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OPEN PEER REVIEW

Oral Melatonin for Colistin-induced Nephrotoxicity Reduction in Intensive Care Unit: A Randomized Placebo Controlled Clinical Trial

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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.

More about open peer review: brieflands.com/knowledgebase/opr

Contents

1 **Original submission** Referee 1 2
2 **Revision 1** Associate Editor, Editor-in-Chief 3
Authors' reply to reviewers 4
Reviewer and editor comments 7
3 **Revision 2** Alireza Soleymanitabar, Associate Editor 8
Authors' reply to reviewers 9
Reviewer and editor comments 12
4 **Revision 3** Associate Editor 13
Authors' reply to reviewers 14
Reviewer and editor comments 15

1 Original submission

1 comment · 23 Feb 2023

Referee 1 Reviewer

MAJOR REVISION 23 Feb 2023

This randomized placebo-controlled clinical study's objective is to investigate the influence of melatonin on reducing the medication-induced kidney damage produced by colistin so that we may be able to use this therapy with fewer side effects. The research compared the outcomes of two treatment groups involving 56 critically ill patients with MDR infections. The melatonin group (intervention) took 3 mg orally at the beginning of their IV colistin treatment, whereas the placebo group (control) took the placebo with their IV colistin treatment. In critically sick patients taking colistin, the investigators could not find any significant change in AKI criteria with the addition of melatonin; nonetheless, no problems were identified.

1. Please rephrase the following sentence in the abstract to improve its clarity:
"Analyzing their details based on age(p-valueo.357), gender (p- valueo.945), weight(p-valueo.438), APACHE score(p-valueo.162)".

2. Please always provide relevant p-values when presenting results. Consider, for example, the following phrase without a p-value:
"We concluded that difference between two groups insignificant and melatonin doesn't cause a decrease in the blood level of creatinine and BUN or prevent the reduction of urinary volume". (p-values???)

3. Please also revise the following sentence:
"We concluded that difference between two groups insignificant and melatonin doesn't cause a decrease in the blood level of creatinine".

4. From my point of view, the background section of the abstract is so long; instead, you can provide the readers with more information in the conclusion section of the abstract.

5. Please revise the following sentence:
"The appearance and spread of antibiotic-resistant(MDR) bacteria and limited number of available antibiotics for lack of new antibiotic development we have to use old antibiotics".

6. The document has several issues with English editing.

7. In the introduction, the word "we" appears many times in sentence constructions.

8. The introduction is a fairly lengthy section. In addition, the authors were unable to express their study aim or the research gap toward the end of the introduction.

9. Put the patient selection criteria (inclusion/exclusion) at the beginning of the method section.

10. The discussion is poorly written and arranged. Please attempt to enhance the quality of the discussion by including relevant studies and comparing their findings to your own.

11. Add a participant flow diagram to your article.

2

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.

Thanks to the reviewers

The comments of the dear reviewers are written below along with the answers

1.please rephrase the following sentence of the abstract to increase the meaning:

Analyzing their details based on age(p-value0.357), gender (p-value0.945), Wight(p-value0.438), APACHI score (p-value 0.162)

Answer: information obtained from recipients was analyzed for age (p-value 0.357), gender (p-value 0.945), Wight (p-value 0.438), APACHI score (0.162).

2.Please always provide relevant p-value when presenting results. Consider for example. The following phrase without p-value: we concluded that difference between two groups insignificant and melatonin doesn't cause a decrease in blood level for creatinine and BUN or prevent the reduction of urinary volume. (p-value??)

Answer: We did not observe a significant difference in AK criteria in two groups. Compared to the control group, melatonin didn't cause a decrease in the blood level of creatinine (p-value 0.110), BUN(p-value0.567), and change in urinary volume (p-value 0.913)

3. please also revise the following sentence:

We concluded that difference between two groups insignificant and melatonin doesn't cause of decrease in blood level of creatinine.

Answer: We did not observe a significant difference in AKI criteria in the two groups. Compared to the control group, melatonin didn't cause a decrease in the blood level of creatinine(p-value0.110), BUN(p-value0.567) and, change in urinary volume(p-value0.913).

4.In my point of view, the back ground section of the abstract is so long; instead, you can provide the readers with more information in the conclusion section of the abstract.

Answer: Background was summarized and the conclusion were rewritten.

Conclusions: It did not reveal any significant difference in the AKI criteria, including blood level of creatinine and BUN and daily urine volume with the addition of melatonin in participants receiving colistin; however, there were no complications observed in the intervention group who received melatonin.

5. Please revise the following sentence:

The appearance and spread of antibiotics-resistance (MDR) bacteria and limited number of available antibiotics for lack of new antibiotic development we have to use older antibiotics

Answer: This sentence was removed from the new text.

6. The document has several issue with English editing

Answer: Ok, will be done

7. in the introduction, the word "we" appears many times in sentence constructions.

Answer: Ok, I tried to reduce the number of "we" words

8.The introduction is a fairly lengthy section. In addition, the authors were unable to express their study aim or research gap towards the end of in the introduction.

Answer: I summarized and simplified the introduction, words 900words to 600words. I tried to reduce gap

9. Put the patient selection criteria (inclusion/exclusion) at the beginning of the method.

Answer: ok done

10. The discussion is poorly written and arranged. Please attempt to enhance the quality of discussion by including relevant studies and comparing their finding to your own.

Answer: The discussion was revised

11. Add participant flow diagram into tour article

Answer: flow diagram was added to the article

2 Revision 1

2 comments · 4 Jul 2023 – 4 Jul 2023

Associate Editor

MINOR REVISION 4 Jul 2023

Minor revision

Editor-in-Chief

MINOR REVISION 4 Jul 2023

Minor Revision

3

Revision 2

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.

Thank the dear reviewers for the valuable comments that will improve the quality of the article

I corrected the sentence with GREEN highlight

I would like the answer to the questions

Reviewer1:

Furthermore in Table 2 you have mentioned : Cr toxicity, Urine toxicity and Nephrotoxicity and Some of the numbers infront of them that are not clear what they represent...

Please tell us about difference between Cr toxicity, Urine toxicity and Nephrotoxicity.

RED highlight is corrected

Creatinine toxicity: creatinine is a toxic substance and is the final product of creatine metabolism. It is life threatening and led to preventing to entry of glucose in to red blood cells, reducing the life of RBCs, and finally lysis of them. Creatinine can also interfere with insulin secretion by the pancreas and disturbance of glucose hemostasis.

Urea toxicity: urea is the end product of nitrogen metabolism, excreted from the kidneys. An increases in blood level of urea lead to uremia and can lead to neuromuscular, endocrine, and metabolism disturbance.

Nephrotoxicity: nephrotoxicity is defined as all factors that causes the rapid deterioration of kidney function due to toxic effect of drug and chemicals. In nephrotoxicity, urinary output decreases and an increases in blood creatinine and urea.

Urine toxicity: It was typing error. Corrected to low urine output.

Reviewer2:

in the introduction: The Content order should be changed. you are supposed to write about the main problem first (that is aki in your study). Second you are supposed to write about the Colistin that is the cause of this problem

In the introduction, a paragraph about AKI was added to the first part, and also the sentence about colistin were changed.

You should mention the burden of this disease and its problems from the most reliable and recent huge studies that investigated this problem.

New references were added to improve the quality of the study.

It's better that you mentioned the figure number two in this part when you are explaining the effects of Colistin and clearly the picture should be related to your text completely. It's better that the figure completes your writing a

Number and location of figures has been corrected.

Finally, in the introduction part you are not supposed to say that what score or what tool you have used and what are your inclusion or exclusion criteria. There are supposed to be in the methods part. At the last of the introduction part, it's better that you say your goal to run this study.

KIDIGO discussion moved from introduction to the setting

figure 1 is prepared 2 times in the manuscript. the first one is so blurred and poor in quality.
figure 2 is

Quality of figure is corrected

first paragraph DOES need references.

References have been added to the first and third paragraphs of discussion.

first line of the second paragraph in the discussion doesn't makes sense. it is unrelated to the rest of the paragraph.
the third paragraph MUST have references.
overall, the structure of text in the dis

First line of second paragraph is corrected. Third paragraph reference was added

overall, the structure of text in the discussion part should be arranged more scientific. for example: line 201 to 204 should be used in a proper paragraph. it should have more explanation and comparison with other studies

The structure of discussion has changed line 201 to 204 changed

3 Revision 2

2 comments · 2 Aug 2023 – 5 Aug 2023

Alireza Soleymanitabar Reviewer

ACCEPT 2 Aug 2023

I have no further comments.

Associate Editor

MINOR REVISION 5 Aug 2023

Minor Revision

4

Revision 3

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.

I would like to thank the dear revivers, I tried to correct the error of article

Commented [A1]: This manuscript needs major revision according to scientific writing structure, statistical analysis, results presentation style, and results interpretation. Comments annexed in the manuscript file that should be applied for next time review.
Answer: Yes, I do

Commented [A2]: These paragraphs should be replacing with more related contents.
Answer: Replace with short and more related contents.

Commented [A3]: Methods should be written according to CONSORT guideline with appropriate subtitles.
Answer: Change according to the CONSORT guideline

Commented [A4]: Duration od intervention should be added.
Answer: Duration added 10 days.

Commented [A5]: Also, mean change from baseline to the end of study, in each group should be calculated using by repeated measure ANOVA or Friedman test, in terms of normality distribution.
Answer: Repeated measured with ANOVA was done.

Commented [A6]: Results and tables should be reported and re-designed according to following well written paper: “Evaluation of the Effectiveness of N-Acetylcysteine in the Prevention of Colistin-Induced Nephrotoxicity: A Randomized Controlled Clinical Trial
Answer: Re-arranged according to this article.

Commented [A7]:
We had no financial support.

Commented [A8]:
The consent form was sent.

[Translated from Persian by the Brieflands editorial office.]

4 Revision 3

1 comment · 14 Sep 2023

Associate Editor

ACCEPT 14 Sep 2023

Accept