Title: Influence of different preoperative fasting times on women and neonates in cesarean section: a retrospective analysis

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Author’s response to reviews:

Dear editor:

Our manuscript entitled “Influence of different preoperative fasting times on women and neonates in cesarean section: a retrospective analysis” has been carefully revised according to the reviewers’ suggestions and also revised according to the preferred format for the journal. The manuscript has been professionally edited for English language readability prior to resubmission to the journal. We have taken all of the comments of the two reviewers into account and wish to respond as follows:

Part A: COMMENTS OF REVIEWER #1

Question (1): This is an interesting study that attempts to address a common issue in the care of women experiencing a caesarean section. This manuscript requires a thorough revision if it is to be published in the English language. Once clarity has been achieved following the revision of
meaning, it would require an additional revision to establish if it will contribute new information to the literature.

Answer: Thanks to the reviewer for their positive comments on our manuscript, and also for the reviewer to give us an opportunity to modify our manuscript. As suggested by this reviewer, the manuscript has been carefully revised regarding a standard writing format and grammar by native English-speakers.

Abstract

Question (1): Please refer to women as women rather than puerperas.

Answer: We would like to express our great appreciation for the comments of reviewer. According to the reviewer's suggestion, we have replaced the word 'puerperas' in the manuscript with 'women' throughout the text.

Question (2): Please define what is meant by 'slag' free fluid - this is not a common term used in most countries; clear fluids means free of particulate matter.

Answer: We very much appreciated this suggestion. In our study, 'slag-free fluid' refers to 'clear fluids'. According to the reviewer, we have replaced the phrase 'slag-free fluid' with 'clear fluids' throughout the text.

Question (3): Requirement - This paper would require a thorough editorial edit to ensure clarity of writing in the English language given the current choice of words that have been used which may have arisen through translation into English.

Answer: As suggested by this reviewer, the manuscript has been carefully revised regarding a standard writing format and grammar by native English-speakers.

Question (4): Eg: 1st sentence, Line 3-4: but also related to abusive use of no medical indication [1]. This could be more accurately described as 'medically driven caesarean which lacks an evidence base / medical indication for the procedure'

Answer: We very much appreciated this suggestion. We found the sentence recommended by the reviewer to be very precise. We have modified the original sentence. Now, we say: ‘The increase in the number of caesarean sections worldwide has to do with the opportunity for women to enter the program when they are needed, but also correlates with medically driven caesarean which
lacks an evidence base/medical indication for the procedure [1]', which is shown on page 3, line 2-4, highlighted in blue.

Question (5): Counter-current mistake inhalation….? Clarity of writing required.

Answer: We have corrected this non-standard title. We replaced 'countercurrent mistake inhalation' with 'regurgitation and aspiration' in text, which is shown on page 3, line 9, 12, 13, highlighted in blue. We very much appreciated this suggestion.

Question (6): Usual symbol for greater than and/or equal to is ≤ or ≥

Answer: We very much appreciated this suggestion. We have corrected this typo ‘≧’ and replaced these wrong symbols with the true ‘≥’. In the text, the corrected symbol is displayed as a highlighted blue.

Question (7): Typographical and grammatical errors need to be corrected throughout the document eg. Line 14 - leas should be least; Line 16-18 - is not a grammatically correct sentence.

Answer: We very much appreciated this suggestion. We have corrected 'leas' to 'least', which is shown on page 2, line 12, highlighted in blue. We also rewritten the sentences of lines 16-18, we say: ‘The preoperative fasting of solid food ≥ 6h < 8h and clear fluids < 2h reduces the incidence of vomiting in women's anesthesia and the risk of hypoglycemia and acidosis in neonates’, which is shown on page 2, line 14-16, highlighted in blue.


Answer: We very much appreciated this suggestion. We replaced 'fasting projects' with 'fasting conditions' in text, which is shown on page 4, line 1, highlighted in blue.

Question (9): The study aim in the abstract appeared to be: This study was to evaluate the impact of different preoperative fasting conditions on puerperas and neonates through a retrospective analysis. In the conclusion of the background, prior to methods, it appeared to focus on outcomes for health of neonates only. Ensure study purpose or aim is consistent and addresses key outcomes.
Answer: We very much appreciated this suggestion. In this study, we are concerned with the potential impact of different fasting conditions of women on the health of women themselves and neonates. The main indicators of women’s observations are: incidence of vomiting; low blood sugar; electrolyte disturbance; and abdominal distension. The main indicators of neonates’ observations are: blood glucose; incidence of hypoglycemia; value of pH; and incidence of pH < 7.2. We have revised the last part of the background and we say: We retrospectively analyzed the data of different preoperative fasting conditions of women before caesarean section in our hospital within two years in order to determine the potential impact of different fasting conditions on the health of women and neonates’, which is shown on page 3, line 22 to page 4, line 2, highlighted in blue.

Question (10): Under Inclusion Criteria: provide definition of what is meant by ‘meeting the indications of caesarean section operation’ as protocols may differ across the world depending on setting, services available, skill level of staff, public vs private setting etc

Answer: We very much appreciated this suggestion. The indication criteria for cesarean section surgery in this study were developed by Obstetrics group, Obstetrics and Gynecology, Chinese Medical Association. We have added this description to the text. We say: (4) meeting the indications of cesarean section operation according to the criteria made by Obstetrics group, Obstetrics and Gynecology, Chinese Medical Association [9], which is shown on page 4, line 14 to 16, highlighted in blue.

Reference:


Question (11): Page 4, Line 5-13 (or 13-24): What is meant by heading 'Objects'. This would be better described as Variable or Data collection.

Answer: We very much appreciated this suggestion. According to the reviewer’s suggestion, we have replaced the heading 'objects' with 'Data collection', which is shown on page 5, line 5, highlighted in blue.

Question (12): Pregnant times (P4, Line 9 pregnant times (times)) - is this gestational age?
Answer: We are very grateful to the reviewer for discovering flaws in our manuscript. The word 'pregnant times' in our context means 'frequency of delivery (times)'. We've corrected this non-standard notation, which is shown on page 5, line 7, highlighted in blue.

Question (13): How did you measure 'huge fetus' - please use standard weight classifications eg macrosomic baby, >4500 grams.

Answer: We very much appreciated this suggestion. In our study, a fetus with a body weight of 4000 grams or more was called a macrosomia. Now, we have made a special note in the text, which is shown on page 5, line 11, highlighted in blue.

Question (14): Page 18-19 - sentence does not make sense: To enhance comparability, the puerperas received a uniform anesthetic method (epidural block) was included puerperas [9].

Answer: We very much appreciated this suggestion. We modified this sentence and we say: Considering that the anesthetic results may affect some physiological conditions of women or neonates, the women included this study received the same anesthetic method (epidural block) [11], which is shown on page 5, line 15-16, highlighted in blue.

Reference:

Question (15): Blood Glucose Level of neonates - check current definition of hypoglycaemia used in most developed countries - appears to be 2.6mmol/L not 2.2 mmol/L as stated in this paper.

…”However the common thresholds for the diagnosis of hypoglycaemia in the newborn (blood glucose <2.0 mmol/l or <2.6 mmol/l) and hyperglycaemia (blood glucose >10 mmol/l) are at the limits of accuracy for many POC glucose analysers."

Australia:https://www.health.qld.gov.au/__data/assets/pdf_file/0019/142156/g-hypogly.pdf  UK: http://fn.bmj.com/content/102/1/F92

Answer: This is a slip of the pen. Thanks to the reviewer for finding this error. The standard of neonatal hypoglycemia in this study was 2.6mmol/L. We have corrected this error, which is shown on page 6, line 7-8, highlighted in blue.
Question (16): The section on Apgar score can be shortened as this is a world wide scoring system; simply reference Apgar. APGAR Score Leslie V. Simon; Bradley N. Bragg. Last Update: November 29, 2017.

Answer: We have simplified this paragraph as much as possible and cited the relevant literature. We say: The clinical state of neonates was evaluated using the Apgar scores system, which based on five physical signs (heart rate, respiratory effort, reflex irritability, muscle tone and colour) presented shortly after birth [14]. The value of Apgar scores range from zero to 10. Scores 7 and above are generally normal, 4 to 6 fairly low, and 3 and below are generally regarded as critically low [15], which is shown on page 6, line 18-21, highlighted in blue.

Reference:

Statistical analysis

This study sample of 1599 mothers and newborns was divided into 5 groups for comparison of outcomes. This requires clear statements relating to sample size calculations that were conducted and assumptions made in order to determine power including which variable this was based on; (assume primary outcome of neonatal BSL? or was it maternal BSL?); normal and skewed distributions - which data these referred to; and parametric and nonparametric tests used - as there was a mixture of means and nonparametric data presented.

Answer: This is a retrospective analysis, and the research ideas are actually very clear. A total of 1599 maternal cases were observed. Maternal women were divided into five groups for analysis. The grouping is based on different fasting conditions for the mother [(A) solid food ≥ 8h; clear fluids ≥ 6h; (B) solid food ≥ 8h; clear fluids ≥ 2h < 6h; (C) solid food ≥ 6h < 8h; clear fluids < 2h; (D) solid food ≥ 2h < 6h; clear fluids < 2h; (E) solid food < 2h; clear fluids < 2h]. Similarly, newborns from 5 groups of women also entered 5 different groups. In general, the generation of grouping depends on the mother. We retrospectively analyzed the data of different preoperative fasting time of women before caesarean section in order to determine the potential impact of different fasting conditions on the health of women and neonates. T-test and variance analysis were used for comparison between groups. The non-normally distributed count data were
analyzed by non-parametric test. For counting data, it is analyzed by multivariance analysis. We have now detailed these statistical ideas in the statistics section. We say: The statistical ideas used in this study are as follows: (1) The measurement data of the normal distribution for comparison between groups, such as the birth weight of the newborn, the gestational age, the Apgar scores, etc., were expressed with mean ± standard deviation and analyzed by Student's T test and variance analysis; (2) The non-normal distribution data, blood glucose and value of pH, were compared with non-parametric test; (3) The counting data, such as postoperative complications in women and general clinical data for neonates, were expressed in terms of rate (%) and a chi-square test was used for comparison between groups; (4) Multifactor logistic regression analysis was used to analyze the relative risk factors on the incidence of hypoglycemia and low-pH value caused by different fasting conditions, (5) SPSS 21.0 statistical software (SPSS Institute, Chicago, USA) was used to analyze the data. P < 0.05 was considered to be statistically significant. These changes were shown on page 7, line 1-10, highlighted in blue.

Results

Question (1): What is meant by number of labor? Was this numbers of previous labours? How was this calculated - pregnancies - previous elective c/sections.

Answer: As the reviewer asks, we apply inappropriate words in our writing. The word ‘number of labor’ in the context refers to ‘frequency of delivery’. That is, the cumulative number of women giving birth, including this delivery. We've corrected the sentence, we say: There were no statistical differences between groups, regardless of narcotic effect (P > 0.05), frequency of delivery (P > 0.05), and body mass index (BMI) (P < 0.05), which is shown on page 7, line 15-17, highlighted in blue.

Question (2): Some summary statements lack clarity - eg what does: To sum up, the general clinical features of puerperas in each group showed no significant difference and had better comparability. (Please clarify comparability 'with what' or using which variable?)

Answer: In this paragraph, we have detailed the results of the comparison of the various variables between the groups. The final concluding remark is really superfluous. Therefore, we removed this extra sentence.

Question (3): Results presentation using the Groups A to E were confusing.
Answer: This comment concerns a matter of far-reaching significance. We very much appreciated this suggestion. Results presentation using the Groups A to E is the need for grouping in the study. Through careful analysis of information on all cases, mothers and neonates were divided into 5 groups according to the conditions of preoperative fasting: (A) solid food ≥ 8h and clear fluids ≥ 6h; (B) solid food ≥ 8h and clear fluids ≥ 2h < 6h; (C) solid food ≥ 6h < 8h and clear fluids < 2h; (D) solid food ≥ 2h < 6h and clear fluids < 2h and (E) solid food < 2h and clear fluids < 2h. We have already highlighted this in two places in the text, which are shown on page 5, line 20 to page 6, line 1, and page 7, line 21 to page 8, line 2, highlighted in blue. We also think that such an arrangement may increase the confusion of the reader's understanding, but there seems to be no better way to write in text.

Question (4): Table1 - Number of production - meaning is not clear - does this mean number of times pregnant, number of times having C/section, number of births?

Answer: The word ‘Number of production’ in Table 1 refers to ‘frequency of delivery’. That is, the cumulative number of women giving birth, including this delivery. We have replaced this inappropriate word, which is shown in Table 1, highlighted in blue.

Question (5): Conclusion - check sentence construction for each of the two sentences in the conclusion to make grammatical sense and improve clarity of meaning/

Answer: We very much appreciated this suggestion. We have reorganized these sentences. We say: ‘The preoperative fasting of solid food ≥ 6h < 8h and clear fluids < 2h had potential advantages to both of women and neonates, which decreased the incidence rate of neonatal hypoglycemia and acidosis as well as the incidence of vomiting of women’, which is shown on page 12, line 17-19, highlighted in blue.

Question (6): References - some of the references used were very dated eg 2002, 1995. Please reference more contemporary sources (<10 years)

Answer: This comment concerns a matter of far-reaching significance. We very much appreciated this suggestion. We re-searched the references for the relevant discussion section and selected the appropriate literature for reference. We have removed the outdated references.
The new references are as follows:


Part B: COMMENTS OF REVIEWER #2

Design: there is no description of how patient allocation happened. Since this was not a randomized study, no explanation is given on why women had different patterns of fasting. This is an important source of bias.

Answer: Thanks you for reviewer’s comments on our work. We have pointed out in the title and background of the study that this is a retrospective analysis. Therefore, the enrolled mother does not have a process of random assignment. A total of 1599 full-term mothers (more than 37 weeks of pregnancy) without obstetric pathology related factors who received the cesarean section at the Guangdong Women and Children Hospital, Guangzhou, China from January 2015 to December 2017 were included in this retrospective study. In order to determine the potential impact of different fasting conditions of women on the health of women and neonates, we grouped women according to different diet management, which were divided into 5 groups according to the time of preoperative fasting: (A) solid food ≥ 8h; clear fluids ≥ 6h; (B) solid food ≥ 8h; clear fluids ≥ 2h < 6h; (C) solid food ≥ 6h < 8h; clear fluids < 2h; (D) solid food ≥ 2h < 6h; clear fluids < 2h; (E) solid food < 2h; clear fluids < 2h. We have explained these contents in the
relevant section, which are shown on page 3, line 22 to page 4, line 2, and page 5, line 20 to page 6, line 1, highlighted in blue.

Although the evidence level of retrospective analysis is not as strong as that of randomized controlled trials, it is also an important method of clinical research. We can't let mothers to follow different fasting plans (This is a very controversial topic) in order to complete the randomization principle, because this involves medical ethics and medical concerns. In addition, most of the cases receiving cesarean section are treated at the emergency department (The timing of the visit to the operation is uncertain depending on mother's condition), which makes it impossible to adhere strictly to established fasting plans. After careful questioning before the operation, the doctor got detailed data about diet. Therefore, this study can only be analyzed retrospectively.

Design: no definition of vomiting is provided. It is not explained how this information was obtained from clinical notes. The time frame of vomiting is not defined (did the authors include vomiting during surgery, the first 6h, the first 24h or what else?).

Answer: This suggestion is helpful to the improvement of our manuscript. We very much appreciated this suggestion. Vomiting is usually preceded by nausea, an unpleasant sensation centered in the epigastrium and retching, a contraction of the abdominal muscles and diaphragm. Vomiting itself is characterized by a violent coordinated contraction of the diaphragm and abdominal muscles accompanied by pyloric constriction and gastroesophageal relaxation. According to the reviewer's questions, we have explained the concept of vomiting in the paper, which is shown on page 5, line 7 to page 9, highlighted in blue. In addition, the vomiting data we observed were: the number of vomiting from the time the mother is anesthetized to the time the baby is born. We have explained the time frame in the paper, which is shown on page 5, line 10, highlighted in blue.

Execution: logistic regression analysis was only performed for hypoglycemia and low-pH. Why? Why were other outcomes not investigated.

Answer: Because the mother's different fasting conditions were related to neonates' hypoglycemia and low-pH (P < 0.05), and we only observed these two indicators, so we performed regression analysis on these two indicators and different fasting conditions. In the analysis process, the study outcomes are these two indicators, and multiple factors are different fasting conditions. Because there are no more outcome indicators, there is no regression analysis of more outcomes.
Execution: Apgar scores at 2 and 3 minutes are of little clinical value. Apgar score at 5 minutes is more relevant clinically, and is usually reported in research. The Apgar score is typically a non-normally distributed variable: it cannot be reported with decimals, nor expressed as mean +/- SD.

Answer: Thanks to the reviewer for raising this question. The initial design of our study was to observe the Apgar scores of 1, 2, and 3 minutes after birth. The reason for this was mainly because the short-term score was more reflective of the actual condition of the neonates, and at the 5 minute assessment, it is possible that the newborn has been given medical intervention.

In our study, although the data of a single individual is an integer, the data of a large sample should be expressed by the mean ± standard deviation, and the statistical data will show the data after the decimal point. The reviewers' questions are very sharp and inspiring to us. We will improve these issues in future research work.

Interpretation: the authors fail to address the issue of bias deriving from group allocation.

Answer: Understanding the meaning of the reviewer, we have already explained this issue in the discussion section. We say: ‘Firstly, this is a retrospective study, not a randomized controlled prospective study, which mainly due to ethical principles and consideration of medical risks. So, it may leads to a bias deriving from group allocation’, which is shown on page 12, line 9 to 11, highlighted in blue.

(In the end)

Thank you very much for your great efforts on our manuscript. We would like to express our great appreciation again to the reviewers and the editing staff at BMC Pregnancy and Childbirth for the manuscript comments.

We look forward to hearing from you, and, as before, please address all communications regarding this manuscript to me as the corresponding author.

Thank you very much for your attention to our paper.

Sincerely yours,

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