OPEN PEER REVIEW

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You can find out more at:
https://sites.kowsarpub.com/kowsar/knowledgebase/category/tree.html#opr.html

Archives of Neuroscience
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Peer Review Report for "The Effect of Low-Dose Atorvastatin on Inflammatory Factors in Patients with Traumatic Brain Injury: A Randomized Clinical Trial"

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Review Timeline:

Submit Date: 27 Jun 2020
Revised Date: 2 Oct 2020
Accepted Date: 9 Oct 2020

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (0) 10 Aug 2020

Dear AE,
The researchers tried to elucidate the impact of low dose Atorvastatin upon ESR and CRP of TBI cases in a single center during one y period of time via RCT. even though the concept is interesting but some points need clarification;
1- introduction is too long and most of the statements better be declared in the discussion.
2- including the cases coined moderate / severe TBI by only knowing them by GCS numbering is certainly wrong (i would say) because so wide a spectrum of pathologic derangement might have occurred in CNS in every case and it is unacceptable to put them together in such a study, especially when the number of the cases are only 30 in each shoulder.
3- there are different medications used in the treatment protocol of TBI cases used routinely or exclusively for each case of TBI. any one of those medications might have a kind of effect on ESR and CRP which are either known or undiscovered yet.
4- awareness of these medications needs a Q sheath long enough for each patient. if such kind of data gathering is done, then log regression analysis might be able to exclude other

possibly effective variants and evaluate Atorvastatin's weight more acceptably.
Thanks.

Hemendra J vekaria: Reviewer | **Revision** (0) 20 Aug 2020

Dear AE,
Overall the objective of the manuscript is quite significant but there are some major limitations with the data content and the way it is written. The manuscript needs to be checked extensively for grammatical errors. In addition, it also needs to be formatted well. Here are the major comments.
1. The grammar of the title needs to be corrected.
2. The age of the patients was in the range of 18-50 years and with the age, the blood parameters mentioned also changes which are not accounted for in the data.
3. There are sex-dependent changes in the blood parameters but are considered as one range that needs to be explained.
4. Figure 1 doesn't show error bars and the labeling of the Y-axis is missing
5. Flow diagram is not properly formatted. Characters are missing.
6. Need an explanation for the first-day drop in WBC count with the atorvastatin group.
7. Table 2, 10th-day data is missing
8. Indicate the statistics properly. Each data set should represent observations. Preferably data need to be presented as graphs with individual points representing the graph for clarity.
9. The phase I and phase II clinical trials of Atorvastatin have already been done for TBI. There is no mention of it in the manuscript. Also need to discuss the positive and negative outcomes of these trials. Additionally, the authors need to give an explanation that how this study is going to be useful in comparison to the previous studies.
Thanks.

REFEREE: Associate Editor | **Revision** (0) 24 Aug 2020

Dear EIC,
The manuscript is studied, and there are some comments which should be addressed by the author. According to the comments, the document needs major revision.
Kind regards,

REFEREE: EIC | **Revision** (0) 24 Aug 2020

Dear Author,
Your article is reviewed by the reviewers carefully. According to their comments, this document needs major revision. Please follow their comments as requested.
Thanks.

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Dear* reviewers*: We corrected all the raised comments and marked the corrections by yellow color to simplify the reviewing process. I appreciate you and your reviewers in advance

Reviewer 1:
the researchers tried to elucidate the impact of low dose Atorvastatin upon ESR and CRP of TBI cases in a single center during one y period of time via RCT. even though the concept is interesting but some points needs clarification;
1- introduction is too long and most of the statement better to be declared in discussion.

Answer: The introduction was shortened and many sentences were deleted.
2- including the cases coined moderate / severe TBI by only knowing them by GCS numbering is certainly wrong (i would say) because so wide spectrum of pathologic derangement might have occurred in CNS in every case and it is unacceptable to put them together in such a study, especially when the number of the cases are only 30 in each shoulder.

Answer: This was corrected in this way ***moderate decrease of GCS (9-13)or severe decrease of GCS (5-8) that they had isolated TBI*** *and who had brain contusions of less than 30 cc volume* ***in brain CT scan.***

3- there are different medications used in the treatment protocol of TBI case used routinely or exclusively for each case of TBI. any one of those medications might have a kind of effect on ESR and CRP which are either known or undiscovered yet.

Answer: That's right
4- awareness of these medications needs a Q sheath long enough for each patient. if such kind of data gathering is done , then log regression analysis might be able to exclude other possibly effective variants and evaluate Atorvastatin's weight more acceptably.

Answer: This comment is completely correct, but we unfortunately did not review all the medications used

Reviewer 2:
Overall the objective of the manuscript is quite significant but there are some major limitations with the data content and the way it is written. The manuscript need to be checked extensively for the grammatical errors. In addition, it also need to be formatted well. Here are the major comments.

1. *The grammar of the title need to be corrected.*

   Answer: We checked extensively for the grammatical errors and corrected

   2. The age of the patients was in the range of 18-50 years and with the age the blood parameters mentioned also changes which is not accounted for in the data.

3. There are sex dependent changes in the blood parameters but are considered as a one range which need to be explain

Answer 2,3: ESRs are higher in women than in men and they also increases with age, although most laboratory reference ranges only take gender into account. It is unclear whether CRP, like ESR, differs between women and men and/or increases with age. However, in this study, the effect of atrovastatin on inflammatory factors was not investigated based on age and sex. This considered in discussion part

4. Figure 1 doesn't show error bars and labelling of the Y axis is missing

Was corrected

5. Flow diagram in not properly formatted. Characters are missing.

Was corrected

6. Need explanation for the first day drop in WBC count with atorvastatin group.

Answer: we did have not the first day drop in WBC count with atorvastatin group than control. We made a mistake in typingand corrected it. 10666.08±1647.93than10334.19±1722.95

7. Table 2, 10th day data is missing

Answer: 10th day data were added.

8. Indicate the statistics properly. Each data set should represent observations. Preferably data need to be presented as graphs with individual points

representing the graph for clarity.

Answer: We Indicate the statistics properly in the tables and in the result section . The data be presented as graphs (figure 1,2,3)

9. The phase I and phase II clinical trials of Atorvastatin has already been done for TBI. There is no mention of it in the manuscript. Also need to discuss the positive and negative outcomes of these trials. Additionally, authors need to give explanation that how this study is going to be useful in comparison to the previous studies.

Answer: Dear reviewer, we explain and compare previous study such as references 16,17,18,19,21 and 25in the discussion part. Also we explained difference of this study with previous studies in the discussion section.

The difference between this study and previous studies :we compare level of CRP, ESR, and WBC in first,10,14,days after receive Atorvastatin and use low dose of this drug for evaluation of its effect.in the previous studies ,evaluation were done CPR,ESR and WBC only after treatment.

Associate Editor's Comments:

Associate Editor 1:
The manuscript needs revision. Please revise based on comments.

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Revision (1)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (1) 16 Sep 2020

Dear AE,
The study is reviewed carefully. According to comments and revisions by the author, this manuscript is accepted.
Thanks

Hemendra J vekaria: Reviewer | **Revision** (1) 24 Sep 2020

Dear AE,
Most of the comments are addressed by the authors. Still there are some grammatical errors and minor issues need to be addressed which are enlisted in the attached files.
Thanks.

REFEREE: Associate Editor | **Revision** (1) 25 Sep 2020

Dear EIC,
The manuscript still needs revision.
Thanks.

REFEREE: EIC | **Revision** (1) 25 Sep 2020

Dear Author,
Your article is reviewed by the reviewers carefully. According to their comments, this document needs minor revision. Please follow their comments as requested.
Thanks.

OPEN PEER REVIEW

Revision (2)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Dear reviewers*: We corrected all the raised*

Reviewer 1:

Most of the comments are addressed by the authors. Still there are some grammatical errors and minor issues need to be addressed which are enlisted in the attached files.

Answer :we corrected all grammatical errors .

Reviewer 2:

u did what possible for u.

Answer: thank you

We mention Diagram and figures in the text

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Revision (2)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

Hemendra J vekaria: Reviewer | **Revision** (2) 6 Oct 2020

Dear AE,
The manuscript looks good now. Still need some grammatical and formatting corrections. I have noted some of them here. With these corrections, I recommend it for publication in the Archives of Neuroscience.
1. Please indicate full forms when appears for the first time: For eg. Erythrocyte Sedimentation Rate (ESR). Similarly, CRP, TBI, GCS. Be consistent in using the full form or short form throughout the manuscript.
2. In the abstract the last sentence there is a repetition of the phrase 'in patients with a traumatic brain injury.
3. Line 18 'in 14th days is a wrong phrase instead use 'in 14 days or if measured only on 14th day then use on '14th day'.
4. In key messages there is again a repetition of the phrase "in patients with a traumatic brain injury.
5. Line 38 and 39 improve sentence grammar. The highlighted text sounds weird "TBI causes an acute opening of the blood-brain barrier and the possibility of circulating white blood cells toward the inside the damaged brain(2).
6. Line 51 'atherovstatin' is it atorvastatin or it's a different drug?
7. Line 174 " Please use correct author name. Its Naghibi et. al.
8. Line 167 uses just 'Robertson et. al.' Be consistent in mentioning the author names throughout the manuscript.
9. Include error bars in Figure 4.
Thanks.

REFEREE: Associate Editor | **Revision** (2) 9 Oct 2020

Dear EIC
Based on the authors' answers to the reviewers' comments, the reviewer(s) have recommended publication.
Kind regards.

REFEREE: EIC | **Revision** (2) 9 Oct 2020

Dear Author,
The document is reviewed carefully by the reviewers. According to their comments and your

revisions as requested, this manuscript is accepted.

Thanks.