Archives of Neuroscience
Volume 10 · Issue 4 · e140241

OPEN PEER REVIEW

Comparison of Ketamine to Haloperidol for Preventing Delirium in ICU Elderly Patients

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SUBMITTED	REVISED	ACCEPTED	DOI
23 Aug 2023	17 Oct 2023	18 Oct 2023	10.5812/ans-140241

About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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1 Original submission

4 comments · 18 Sep 2023 – 26 Sep 2023

Referee 1 Reviewer

MAJOR REVISION 18 Sep 2023

Dear AE,
Below you can find my review:
The manuscript titled "Ketamine Compared to Haloperidol for Preventing Delirium in ICU Elderly Patients" discusses the results of a randomized clinical trial comparing the safety and efficacy of ketamine and haloperidol in preventing delirium in elderly ICU patients. Overall, the study is well-structured and provides valuable insights into the potential use of ketamine for delirium prevention in this patient population. However, there are several areas that require clarification and improvement.

Specific Comments:

Abstract Clarity and Completeness: The abstract provides a good summary of the study but could benefit from a more concise and structured format. Additionally, the abstract should include the key findings, conclusions, and implications of the study.

Introduction:

The introduction should provide a more comprehensive background on the significance of delirium in ICU patients, particularly in the elderly. Additionally, it would be helpful to cite more recent literature since the knowledge cutoff date is in September 2021.
The hypothesis should be stated more explicitly in the introduction section.
Methods:

The methods section should provide more details about the randomization process, including how the random number tables were generated.
The exclusion criteria should be explained in more detail, including the specific criteria related to psychosis and cardiovascular disease.
The dosages of ketamine and haloperidol used in the study should be compared to dosages used in other studies, if available.
The method of blinding (single-blind, double-blind) should be mentioned, as it can impact the study's validity.
It's important to describe the statistical methods in more detail, including how the t-test and repeated-measures ANOVA were applied.
Discussion:

The discussion should focus on interpreting the results, comparing them to existing literature, and discussing the clinical implications of the findings.
The limitations of the study should be addressed in more detail, and potential sources of bias or confounding factors should be discussed.
While the manuscript mentions the anti-inflammatory properties of ketamine, it could delve deeper into the potential mechanisms by which ketamine might reduce delirium.
The discussion section should address the clinical applicability of the findings and potential future research directions.
Language and Clarity:

The manuscript contains some grammatical errors and awkward sentences that need revision for clarity. For instance, the sentence, "The P-value between the groups was 0.168 (Effect Size = 0.042), while the P-value

within the groups was <0.001 (Effect Size = 0.601)," could be rephrased for better readability.
Conclusion:

The conclusion should succinctly summarize the main findings of the study and emphasize their clinical relevance.

Peyman Saberian Reviewer

ACCEPT 26 Sep 2023

Dear AE,
The manuscript is acceptable in my view.

Associate Editor

MAJOR REVISION 26 Sep 2023

Dear EIC,
I thank the authors and express my appreciation to the researchers. The manuscript is a valuable piece of research. But some revisions are needed. The authors should revise it based on the comments.

Editor-in-Chief

MAJOR REVISION 26 Sep 2023

Dear Author,
Thank you for submitting the article. It needs some revision. Please revise it based on the reviewers' and AE's comments.

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Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

October 2023

Dear Reviewer

Many thanks for allowing us to revise our manuscript. We appreciate the positive and constructive comments and suggestions on our manuscript entitled **"Ketamine Compared to Haloperidol for Preventing Delirium in ICU Elderly Patients**" [ID: 140241].

The comments were valuable and helpful in improving our manuscript. We carefully reviewed the comments and revised the manuscript accordingly, with the revised portions marked in yellow throughout the text. We hope that the revised manuscript will be acceptable for publication. We would like to express our gratitude to your precise guidance.

Response to the reviewer 2 comments:

Specific Comments:

1. Abstract Clarity and Completeness: The abstract provides a good summary of the study but could benefit from a more concise and structured format. Additionally, the abstract should include the key findings, conclusions, and implications of the study.

Response: Thanks for your valuable comment, we rewrite the manuscript according to your valuable suggestion.

Introduction:

2. The introduction should provide a more comprehensive background on the significance of delirium in ICU patients, particularly in the elderly.

Response: We rewrite introduction according to your valuable suggestion (line 48-71).

3. Additionally, it would be helpful to cite more recent literature since the knowledge cutoff date is in September 2021.

Response: Based on your valuable suggestion, we use the recent literature in the revised manuscript.

4. The hypothesis should be stated more explicitly in the introduction section.

Response: Based on your valuable comment, we explain the hypothesis in more details. (line: 91-97)

Methods:

5. The methods section should provide more details about the randomization process, including how the random number tables were generated.

Response: Thank you for the valuable feedback and acknowledge their suggestion to include more details about the randomization process in the methods section (line 122-126).

6. The exclusion criteria should be explained in more detail, including the specific criteria related to psychosis and cardiovascular disease.

Response: Thank you for your comment regarding the need for more detailed explanation of the exclusion criteria related to psychosis and cardiovascular disease. In response to your feedback, we will provide a more comprehensive description of the exclusion criteria in the revised manuscript (line 111-115).

7. The dosages of ketamine and haloperidol used in the study should be compared to dosages used in other studies, if available.

Response: Thank you for your comment. In the discussion section, we compared the dosages of ketamine and haloperidol used in our study with those reported in other relevant studies.

8. The method of blinding (single-blind, double-blind) should be mentioned, as it can impact the study's validity.

Response: according to your valuable comment, we mention the method of blinding in study design section.

9. It's important to describe the statistical methods in more detail, including how the t-test and repeated-measures ANOVA were applied.

Response: The details of statistical methods were applied. (line 151-156)

Discussion:

10. The discussion should focus on interpreting the results, comparing them to existing literature, and discussing the clinical implications of the findings.

Response: According to your valuable comments, the discussion section revised (line 226-244) (line 262-269)

11. The limitations of the study should be addressed in more detail, and potential sources of bias or confounding factors should be discussed.

Response: The study limitations were written in more detail in revised manuscript (line 331-351)

12. While the manuscript mentions the anti-inflammatory properties of ketamine, it could delve deeper into the potential mechanisms by which ketamine might reduce delirium.

Response: The manuscript rewrite, according to your valuable comments (line 292-320)

13. The discussion section should address the clinical applicability of the findings and potential future research directions.

Response: The manuscript rewrite, according to your valuable comments (line 321-329)

Language and Clarity:

14. The manuscript contains some grammatical errors and awkward sentences that need revision for clarity. For instance, the sentence, "The P-value between the groups was 0.168 (Effect Size = 0.042), while the P-value within the groups was <0.001 (Effect Size = 0.601)," could be rephrased for better readability.

Response: Thanks for your valuable comment, a native English speaker edited our manuscript for improved clarity and readability.

Conclusion:

15. The conclusion should succinctly summarize the main findings of the study and emphasize their clinical relevance

Response: The manuscript rewrite, according to your valuable comments (line 353-370)

2 Revision 1

3 comments · 18 Oct 2023 – 18 Oct 2023

Referee 1 Reviewer

ACCEPT 18 Oct 2023

Dear AE,
I reviewed the manuscript again. The great effort in improving the manuscript is highly appreciated.
The authors have addressed all comments.
Thank you

Associate Editor

ACCEPT 18 Oct 2023

Dear EIC,
I read the manuscript, and the authors corrected the requested items. The article could be accepted at this stage.
Sincerely;

Editor-in-Chief

ACCEPT 18 Oct 2023

Dear Author,
Thank you for paying attention and responding to the reviewer's comments. The manuscript is acceptable now.