

Dear Sir,

Thank you for your e-mail and the valuable comments/suggestions of the reviewers.

Please find enclosed our manuscript entitled "**Role of Melatonin in Management of COVID-19: A Systematic Review**" modified according to the valuable recommendations of the reviewers; Modifications in RED.

Here we answer all inquiries/suggestions of the reviewers:

FIRST ROUND

Reviewer A:

1. Relevance of the title to the content of the article: Regular

Answer: Thank you.

2. Summary: Regular

Answer: Thank you.

3. Introduction: Regular

Answer: Thank you.

4. Methodology: Poor

Answer: Modified and updated.

5. Ethical aspects. Yes

Answer: Systematic reviews and Meta-analysis are exempted from Ethical Committees Approvals.

6. Results: Regular

Answer: Modified and updated.

7. Discussion: Regular

Answer: Modified and updated.

8. Conclusions: Regular

Answer: Modified and updated.

9. References. Poor

Answer: All references now follow Vancouver style.

10. Redaction. Requires a thorough assessment of grammar and spelling

Answer: English style was improved.

11. Contributions.

Answer: Done. Modified and updated.

Reviewer B:

1. Relevance of the title to the content of the article: Regular

Answer: Thank you.

2. Summary: Regular. To conclude this hypothesis it would be necessary to perform another type of study such as a clinical trial.

Answer: A quantitative review of RCTs was conducted; Level 1 Evidence.

3. Introduction: Summarise the effects of melatonin and its relationship with covid
Your work lacks objectives, hypothesis and justification, as these are important components especially for the reader in case of possible publication.

Answer: Modified and updated.

Objective: The aim of the current systematic review was to clarify the efficacy of melatonin in management of COVID-19 patients and its contribution in faster return of patients to baseline health.

4. Methodology: Regular

Answer: Modified and updated.

5. Ethical aspects. No

Answer: Systematic reviews and Meta-analysis are exempted from Ethical Committees Approvals.

Ethical Considerations: Added after the statistical analysis section.

6. Results: Regular

Answer: Modified and updated.

7. Discussion: Regular

Answer: Modified and updated.

8. Conclusions: Regular

Answer: Modified and updated.

9. References: Regular

Answer: All references now follow Vancouver style.

10. Redaction. Acceptable

Answer: English style was improved.

11. Contributions: A systematic review you cannot conclude or assure that melatonin reduced mortality in covid patients as this may be biased by confounding factors such as comorbidities, age...so it is recommended that you mention the results but conclude as a probability, since to conclude this hypothesis it would be necessary to perform another type of study such as a clinical trial.

Answer: A quantitative review of RCTs was conducted; Level 1 Evidence.

Reviewer C:

1. Relevance of the title to the content of the article: Good

Answer: Thank you.

2. Summary: Poor

Background does not include information about melatonin as an intervention for SARS-CoV-2.

Answer: Added. Modified and updated.

3. Introduction: Regular. Citation is not suitable.

Answer: Modified and updated.

4. Methodology: Regular

Answer: Modified and updated.

5. Ethical aspects. No

Answer: Systematic reviews and Meta-analysis are exempted from Ethical Committees Approvals.

Ethical Considerations: Added after the statistical analysis section.

6. Results: Regular

Answer: Thank you.

7. Discussion: Regular

Answer: Thank you.

8. Conclusions: Regular

It is recommended that "Conclusion" was made as a conditional result, since these studies can not grant a general conclusion.

Answer: A quantitative review of RCTs was conducted; Level 1 Evidence.

9. References. Good

Answer: All references now follow Vancouver style.

10. Redaction. Needs some language corrections

Answer: English style was improved.

11. Contributions. One of the main weaknesses is that implies a general conclusion.

Answer: A quantitative review of RCTs was conducted; Level 1 Evidence.

Limitations: Pooling results of small number of studies.

SECOND ROUND REVIEWERS'S COMMENTS

Reviewer A:

Are there controversies in this field? What are the most recent and important achievements in the field? In my opinion, answers to these questions should be emphasized. Perhaps, in some cases, novelty of the recent achievements should be highlighted by indicating the year of publication in the text of the manuscript.

Answer: Introduction was modified to justify the study and a new recent reference was added; Mubashshir et al., 2023.

The discussion section is modest.

Answer: Discussion was modified and improved.

Abstract: not properly written.

Answer: Abstract was modified and re-written.

Conclusion: The section devoted to the explanation of the results suffers from the same problems revealed so far. Your storyline in the results section (and conclusion) is hard to follow. Moreover, the conclusions reached are really far from what one can infer from the empirical results.

Answer: Conclusion was modified and re-written.

The discussion should be rather organized around arguments avoiding simply describing details without providing much meaning.

Answer: Discussion was modified and improved.

Reviewer B:

The wording and structure of the paper have significantly improved, although the introduction and discussion sections could be further refined.

Answer: Introduction and Discussion were modified and improved.

In the introduction: it is recommended to summarize/synthesize the concept of virus composition and structure as the information is scattered and does not focus on how melatonin may affect the virus structure or the immune response, which can lead to confusion and fail to clarify its benefits.

Answer: Introduction was modified.

In the discussion: Improve the wording and avoid making absolute statements or conclusions about the direct effect of melatonin on improving Covid patients, and despite the study being a quantitative review of RCTs, the results indicate probabilities.

Answer: Done.

Reviewer C:

- In the RCT standard care was compared to melatonin intervention? It should be mentioned, in order to avoid bias

Answer: Modified in the Methodology; Types of interventions.

- In Conclusion, no affirmations must be made. Try writing "Melatonin may decrease mortality rate among..." instead of "Melatonin decreased the mortality..."

Answer: Done.
