

Dear Editors and Reviewers:

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "Safety and effectiveness of butorphanol in epidural labor analgesia: A protocol for a systematic review and meta-analysis" (ID: 89773). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. Revised portion are marked with yellow color in the paper. The main corrections in the paper and the responds to the reviewer's comments are as flowing:

Responds to the reviewer's comments:

Reviewer #1:

1. Response to comment: This research initiative represents a commendable effort to address the gap in knowledge regarding the safety and efficacy of butorphanol in epidural labor analgesia. By conducting a thorough and comprehensive search of various reputable databases, the study aims to provide a solid foundation for evidence-based decision-making in clinical practice. The inclusion of randomized controlled trials in the review design is a strength, as it ensures a rigorous methodology that can contribute to robust conclusions. This approach enhances the reliability and validity of the findings, adding credibility to the assessment of butorphanol's effectiveness and safety in comparison to other opioids combined with local anesthetics. The consideration of primary outcomes, such as the visual analog scale score for the first stage of labor, fetal effects, and Apgar scores, reflects a comprehensive evaluation of both maternal and neonatal well-being. This approach aligns with the holistic nature of labor analgesia research and provides valuable insights into potential impacts on both mothers and infants. **Response:** We appreciate that the reviewer acknowledged the efforts of our staff.

2. Response to comment: While the inclusion of various databases is comprehensive, it would be beneficial to explicitly mention the search strategy and criteria to enhance transparency and reproducibility. Clear documentation of the search process would contribute to the robustness of the systematic review. Consider specifying the criteria for the selection of studies and potential sources of heterogeneity in the protocol. This will enhance the clarity

of the methodology and facilitate a better understanding of the factors influencing the outcomes.

Response: We have made appropriate corrections based on the reviewer's comments, such as: **“Types of studies” section:** This systematic review will include randomized controlled trials (RCTs) examining the use of butorphanol as an epidural analgesic during labor.

“Search strategy” section: All database searches will be tailored to the specific database using a combination of Medical Subject Headings (MeSH) and free terms. The following terms will be used: butorphanol, parturient, epidural anesthetic, epidural labor analgesia, and randomized controlled trial

3. Response to comment: The commitment to evaluating publication biases and heterogeneity through Egger's or Begg's tests and the Cochran Q test demonstrates a meticulous approach to methodological quality. This awareness of potential biases and variations in study results is crucial for the accurate interpretation of the overall findings.

Response: We appreciate that the reviewer acknowledged the efforts of our staff.

We tried our hardest to improve the manuscript and made some adjustments.

These modifications will have no effect on the paper's content or structure.

We sincerely thank the Editors/Reviewers for their hard work and hope that the adjustment is accepted.

Thank you for your comments and recommendations once more.

Sincerely,

Yan Cheng

January 8, 2024