

Dear Editor,

Thank you very much for your decision letter and advice on our manuscript (Manuscript: 74336) entitled “Impact of Preoperative Carbohydrate Loading on Gastric Volume in Patients with Type 2 Diabetes”. We also thank the reviewers for the constructive comments and suggestions. We have revised the manuscript accordingly, and all amendments are indicated by red font in the revised manuscript. In addition, our point-by-point responses to the comments are listed below this letter.

This revised manuscript has been edited and proofread by *Medjaden Inc.*.

The authors Jianxin Lin's email (13799610686@163.com) and Xiaochun Zheng (zhengxiaochun2021@163.com) did not receive CLA email. We sent emails many times and asked you to send the link again, but we didn't receive a reply, so we prepared a manually signed copyright license agreement (CLA).

We hope that our revised manuscript is now acceptable for publication in your journal and look forward to hearing from you soon.

With best wishes,

Yours sincerely,

Xiaochun Zheng

First of all, we would like to express our sincere gratitude to the reviewers for their constructive and positive comments.

Replies to Reviewer 1

Specific Comments

1. The conclusion in abstract section should describe better the outcome of research.

Response: Thank you for your insightful suggestion. Several sentences have been changed in the Conclusion of the revised manuscript to address this issue.

Page 3-4, Lines 80-85: Preoperative carbohydrate loading <300 mL 2 h before induction of anesthesia in patients with T2D did not affect GV or increase the risk of reflux and aspiration. Blood glucose level did not change significantly with preoperative carbohydrate loading of <200 mL. However, 300 mL carbohydrate loading may increase blood glucose levels in patients with T2D before induction of anesthesia.

2. Please use more relevant keyword.

Response: Thank you. We have added three new keywords more related to the article.

Page 4, Lines 86-87: Preoperative; Carbohydrate loading; Ultrasound assessment

3. Please replace references 22-23-25 and use recent related work.

Response: Thank you for your advice. We have replaced the references using recent related work. References 22 and 23 are replaced with 21, reference 25 is replaced with 26.

Page 16, Lines 409-412 and Line 428-429.

21. He XD, Guo YM, Goyal RK. Effect of Hyperglycemia on Purinergic and Nitroergic Inhibitory Neuromuscular Transmission in the Antrum of the Stomach: Implications for Fast Gastric Emptying. *Front Med (Lausanne)*. 2018;5:1.

26. Van de Putte P, Vernieuwe L, Bouvet L. Gastric ultrasound as an aspiration risk assessment tool. *Indian J Anaesth*. 2019;63(2):160-1.

4. In the conclusion section explain about benefits of this works and suggestions for future research.

Response: Thank you for your suggestion. We added benefits of our study and suggestions for future research.

Page 13, Lines 336-339: In conclusion, it is safe for patients with type 2 diabetes to drink 200ml 14.2% carbohydrate 2 hours before surgery. In the future, we will study whether the preoperative consumption of 200 mL 14.2% carbohydrate can reduce postoperative insulin resistance and promote patients' recovery.

Replies to Reviewer 2

Specific Comments

1. Concentration of glucose drink must be detailed in Methods.

Response: Thank you for your advice. We have described the glucose drink in Methods section.

Page 8, Line 189-191: Each group uses the same concentration of carbohydrate drink which contains 14.2g carbohydrate per 100ml (Yichang Human Medical Food Co., Ltd.).

2. Was 200 or 300 ml consumption superior in previous studies? What if the carbohydrate amount is reduced for the 300ml one, e.g. the same amount which was added to 200ml, just diluted to a larger volume?

Response: Thank you for your question. We did not see a study comparing preoperative carbohydrate loading of 200 or 300 ml in patients with type 2 diabetes. For non-diabetic patients, preoperative carbohydrate loading < 400 mL 2 h before anesthesia induction is safe. Considering blood glucose and delayed gastric emptying, we set 300ml as the safe dose and compared 100ml, 200ml and 300ml groups respectively. In our study, the concentration of carbohydrates in each group is the same. Our results showed that preoperative carbohydrate loading < 300 mL 2 h before

anesthesia induction in patients with T2D did not affect gastric volume. The increased level of blood glucose should be related to the sugar content of carbohydrates consumed by patients, not to the volume.

3. Statistical methods must be revised! - Comparing 4 groups must be done with one-way ANOVA / Kruskal-Wallis + post-hocs, and not by t-tests. - Why did authors use both chi-square and Fisher exact tests? The latter one is good for both parametric and non-parametric data. - To analyse the longitudinal data, a mixed effect model would be more elegant, than the repeated measure ANOVA.

Response: Thank you for your suggestion. In the current manuscript, we have corrected the statistical methods.

Page 9-10, Lines 234-244: Normally distributed continuous data are presented as mean \pm standard deviation (M \pm SD). Categorical data is presented as frequency or rate. Age, height, weight, BMI, course of the disease, HbA1c (%) and fasting blood glucose were compared using one-way ANOVA. This is a comparison of categorical variables. The comparison of categorical variable data of multiple groups of samples can use the chi-square test, but it must meet the application conditions. Some of the data in this paper meet the application conditions of the chi-square test, so we choose the chi-square test. For those that did not meet the chi-square test, Fisher exact tests were performed. For data with missing values, the mixed effect model does have more advantages. The data in this paper have no missing values and meet the hypothesis test. Therefore, the repeated measures analysis of variance was used.

4. An additional table is recommended about diabetic properties of the patients: duration of diabetes, treatment data in a more detailed manner than oral/insulin, diabetic complications, etc.

Response: Thank you for your advice. In Table 1, we have information about the courses of diabetes, the HbA1c level, fasting blood glucose, and blood glucose control. Previous studies have shown that gastric emptying is not related to age, weight, duration of diabetes or diabetic complications ^[1]. Therefore, taking into account

various types of oral diabetes drugs and insulin, it is difficult to describe the diabetic properties in detail.

1 Halland M, Bharucha AE. Relationship Between Control of Glycemia and Gastric Emptying Disturbances in Diabetes Mellitus. *Clin Gastroenterol Hepatol* 2016; **14**: 929-936 [PMID: 26717862 DOI: 10.1016/j.cgh.2015.11.021]

Minor issues:

1. Resolve the abbreviation of ERAS in the abstract.

Response: We have described the abbreviation of ERAS in the abstract.

Page 3, Line 53: Enhanced Recovery After Surgery (ERAS)

2. Abstract (line 53): empty -> emptying

Response: We have corrected the word “empty” into “emptying” (Page 3, Line 55).

3. Resolve all abbreviations in Core Tip

Response: We have resolved all abbreviations in Core Tip (Page 4-5, Line 108-118).

4. Line 106: "Delayed gastric emptying" -> Delayed gastric emptying (gastroparesis)

Response: We have replaced “delayed gastric emptying” into “delayed gastric emptying (gastroparesis)” (Page 6, Line 132).

5. Line 118: Please give a general, 1-sentence description of what the Perlas scores are used for

Response: Thank you for your advice. We have described the Perlas scores in detail in the corrected manuscript.

Page 6-7, Lines 145-151: Perlas used ultrasound to grade gastric volume, which was measured in the right decubitus and supine positions to assess the risk of aspiration, The visualization of gastric antrum content was scored using the Perlas grading system: Grade 0, no content visible in the supine or RLD position; grade 1, clear gastric fluid content only in the RLD position, but not in the supine position; and

grade 2, clear gastric fluid content visible in both supine and RLD positions.

6. Line 142-143: two "(7)"-s are present 7.

Response: We have corrected the description (Page 7, Line 177).

7. Line 186-188: citation needed

Response: The sample size was determined based on our preliminary study rather than other studies. We have corrected the description in the current manuscript.

Page 9, Lines 224-229: The sample size was determined on the basis of the GV/W at different time periods. The average GV/W at T0, T1, and T2 in the control group was 0.66, 0.64, and 0.70 mL/kg, respectively, in our preliminary study. The values at T0, T1, and T2 in groups receiving 100 mL, 200 mL, and 300 mL carbohydrate drink were 0.45, 1.2, and 0.53 mL/kg; 0.70, 3.20, 0.85 mL/kg; and 0.65, 4.67, 0.8 mL/kg, respectively.

8. Line 189: "groups 1, 2, and 3" -> what were these groups? Most readers do not like to open a separate article, please include the information.

Response: Thank you for your advice. We have described the groups in detail.

Page 9, Line 226-229: The values at T0, T1, and T2 in groups receiving 100 mL, 200 mL, and 300 mL carbohydrate drink were 0.45, 1.2, and 0.53 mL/kg; 0.70, 3.20, 0.85 mL/kg; and 0.65, 4.67, 0.8 mL/kg, respectively.

9. Line 196-197: "The correlations between treatment category and clinicopathological characteristics were" -> shouldn't it be "The comparisons between treatment categories and clinicopathological characteristics were" ?

Response: We have corrected the description in the current manuscript.

Page 9-10, Line 234-234

10. Line 241: "In addition, glycemia was well controlled" -> hypo or hyper?

Response: We described the well-controlled glycemia in the current manuscript.

Page 11, Line 286-290: In addition, in our study preoperative fasting blood glucose

level was controlled less than 10mmol/l, which may reduce the incidence of delayed gastric emptying in T2D. Previous studies have shown that acute severe hyperglycemia may lead to delayed gastric emptying.

11. Line 272: "controlled and <10 mmol/L." -> "controlled and their preoperative FPG was <10 mmol/L."

Response: We have replaced the description (Page 12, Line 321).