Author’s response to reviews

Title: Efficacy and safety of prophylactic use of ketamine for prevention of postanesthetic shivering: A systematic review and meta analysis

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The BMC Anesthesiology Editorial Office

To Associate Editor:

Dear Editors:

Thank you for your attention and the reviewers’ evaluation and comments on our paper. We have revised our manuscript according to your kind suggestions. We made responses to the reviewers point-by-point in this cover letter. We sincerely hope this manuscript could be acceptable to be published on BMC Anesthesiology.

Thank you very much for your help and we are looking forward to hearing from you soon.

Best regards
Response to the reviewers’ comments

Reviewer 1

Comment 1: Results: Secondary outcomes: Page 13 Line 29: Please elaborate on 'the other side effects'
Response: Thank you for your kind suggestion. We have explained the other side effects' in Page 13 Line 29.

Comments 2: Page 13 Line 42: please change 'dominant' to 'prevalent' and list the prevalence of hallucinations Consider removing Page 13 Lines 46 though 55, as this does not significantly contribute to the text.
Response: Sorry for the incorrect word we used, we have changed it into 'prevalent' (Page 13 Line 42). The introduction of sedation score seems irrelevant to the topic, we have deleted it.

Comment 3: Page 13 Line 58: please change 'higher' to 'more sedated'
Response: Thank you for your kind suggestion. We have changed the expression (Page 13 Line 58).

Comment 4: Discussion: Page 15 line 15: please change 'included' to 'observed'
Page 15 line 56: please change outcome to sedation
Page 15 line 60: please add a transition to the beginning of this paragraph.
Response: Sorry for our carelessness. You can see the revisions in Page 15 line 15, Page 15 line 56 and Page 15 line 60.

Comment 5: The Abbreviations section still does not contain all abbreviations used throughout the manuscript.
Response: We have added the explanation of 'CNS ' in the abbreviation section.

Comment 6: Table 2 is very cluttered and hard to read. Please simplify this table.
Response: Thank you for your notice. Table 2 is generated automatically by GRADE profile which we thought could provide detailed information about the quality of the evidence.

Reviewer 2

Comment 1: Conclusion: "We found that ketamine reduced the incidence rate of shivering." - you should add "compared to the placebo".
Response: Thank you for your kind suggestion. You can see the revision in Conclusion section, Line 3.

Comments 2: Tables and figures: the list of the papers is aligned by alphabetical order of the author's last name. The trends due to chronological advancement, if any, would be more interesting. Please re-align all studies chronologically in all tables and figures.
Response : Thank you for your kind suggestion. We have e-aligned all studies chronologically in figures 3, 4, 5, 6, 7 and table 1, 4.

Comment 3: References #10 and #17 are not cited fully. Reference #30 should be "Anesthesiology 2002; 96:467-84". I do not have a time to check all references; however, I have a concern whether the authors cited the other references properly. Please recheck citation information of all references and the authors should strictly adhere to the journal's citation instruction.
Response: We are sorry for our mistakes. We have added necessary information for the citations.

Reviewer 3

Comment 1: Abstract Please re-write the abstract as currently, there might be some confusion between the main 'purpose' (linked to ketamine?) and primary (incidence rate of shivering- add between ketamine and placebo) and secondary outcomes (side effects of drugs?-Add ketamine here as well).
Response: Thank you for your kind suggestion. We have re-written the abstract following your advice (See Abstract-Methods-Line4-7).

Comment 2: Methods. Language restrictions were not used. Please re-write this as surely literature was excluded if content was not understood by the authors? Perhaps add which languages are understood by the authors.

Response: We truly did not set language restrictions when selecting the qualified articles in. We did found some articles written in German or French when we selected studies, but the abstract part of them were in English version which we excluded them after reading the abstract part based on our inclusion criteria.

Comment 3: Studies were excluded if other drugs besides ketamine were used. This seems to contradict the overall conclusion that large RCT are needed with anti-shivering regimens (If this implies multimodal regimens, perhaps these studies are already conducted but 'excluded' from this meta-analysis…) Please explain.

Response: What we wanted to find out was whether the single administration of ketamine could reduce the incidence of postoperative shivering. And common meta-analysis is conducted to find out the effect of one specific intervention compared with other interventions. However, the multimodal regimens make the results uncomparable unless we conducted our work in network meta-analysis. We did conclude that multimodal regimens should be carried out in large RCTs but it did not mean that it should be included in our current analysis. We hope we have made us understood to you.

Comments 4: Discussion Please restructure the discussion as following: "In the present study… In total… Were analysed…. Ketamine was first synthesized in the early 1960s as a safe alternative to phencyclidine [26]…. Ketamine is predominantly utilized as an anaesthetic agent that induces analgesia but for a long time it has been criticized for some of its side effects which include the induction of a psychedelic state causing agitation and hallucinations [30]. The key finding of our analysis… "

Response: Sorry for the wrong arrangement of discussion part, we have re-aligned it.
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