Journal of Reports in Pharmaceutical Sciences
Volume 13 · Issue 1 · e149927

OPEN PEER REVIEW

Atorvastatin Attenuated the Inflammatory Outcomes of COVID-19: A Double-Blind, Randomized Controlled Trial

Hajar Shokri-Afra, Shahab Moghadam, Ziaeddin Oladi, Masoud Lotfizadeh, Mohammad Mehdi Mirforoughi, Mohammad-Hassan Arjmand, Ahmad Raeisi

SUBMITTED	REVISED	ACCEPTED	DOI
11 Jun 2024	30 Nov 2024	19 Jan 2025	10.5812/jrps-149927

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** Mohammad Babaeian, Associate Editor, Editor-in-Chief 2
2 **Revision 1** Associate Editor, Editor-in-Chief 3
Authors' reply to reviewers 4
Reviewer and editor comments 8

1 Original submission

3 comments · 19 Oct 2024 – 27 Oct 2024

Mohammad Babaeian Reviewer

REJECT 19 Oct 2024

Dear authors,
You have carried out a valuable study.
- I want to ask you to polish the English of your manuscript.
- Please finalize the manuscript file; there are some blank highlighted spaces in the text.
- I am pretty sure that you were supposed to write this sentence differently: "They were randomly assigned to receive remdesivir plus atorvastatin 40 mg/day for 14 days or a placebo after fulfilling the inclusion criteria."
- Why did you choose 40 mg of atorvastatin? Why for 14 days?
- Why is the rate of "Muscular pain" higher in the Atorvastatin Group?

Regards

Associate Editor

MAJOR REVISION 27 Oct 2024

Dear Authors,

I hope this message finds you well. I am writing to inform you that your manuscript entitled “Atorvastatin Attenuated the Inflammatory Outcomes of COVID-19: A Double-Blind, Randomized Controlled Trial” has been reviewed and requires major revisions before it can be considered for publication in the Journal of Reports in Pharmaceutical Sciences.
Best regards,
E.I.C

Editor-in-Chief

MAJOR REVISION 27 Oct 2024

Dear Authors,

I hope this message finds you well. I am writing to inform you that your manuscript entitled “Atorvastatin Attenuated the Inflammatory Outcomes of COVID-19: A Double-Blind, Randomized Controlled Trial” has been reviewed and requires major revisions before it can be considered for publication in the Journal of Reports in Pharmaceutical Sciences.
Best regards,
E.I.C

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.

Point-by-point responses to reviewers

Dear Editor in Journal of Reports in Pharmaceutical Sciences

This is an accompanying letter outlining how the reviewers' comments were addressed in the revised manuscript entitled " **Atorvastatin attenuated the inflammatory outcomes of COVID-19: A double-blind, randomized controlled trial**", with submission-ID 149927.

First of all, we deeply appreciate the editors and reviewers who paid much attention to our manuscript. We received very valuable comments that we believe will greatly improve our manuscript. So, we paid close attention to all the comments provided and applied the requested changes to the manuscript. All changes were marked with highlights in the revised manuscript. We tried our best to apply the comments of both referees in a detailed and scientific manner in order to cover the referees' requests adequately.

Reviewers' Comments:

Reviewer 1:

In the article titled "Atorvastatin Attenuated the Inflammatory Outcomes of COVID-19: A Double-Blind, Randomized Controlled Trial," the authors investigated the role of atorvastatin in managing inflammatory markers in COVID-19 patients. Below are the reviewer's concerns and recommendations:

1. Is this study registered with a recognized clinical trial registry? If so, the registration code should be provided in the methods section.

Author's response: According to the journal instructions, we had to send a blind manuscript file without the authors' names and affiliations, so these, the name of pharmaceutical company and IRCT-related information were sent in a separate file as the **"Title page**". Given your comment, related information was added in the Methods section.

2. How was patient consent obtained for this study? Was an informed consent form provided for participants?

Author's response: Thank you for your attention. Yes, "All patients provided informed consent to participate in the study before initiating the treatments". According to your comment, this sentence was added in the Methods section

3. The name of the pharmaceutical company is not mentioned in the manuscript, and this has been highlighted.

Author's response: As mentioned in the answer to the first question, this subject was not included in the manuscript to avoid reviewer bias. Therefore, this part was empty. But now we added to the text.

Point-by-point responses to reviewers

4. In my opinion, the inclusion and exclusion criteria should be more comprehensive, as factors like pregnancy and breastfeeding are not currently considered.

Author's response: Thank you for your attention to the inclusion and exclusion criteria. We tried to add the remaining items in this section to make it more comprehensive.

5. Primary and secondary outcomes should be specified separately.

Author's response: In the methods section of the abstract and the outcome measures section of the Methods, we noted that "inflammatory markers" were assessed as the main (primary) outcome, and the other dependent variables were considered secondary outcomes.

If the respected reviewer has another suggestion to clarify this part better and fix the flaws, we will gladly welcome it.

6. In the table of basic patient characteristics, appropriate statistical analyses should be conducted for all variables, including age and sex, and the p-values should be included in the table.

Author's response: In Tables 2 and 3, the comparisons and their significance are written at baseline and at two other times, so we omitted to write the p-value in Table 1 to avoid re-reporting the results. Only the p-values related to age, gender, and BMI are not written in the manuscript, which clearly shows that there is no significant difference between the two groups.

7. In several instances, p-values exceeding one have been reported (e.g., 163 and 457), which is statistically incorrect, as p-values must range between zero and one.

Author's response: You are absolutely right. This was a typographical error and all items have been corrected. Thank you for your careful comment.

8. On page 7, second line, is the value of p written correctly as (p > 0.001)?

Author's response: Thank you for your attention. This was a typographical error that has been corrected.

9. Is the total number of patients included in the analysis 80 or 81? Table 1 mentions 40 individuals in each group, but the text states 81.

Author's response: We are very glad that you read our manuscript so carefully. As shown in the study diagram (Figure 1), the final number of included patients was 81, and this was also a typographical error in Tables that was corrected. Thank you again for your attention.

Reviewer 2:

Point-by-point responses to reviewers

Dear authors,

You have carried out a valuable study.

- I want to ask you to polish the English of your manuscript.

Author's response: The written language was rechecked with the relevant software (Grammarly and chatGPT). It also improved by a researcher at the University of Manchester.

- Please finalize the manuscript file; there are some blank highlighted spaces in the text.

Author's response: According to the journal instructions, we had to send a blind manuscript file without the authors' names and affiliations, so these, the name of pharmaceutical company and IRCT-related information were sent in a separate file as the "**Title page**". Given your comment, related information was added in the Methods section.

- I am pretty sure that you were supposed to write this sentence correctly different: "They were randomly assigned to receive remdesivir plus atorvastatin 40 mg/day for 14 days or a placebo after fulfilling the inclusion criteria."

Author's response: Thank you for your attention. The above sentence was rewritten to clear the ambiguity. I hope this amendment is accepted.

- Why did you chose 40 mg of atorvastatin? Why for 14 days?

Author's response: The purpose of this study was to investigate the anti-inflammatory effect of statins, and considering that this effect is obtained by consuming high doses of these drugs, a dose of 40 mg of atorvastatin was used. As referenced in the article entitled "Comparison of anti-inflammatory effect of atorvastatin with rosuvastatin in patients of acute coronary syndrome": [Atorvastatin has been shown in clinical studies to produce reduction in CRP of 39% to 60% across the dose range of 10 to 80 mg [15,16]].

On the other hand, considering that systemic inflammation is the mechanism of pathogenesis and damage caused by SARS-CoV-2 in the first two weeks, atorvastatin was prescribed during these first two weeks of the treatment start.

- Why the rate of "Muscular pain" is higher in the Atorvastatin Group?

Author's response: The rate of "muscle pain" is not higher in the atorvastatin group. Table 2 shows that 31 in the statin group and 27 in the placebo group had no significant difference at the baseline (0.317), and until the end of the study, the difference between the two groups was not significant.

Regards

Point-by-point responses to reviewers

Associate Editor's Comments:

EIC Decision:

Associate Editor 1:

Dear Authors,

I hope this message finds you well. I am writing to inform you that your manuscript entitled "Atorvastatin Attenuated the Inflammatory Outcomes of COVID-19: A Double-Blind, Randomized Controlled Trial" has been reviewed and requires major revisions before it can be considered for publication in the Journal of Reports in Pharmaceutical Sciences.
Best regards,

E.I.C

Author's response: Thank you again for your attention. We tried to apply the reviewers' and Editor's comments in the manuscript. We hope it is within your criteria.

2 Revision 1

2 comments · 19 Jan 2025 – 19 Jan 2025

Associate Editor

ACCEPT 19 Jan 2025

Dear Authors,
I am writing to extend my heartfelt congratulations on the acceptance of your manuscript entitled "Atorvastatin Attenuated the Inflammatory Outcomes of COVID-19: A Double-Blind, Randomized Controlled Trial" by the reviewers of the "Journal of Reports in Pharmaceutical Sciences".
Thank you for your dedication and hard work in advancing pharmaceutical sciences. Your findings will undoubtedly inspire further research and hold promise for future clinical applications.

Warm regards,
E.I.C

Editor-in-Chief

ACCEPT 19 Jan 2025

Dear Authors,
I am writing to extend my heartfelt congratulations on the acceptance of your manuscript entitled "Atorvastatin Attenuated the Inflammatory Outcomes of COVID-19: A Double-Blind, Randomized Controlled Trial" by the reviewers of the "Journal of Reports in Pharmaceutical Sciences".
Thank you for your dedication and hard work in advancing pharmaceutical sciences. Your findings will undoubtedly inspire further research and hold promise for future clinical applications.

Warm regards,
E.I.C