Author’s response to reviews

Title: Continuous intravenous infusion of remifentanil improves the experience of parturient undergoing repeated cesarean section under epidural anesthesia, a prospective, randomized study

Authors:

wei yan (m18768389432@163.com)
Yun Xiong (jxeyxy@126.com)
Yu Yao (weiqiuair@hotmail.com)
Feng-jiang Zhang (fengjiang_zhang@126.com)
Li-an Yu (zryulina@zju.edu.cn)
Min Yan (zryanmin@zju.edu.cn)

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Author’s response to reviews:

Dear Dr. Mohamed El-Tahan,

First of all, we thank both reviewers and editor for their positive and constructive comments and suggestions.

According to the comments and suggestions of reviewers and editor, we have revised the manuscript, and responded, point by point to, the comments as listed below.

I would like to re-submit this revised manuscript “Continuous intravenous infusion of remifentanil improves the experience of parturient undergoing repeated cesarean section under epidural anesthesia, a prospective, randomized study” (BANE-D-19-00032R2) to BMC Anesthesiology, and hope it is acceptable for publication in the journal.

Looking forward to hearing from you soon.

With kindest regards,

Yours sincerely,

Min Yan. M.D.
Professor and Chief of Anesthesiology Department
The Second Affiliated Hospital of Zhejiang University School of Medicine
88 Jiefang Road, Hangzhou, China
Editor Comments:

1. Reviewer comments
   -- Please address the remaining comments from reviewer 3, seen below.
Response: Thanks. We have addressed the remaining comments from reviewer 3 as listed below

2. Trial registration
   -- I am currently unable to find your trial registration details with the current identifier provided (ChiCRT1800018423). Please ensure that this is the correct identifier.
Response: Thanks. This study was pre-registered at http://www.chictr.org.cn/index.aspx (ChiCRT1800018423) on 17/09/2018
   -- The last section of the abstract should be Trial Registration: listing the trial registry and the unique identifying number, e.g. Trial registration: Current Controlled Trials ISRCTN73824458, as well as the date of registration. Please note that there should be no space between the letters and numbers of the trial registration number. If registration took place after the first participant was enrolled, please state also “Retrospectively registered” at the end of this section.
Response: We have added the Trial Registration information to the last section of the abstract.

3. Authors' contributions
   -- We have noted that author [YY] is missing in the listed authors' contributions. The individual contributions of ALL authors to the manuscript should be specified in the Authors’ Contributions section. Guidance and criteria for authorship can be found here: http://www.biomedcentral.com/submissions/editorial-policies#authorship
Response: We are sorry for the mistake and we have revised it. “YY helped to conduct the study and revise the manuscript for important intellectual content.” See the section of Authors’ Contributions.
   -- Please provide further clarifications on the contributions of YX and FJZ. An ‘author’ is generally considered to be someone who has made substantive intellectual contributions to a published study. To qualify as an author one should 1) have made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; 2) have been involved in drafting the manuscript or revising it critically for important intellectual content; and 3) have given final approval of the version to be published. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content. Acquisition of funding, collection of data, or general supervision of the research group, alone, does not justify authorship.
Response: Thanks. We have revised it in our manuscript. “WY has contributed to study design, patient recruitment, data collection and original draft of the manuscript writing; YX helped to conduct the study, interpret of the results and revise the manuscript for important intellectual content; YY helped to conduct the study and revise the manuscript for important intellectual content; Feng-jiang Zhang helped to conduct the study, analyze the data; LNY helped to analyze the data; MY helped to design the study and revise the manuscript. All authors read and approved the final manuscript.”
   -- Please represent authors' names using their full initials, not their full name, in the Authors’ Contributions section. If there are any duplicated initials, please differentiate them to make it clear that the initials refer to separate authors.
Response: Thanks. We have revised it in our manuscript. “WY has contributed to study design, patient recruitment, data collection and original draft of the manuscript writing; YX helped to conduct the study, interpret of the results and revise the manuscript for important intellectual content; YY helped to conduct the study and revise the manuscript for important intellectual content; Feng-jiang Zhang helped to conduct the study, analyze the data; LNY helped to analyze the data; MY helped to design the
4. Availability of data and materials
-- Data availability statements can take one of the following forms (or a combination of more than one if required for multiple datasets):
• The datasets generated and/or analysed during the current study are available in the [NAME] repository, [PERSISTENT WEB LINK TO DATASETS]
• The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.
• All data generated or analysed during this study are included in this published article [and its supplementary information files].
• The datasets generated and/or analysed during the current study are not publicly available due [REASON WHY DATA ARE NOT PUBLIC] but are available from the corresponding author on reasonable request.
• Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.
• The data that support the findings of this study are available from [third party name] but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of [third party name].
Response: Thanks. We have revised it in our manuscript. “Availability of data and materials: The datasets used and/or analysed during the current study available from the corresponding author on reasonable request (Email: m18768389432@163.com).”

5. Raw data file
-- Please upload an English language version of your raw data file and ensure this is cited within the main text. Alternatively, as this file contains raw data, and therefore does not contain critical information for understanding your study, please remove it and state "The datasets used and/or analysed during the current study available from the corresponding author on reasonable request" in the data availability section.
Response: OK. Thanks. We have uploaded the raw data file and stated the data availability in the data availability section. See page 12.

6. CONSORT
-- Please include a statement within your methods section to indicate that your study adheres to CONSORT guidelines.
Response: Thank you very much. We have added it to our manuscript. “Our study adheres to CONSORT guidelines.”See page 4.

7. Section
-- Please upload your revised manuscript to the "Pain management and analgesia" section.
Response: OK. Thanks.

8. Clean copy
-- At this stage, please upload your manuscript as a single, final, clean version that does not contain any tracked changes, comments, highlights, strikethroughs or text in different colours. All relevant tables/figures/additional files should also be clean versions. Figures (and additional files) should remain uploaded as separate files. Please ensure that all figures, tables and additional-supplementary files are cited within the text.
Response: Thanks. We have removed the highlights in our revised manuscript.

BMC Anesthesiology operates a policy of open peer review, which means that you will be able to see the names of the reviewers who provided the reports via the online peer review system. We encourage you to also view the reports there, via the action links on the left-hand side of the page, to see the
names of the reviewers.
Response: OK. Thanks.
Reviewer reports:
Ohashi Yayoi (Reviewer 3): Thank you for revising your manuscript according to my comments.
Response: Thank you for your positive and constructive comments and suggestions.
P3, "Many studies have shown that remifentanil (an off label drug for parturient) has less adverse neonatal or maternal effects during cesarean section". - This statement doesn't quite include my concern mentioned last time. I would suggest you to state that "Whilst remifentanil is an off label drug for parturients and some serious adverse effects with remifentanil have previously been reported, it has been recently said that remifentanil is effective, has less adverse effects compared to other opioid medications and is safe to use in controlled circumstances." - reference1) Remifentanil patient-controlled analgesia in labour: six-year audit of outcome data of the RemiPCA SAFE Network (2010-2015). International Journal of Obstetric Anesthesia 2019; 39, 12-21. reference2) Wilson et al. Intravenous remifentanil patient-controlled analgesia versus intramuscular pethidine for pain relief in labour (RESPITE): an open-label, multicentre, randomised controlled trial. Lancet 2018; 392: 662-72. reference3) Radhika et al. Remifentanil versus fentanyl for intravenous patient-controlled labour analgesia: an observational study. Canadian Journal of Anesthesia 2012; Vol.59: 246-254
Response: Thank you very much for your help. In our revised manuscript, we have rewritten it and replaced the references based on your suggestions. See page 3.
P4 Method, Please insert a sentence "Therefore readers know that you monitor patients appropriately with the use of remifentanil.
Response: Thanks. We have added the sentence” RR was measured by carbon dioxide sampling” in our revised manuscript. See page 4.
P7 Result, Ketamine administration did not differ despite the VAS was lower in Group R. - you answered my question. Please include your comment/answer in the discussion part.
Response: Based on your suggestions, we have revised it in our manuscript. “ It is worth noting that ketamine administration dose did not differ from the two groups even though the VAS was lower in parturients with remifentanil. It was because some parturients thought that it was unacceptable using ketamine during repeated cesarean section.” See page 8.