2 diabetes, may profoundly impact gastric emptying. In this context, this study explores the rationale for current glycaemic targets and the implications of dysglycaemia and its management in hospitalised and critically unwell populations. In my opinion, this manuscript can be published once some revisions are done successfully. This study did not address the methods of original studies reviewed and the issues of their external validity. I strongly suggest the authors to address these issues in much greater detail.

Response: *We thank the reviewer for the detailed and constructive comments. We have now clarified that some of the original studies exploring the relationship between gastric emptying and glycaemia are experimental in nature. This is unavoidable given that the relationship is bi-directional and in order to explore the role of one factor, the other must be controlled. For example, the blood glucose level must be kept constant to study the impact of an intervention on gastric emptying and vice-versa. The conclusions of these studies should, therefore, be considered as “proof-of-principle”. We have now explicitly stated this on page 7.*

Reviewer #2:

Specific Comments to Authors: The manuscript requires edition to increase the attention of readers. a) The comparison of movements in healthy humans and those patients with disorders must be clear and with some quantitative data.

b) Illustrations and plots are desirable to compare the differences and putative mechanisms.

Response: *We thank the reviewer for their comments. We have tried to maintain the focus of the review on two inter-related areas: current knowledge of GE (focussing only on the physiology in health and illness) and the inter-relationships between GE and glycaemia, including the clinical implications of these insights in hospitalised patients with diabetes, and for critical illness as clarified in the introduction. Thus, the illustration (Fig. 1) only refers to methods of GE measurements to avoid repetition. We have described the ‘movement in healthy individuals’ (we assume that the reviewer is referring to gastric motility) on pages 5 – 6 in the section and described the phenomenon of gastroparesis (or abnormally delayed emptying in those with diabetes) on page 7.*

c) Fig. 1 is illegible.

Response: *Thank you for this comment. We have resubmitted Fig. 1 in the specified format (.pptx) to ensure legibility.*

d) The advances in the last years should be clear in both, abstract and conclusions.

Response: *Thank you for this comment. We have alluded to the advances to the field in the abstract now but a comprehensive discussion is accordingly impossible. The conclusion section similarly refers to the advances.*

e) The advances could be divided by those using an insulin-like and not-insulin-like peptide; and other non-peptides (In the present form the manuscript seems just to mention GLP-1 and -as data are limited or are often published- almost nothing about

other recent molecules relevant in this field (the treatment of disorders in gastric emptying). As well as regarding the observations by an endogen or exogen agents.

Response: *Thank you for this comment. We have provided the rationale for including a section on GLP-1 RA therapy on page 11 (as their mechanism of action is fundamentally linked to the rate of gastric emptying and they are widely used in clinical practice). We consider that the inclusion of other molecules is beyond the scope of this review.*

EDITORIAL OFFICE'S COMMENTS

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

(1) Science editor:

The manuscript has been peer-reviewed, and it's ready for the first decision.

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, the full text of the manuscript, the relevant ethics documents, and the English Language Certificate, all of which have met the basic publishing requirements of the World Journal of Diabetes, 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. Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file. 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):

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figures published elsewhere, or that is copyrighted, the author must provide documentation that the previous publisher or copyright holder has given permission for the figure to be re-published; and correctly indicating the reference source and copyrights. For example, “Figure 1 Histopathological examination by hematoxylin-eosin staining (200 ×). A: Control group; B: Model group; C: Pioglitazone hydrochloride group; D: Chinese herbal medicine group. Citation: Yang JM, Sun Y, Wang M, Zhang XL, Zhang SJ, Gao YS, Chen L, Wu MY, Zhou L, Zhou YM, Wang Y, Zheng FJ, Li YH. Regulatory effect of a Chinese herbal medicine formula on non-alcoholic fatty liver disease. World J Gastroenterol 2019; 25(34): 5105-5119. Copyright ©The Author(s) 2019. Published by Baishideng Publishing Group Inc[6]”. And please cite the reference source in the references list. If the author fails to properly cite the published or copyrighted picture(s) or table(s) as described above, he/she will be subject to withdrawal of the article from BPG publications and may even be held liable.

Response: *We thank the Editor-in-chief for their consideration of the manuscript. We have modified the figure as advised.*