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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Author’s response to reviews:

List of responses to Reviewers:

Dear Reviewers,

Thank you for your letter and comments concerning our manuscript entitled “Efficacy and safety of prophylactic use of ketamine for prevention of postanesthetic shivering: A system review and meta analysis” (manuscript ID:BANE-D-19-00344). These 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 in red in the paper. The main corrections in the paper and the responds to the reviewer’s comments are as following (Original comments in blue, response in regular font).
Reviewer 1

Comments 1: The entire manuscript is written in a mix of the first- and third-persons (example: '2 authors...' vs. 'we...'). One person/viewpoint (preferably the third-person) needs to be selected and carried throughout the manuscript. Having a native English speaker review the manuscript will help with this.

Response: Thank you so much for your suggestions. We are very sorry about the misusage of language. We re-wrote the manuscript totally and submit our manuscript to Wolters Kluwer Author Services (https://app.wk.editage.com) for helping us improve the overall quality of the readability of this manuscript. The certification number of it is YESHJ_6. All the fixed parts have been marked as red color.

Comment 2: Several of the graphs/tables are unreadable. Please reformat/use larger font so reviewers and readers are easily able to see the information being presented.

Response: We are very appreciated your valuable advice. We have changed the font of our graphs/tables to make the manuscript more readable to readers in the revised manuscript.

Comment 3: I recommend to only include tables and figures that add value and enhance the text of the manuscript. This version has numerous figures and tables, some of which I believe can be removed (figure 2, table 3, table 4).

Response: Thanks for your time and your valuable comments. We think both figures are necessary. Figure 2 is ‘Risk of bias graph and summary’ which can represent the bias of included studies, it is complementary to Figure 3.

Comment 4: Under abbreviations, the authors state, 'no abbreviations in the text were used'. However, there are numerous abbreviations throughout the manuscript which need to be defined.

Response: We are very sorry for our negligence. We added all used abbreviations under abbreviations in our revised manuscript.

Thanks again for your time and your valuable comments.
Reviewer 2

Comment 1: Abstract: "Ketamine did reduced the incidence rate of postanesthetic shivering compared with placebo (odds ratio [OR]: 0.13, 95% confidence interval [CI]: 0.06 to 0.26, P < 0.00001)." vs. "No significant difference was found in the incidence of postanesthetic shivering for all comparisons between ketamine and other pharmacological interventions. - These statements are contradictory. Please clarify.

Response: Thanks for your comment. We have re-edited the part of abstract in the revised manuscript.

Comment 2: "Usage of ketamine was associated with a lower rate of hypotension and bradycardia when compared with placebo." Vs. "The occurrence of side effects caused by ketamine or other study drugs was similar with an exception of the comparison between ketamine and ondansetron where ketamine lowered the incidence of hypotension" - repetition to me. Please combine the statements.

Response: Thank you for your kind suggestion. We have re-edited the part of abstract in the revised manuscript.

Comment 3: The following search-term strategy was used: 1) shivering; 2) tremor; 3) shake; 4) hypothermia; 5) anesthesia; 6) postanesthetic; 7) postoperative; 8) surgery; 9) ketamine; 10) 1 or 2 or 3 or 4; 11) 5 or 6 or 7 or 8; 12)9 and 10 and 11 - It is not clear the search strategy in this description. Please clarify.

Response: Thanks for your time and your valuable comments. We use the similar expressions of shivering such as ‘shivering’, ‘tremor’, ‘shake’, ‘shake’ to make sure we include the study population as many as possible. The similar expressions were combined when we searched the related studies, for example we use item 10) to express the issue ‘shivering’. In the end, we got our final search result via item 12).

Reviewer 3

Comment 1: Abstract: results:'Ketamine did reduced' to 'ketamine did reduce'

'Usage of ketamine... when compared with placebo.' to 'when compared to placebo'.

'The occurrence of side effects...but with a relatively higher incidence of...' to 'but was associated with a relatively higher...'
Response: Thank you for your kind suggestion. We have made changes according to your suggestion and a native English speaker reviewed and re-edited the revised manuscript.

Comment 2: Key points summary: Please rewrite the question into a more simple phrase.

Response: Thank you for your kind suggestion. We have re-edited the part in the revised manuscript.

Comment 3: Background:

Please change the following:

'which may cause aggravated pain' to 'complication of anesthesia, perhaps even aggravating pain'.

'Moreover,... which increases...' to 'Moreover,... which increase...'

Results:

Please change the following:

'In 15 trials participants were adults over 18 years...' to 'In 15 trials... adults, ...'

In 13 trials... compared against' to 'In 13 trials ... compared to...

Please change 'compared with' to 'compared to'...

Please change 'in 4 trials included patients receiving' to in 4 trials... having undergone orthopedic surgery'

Secondary outcomes

Ketamine vs placebo:

Please change the following:

'The incidence of hallucination was.. in patients received... to 'in patients who received...'

'significant' to significant'

Response: Thanks for your time and your valuable comments. We have made changes according to your suggestion and re-edited the part in the revised manuscript.
Comment 4: Discussion:

Please do not call postoperative shivering an emotion.

The discussion does not mention the 'dissociative state' that ketamine causes.

Please change 'ketmaine' to 'ketamine'.

Please explain with what you mean with idealising the beneficial aspects of ketamine...

Response: Thank you for your kind suggestion. We have made changes according to your suggestion and re-edited the part in the revised manuscript.

We added a brief introduction of ‘dissoactive state’ of ketamine in the discussion section.

‘idealising the beneficial aspects of ketamine’ means that we want to find out whether ketamine could reduce the rate of postoperative shivering which is not be highlighted in any medical guidelines. If ketamine could help reducing the rate of postoperative shivering, we want to clarify it and provide evidence of this particular effect.

Comment 5: Please rewrite/ reorder the part about forced air heating... Was the comparison of ketamine to non-pharmacological treatments excluded (since a study comparing ketamine to forced air warming was removed...?)

Response: Thank you for your kind suggestion. We have made changes according to your suggestion and re-edited the part in the revised manuscript.

Thanks again for your time and your valuable comments.

Reviewer 4

Comment 1: One trial on pediatric patients were included that I recommend to remove that study from the meta-analysis and repeat analysis.

Response: Thank you for your kind suggestion. Based on our subgroup analysis, we found out that the inclusion of pediatric patients does not influence the primary outcome.
Comments 2:

Response: Please clarify the search strategy.

Response: Thank you for your kind suggestion. We use the similar expressions of shivering such as ‘shivering’, ‘tremor’, ‘shake’, ‘shake’ to make sure we include the study population as many as possible. The similar expressions were combined when we searched the related studies, for example we use item 10) to express the issue ‘shivering’. In the end, we got our final search result via item 12).

Comment 3: Authors mentioned that search study was not limited for language. I was wondering if any non English article was included in the study.

Response: Thanks for your comment. We wanted to collect as many related studies as possible, and actually we could not find any non English articles according to our inclusion and exclusion criteria in the present study.

Comment 4: It was stated that if other antishivering medications were used they excluded the trial. I was wondering which medications were considered in their list and how authors interpreted data if other perioperative medications were not reported (does not necessarily mean those medications were not administered).

Response: We are very appreciated your valuable advice. ‘Other antishivering medications’ means any drugs that were not the main study subject. In the included articles the researchers reported the perioperative medications, otherwise they were excluded in the present study.

Thanks again for your time and your valuable comments

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper. And here we did not list the changes but marked in red in revised paper.

We appreciate for Editors/Reviewers’ warm work earnestly, and hope that the correction will meet with approval.

Once again, thank you very much for your comments and suggestions.

Please feel free to contact me if you have any questions.
Yours sincerely,

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