OPEN PEER REVIEW

Open Peer Review (OPR)

As a new feature for progressing towards transparency, we decided to open a new window for all of our editors as well as authors titled "**Open Peer Review**". We hope by this new facility, our reviewers will be more motivated and authors will be more satisfied with the review process. We believe that publishing our peer review reports could make a transparent and clear environment for all our efforts within a journal, but not all reviewers tend to publish their comments.

What is "Open Peer Review" process?

An "Open Peer Review" process is making the details of all review process (including reviewers, associate editors, and EICs comments) as "Public" as it is agreed by EIC, Authors, and reviewers.

Advantages of "Open Peer Review" process

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- Authors' satisfactions from the review process: Increases honesty between authors and reviewers
- Education of both authors and new students
- Prevents reviewers from following their individual agendas and leading to the detection of reviewers' conflicts of interests

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

Iranian Journal of Psychiatry and Behavioral Sciences
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Peer Review Report for "Comparison of Adjunctive Quetiapine Versus Adjunctive Haloperidol in Combination with Sodium Valproate for Treatment of Patients with Mania or Mixed Feature Bipolar I Disorder: A Randomized Double-Blind Clinical Trial Study"

Author(s): Mercedeh Samiei, Zahra Sepehrifar, Reza Daneshmand, Gita Sadighi

Review Timeline:

- Submit Date: 3 Feb 2019
- Revised Date: 2 May 2020
- Accepted Date: 21 Nov 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) 11 Mar 2019

Dear AE,
I have read the manuscript with interest.
The title is A Comparison of Adjunctive Quetiapine Versus Adjunctive Haloperidol in Combination with Sodium Valproate for Treatment of Patients with Mania or Mixed Feature Bipolar I Disorder.
I have a few minor points about the manuscript:
1. As I read the whole parts of the manuscript, I personally hold the opinion that it is better to modify the title of the manuscript as fallow:
“A Comparison of Adjunctive Quetiapine Versus Adjunctive Haloperidol in Combination with Sodium Valproate for Treatment of Patients with Mania or Mixed Feature Bipolar I Disorder A randomized double blind clinical trial study”
2. Is there any significant statistical difference between the number of patients with “Bipolar I disorder” with the mixed features in two classified groups? The same question has to be

answered for patients with “Bipolar I disorder experiencing episodes of mania”.
3. Please explain about adverse effects of Haloperidol and Quetiapine in patients. Did any subjects experience any kind of Extrapyramidal symptoms in the Haloperidol group or not? How about depression in the 6th week of the Haloperidol group?
4. Page 3 Paragraph 3 . line 7: Valproate Sodium is classified as an anticonvulsant drug, not an Antipsychotic drug.
Minor revision is deemed necessary for this manuscript before publication.
Thanks.

REFEREE: Reviewer | **Revision** (0) 22 Apr 2019

Dear AE,
In the manuscript entitled “A Comparison of Adjunctive Quetiapine Versus Adjunctive Haloperidol in Combination with Sodium Valproate for Treatment of Patients with Mania or Mixed Feature Bipolar I Disorder” authors have compared the effect of two antipsychotics on treating mania. The result of this study can be of great help in clinical practice. The manuscript is easy to read and comprehend, and it follows a standard structure.
There are some minor comments:
- The first 9 lines of the introduction do not relate to the study. Discussing the treatment of mania in more detail would be more appropriate.
- Table1: You may split the row for age from the Mean and SD row.
- Page 7: Table 2: According to the data given for pre-test scores, the two groups do not seem to be significantly different. You may want to double check the P-value
- Page 7: “As shown in table 2, mean score of YMRS was higher in the group of Quetiapine receivers, compared to the Haloperidol group and also increased in the Quetiapine receivers after three weeks from the initiation of the study”
No increase is shown after three weeks in quetiapine receivers according to the table.
- Page 7: “In addition, mean score of the YMRS was increased again in the group of Quetiapine receivers, compared to the Haloperidol receivers after completion of the intervention program (week 6)”
No increase is shown after six weeks in quetiapine receivers according to the table.
- Page 10, line 12: “although we observed that Quetiapine was clearly more efficient in resolving participant’s symptoms, in comparison with Haloperidol”
Your data does not support this observation
- The main limitation of the study is not having a placebo group; thus it cannot be concluded that a combination of sodium valproate with haloperidol or quetiapine is effective. The effectiveness can be attributed to sodium valproate only.
Thanks.

REFEREE: Reviewer | **Revision** (0) 1 May 2019

Dear AE,
I found the subject interesting, but I think the manuscript needs some revisions:
1- study design should be mentioned in the title.
2- Abstract should be structured as below:
Background, objective, material/patients and methods, results and conclusion. This matter has not been considered in the manuscript. Also structure of the article body is

inappropriate.
3- p value should be mentioned in the abstract.
4- Some key words are not selected from MESH.
5- Sample size calculation is not clear.
6- There is not clear explanation about randomization and blindness of the subjects and researches.
7- References needs some editions; Journal name abbreviations should be mentioned in the journal references. Please mention PMID and DOI of the articles in the references part.
My decision: minor revision
Best regards

REFEREE: Associate Editor | **Revision** (0) 1 May 2019

Dear EIC,
Many thanks for submitting" A Comparison of Adjunctive Quetiapine Versus Adjunctive Haloperidol in Combination with Sodium Valproate for Treatment of Patients with Mania or Mixed Feature Bipolar I Disorder". I received comments from reviewers have expertized on the manuscript. Although the reviewers found considerable strengths in your paper, they also identified some concerns and believed that the paper needs some revisions. I conclude that the manuscript has the potential for consideration for publication after satisfactorily addressing reviewers concerns. Therefore, I invite the authors to reply to the reviewers' comments and resubmit their revised manuscript for further review. If they choose to revise the submission please upload their revised manuscript and an annotated list addressing the reviewers' comments and highlighting where changes have been made to the paper.
My decision: minor revision
Sincerely yours

REFEREE: EIC | **Revision** (0) 3 May 2019

Dear Authors,
Your paper has been evaluated by external peer reviewers. Please do your revisions according to the reviewers' comments. I appreciate you doing the revisions as soon as possible by using the track changes mode in MS Word and using colored text.
After revision authors are obliged to upload reviewers' comments word file in which they have replied to all comments one by one.
Besides, please pay attention to the word count limitation: Word Count (including references and title page) should not be more than 3500 words. Original articles' maximum number of references is 55, maximum Number of illustrations/Tables is 5. Otherwise, you should pay extra charge to the publisher.
Word count limits are declared in this link: http://kowsarpub.com/en/index.php/services/for-authors/895-word-count
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 Honored Reviewers and Associate Editor,

I highly appreciate your valuable comments on the manuscript. I would like to inform you that I have revised the manuscript in accordance with the reviews. All of the comments are considered and changes are made based on every single comment.

Kind regards,

Reviewers' Comments:

Reviewer 1:

Dear author

I found the subject interesting, but I think the manuscript needs some revisions:

1- study design should be mentioned in the title.

2- Abstract should be structured as below:

Background, objective, material/patients and methods, results and conclusion. This matter has not been considered in the manuscript. Also structure of the article body is inappropriate.

3- p value should be mentioned in the abstract.

4- Some key words are not selected from MESH.

5- Sample size calculation is not clear.

6- There is not clear explanation about randomization and blindness of the subjects and researches.

7- References needs some editions; Journal name abbreviations should be mentioned in the journal references. Please mention PMID and DOI of the articles in the references part.

My decision: minor revision

Best regards

Reviewer 2:

In the manuscript entitled “A Comparison of Adjunctive Quetiapine Versus Adjunctive Haloperidol in Combination with Sodium Valproate for Treatment of Patients with Mania or Mixed Feature Bipolar I Disorder” authors have compared the effect of two antipsychotics on treating mania. The result of this study can be of great help in clinical practice. The manuscript is easy to read and comprehend, and it follows a standard structure.

There are some minor comments:

- The first 9 lines of the introduction does not relate to the study. Discussing the treatment of mania in more details would be more appropriate.

- Table1: You may split the row for age from Mean and SD row.

- Page 7: Table 2: According to the data given for pre-test scores, two groups do not seem to be significantly different. You may want to double check the P-value

- Page 7: “As shown in table 2, mean score of YMRS was higher in the group of Quetiapine receivers, compared to the Haloperidol group and also increased in the Quetiapine receivers after three weeks from the initiation of the study”

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- Page 7: “In addition, mean score of the YMRS was increased again in the group of Quetiapine receivers, compared to the Haloperidol receivers after completion of the intervention program (week 6)”

No increase is shown after six weeks in quetiapine receivers according to the table.

- Page 10, line 12: “although we observed that Quetiapine was clearly more efficient in resolving participant’s symptoms, in comparison with Haloperidol”

Your data does not support this observation

- The main limitation of the study is not having a placebo group; thus it cannot be concluded that combination of sodium valproate with haloperidol or quetiapine is effective. The effectiveness can be attributed to sodium valproate only.

Reviewer 3:

I have read your manuscript with interest.

Title is: A Comparison of Adjunctive Quetiapine Versus Adjunctive Haloperidol in Combination with Sodium Valproate for Treatment of Patients with Mania or Mixed Feature Bipolar I Disorder.

I have a few minor points about the manuscript:

1. As I read the whole parts of manuscript, I personally hold the opinion that it is better to modify the title of manuscript as fallow:

“A Comparison of Adjunctive Quetiapine Versus Adjunctive Haloperidol in Combination with Sodium Valproate for Treatment of Patients with Mania or Mixed Feature Bipolar I Disorder: A randomized double blind clinical trial study”

2. Is there any significant statistical difference between the number of patients with “Bipolar I disorder” with mixed feature in two classified groups? Same question has to be answered for patients with “Bipolar I disorder experiencing episodes of mania”.

3. Please explain about adverse effects of Haloperidol and Quetiapine in patients. Did any subjects experience any kind of Extrapyramidal symptoms in Haloperidol group or not? How about depression in 6th week of Haloperidol group?

4. Page 3 Paragraph 3 . line 7: Valproate Sodium is classified as an anticonvulsant drug not Antipsychotic drug.

Minor revision is seems necessary for this manuscript before publication.

Associate Editor's Comments:

Associate Editor 1:

Dear author

Many thanks for submitting" A Comparison of Adjunctive Quetiapine Versus Adjunctive Haloperidol in Combination with Sodium Valproate for Treatment of Patients with Mania or Mixed Feature Bipolar I Disorder”. I received comments from reviewers have expertized on the manuscript. Although the reviewers found considerable strengths in your paper, they also identified some concerns and believed that the paper needs some revisions. I conclude that the manuscript has the potential of consideration for publication after satisfactorily addressing reviewers concerns. Therefore, I invite you to reply to the reviewers comments and resubmit your revised manuscript for further review. If you choose to revise your submission please upload your revised manuscript and an annotated list addressing the reviewers comments and highlighting where changes have been made to the paper.

My decision: minor revision

Sincerely yours

OPEN PEER REVIEW

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) 26 Dec 2019

Dear AE,
Thanks for submitting the revised manuscript.
1. I suggest this sentence for background: Acute mania causes many problems for the patient and others. Therefore, it is very important to eliminate the symptoms quickly.
2. In introduction: The second sentence of the introduction needs to be edited. I suggest this sentence: A series of recent studies demonstrated in eleven different European, American and Asian countries that prevalence of Bipolar I disorder as about 0.6%.
3. Did patients have any medical or drug history? If yes, how did you eliminate these confounding factors?
Thanks.

REFEREE: Reviewer | **Revision** (1) 27 Dec 2019

Dear AE,
In my view, the submitted paper is an interesting piece of work, and generally a well-designed experiment; thus, it has the potential to be published in the IRANIAN JOURNAL OF PSYCHIATRY AND BEHAVIORAL SCIENCES.
Comments for the authors:
• Applying an online plagiarism checker to detect plagiarism, there was less than 5% of plagiarism detected in the manuscript, which is in an acceptable range.
• The Materials & Methods part of the manuscript is clear and it is easy to understand what the author exactly measured. Moreover, considering the type of study, the applied measures for data analysis are relevant and of an appropriate choice.
• The observation made and reported is not something new; however, it reproduces previously made observations in detail.
• The presentation of the obtained study data is adequate. There is important information outlined and explained in detail.
• The citations and references seem to be correctly mentioned in the manuscript and the references part.
• The submitted paper is a clear and concise manuscript. In addition, the study appears to be sound, and the manuscript is well written. All parts of the manuscript are written accurately. Editing by a native English speaker or professional translator is not required.
• The title of the paper is appealing, because it clearly conveys the topic, and the writing is strong.

• The discussion part reflects the data in the article reports. In addition, necessary conjectures or founded conclusions that are based on the evidence are presented. Besides, a possible strength of this approach is mentioned.
Thanks.

REFEREE: Reviewer | **Revision (1)** 31 Mar 2020

Dear AE,
Most of the comments have been answered completely, but comment No 4 (page 3 paragraph 3 line 7, sodium valproate is classified as an anticonvulsant drug, not the antipsychotic drug) has not been applied in the manuscript yet! The manuscript can be published in the "Iranian Journal of Psychiatry and Behavioral Sciences" only when the complete answer to the mentioned comment is raised.
Thanks.

REFEREE: Associate Editor | **Revision (1)** 7 Apr 2020

Dear EIC,
Many thanks for revising ” A Comparison of Adjunctive Quetiapine Versus Adjunctive Haloperidol in Combination with Sodium Valproate for Treatment of Patients with Mania or Mixed Feature Bipolar I Disorder". I received comments from reviewers who believed that some of the necessary revisions have been done but some of them identified concerns and think that the manuscript needs some other revisions (some of the comments were also mentioned previously). Therefore, I conclude the manuscript has the potential for consideration for publication after satisfactorily addressing reviewers' concerns. Thus, I invite the authors to reply to all of the reviewers' comments and resubmit their revised manuscript for further review. (Also, please mention DOI and PMID of the articles in the references part.)
My decision: minor revision
sincerely yours

REFEREE: EIC | **Revision (1)** 19 Apr 2020

Dear Authors,
Thank you for your recent revisions.
Your paper has now been evaluated again. According to the reviewers’ and associate editor’s comments, it needs some more revisions. Please do your revisions according to these comments. I appreciate you doing the revisions as soon as possible by using the track changes mode in MS Word and using colored text.
Besides, please pay attention to the word count limitation.
Word count limits are declared in this link: http://kowsarpub.com/en/index.php/services/for-authors/895-word-count
We look forward to receiving your revised manuscript. Thank you for sending your work to the Iranian Journal of Psychiatry and Behavioral Sciences.
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.

Reviewers' Comments:

Reviewer 1:

In my view, the submitted paper is an interesting piece of work, and generally a well-designed experiment; thus, it has the potential to be published in the IRANIAN JOURNAL OF PSYCHIATRY AND BEHAVIORAL SCIENCES.

• Applying an online plagiarism checker to detect plagiarism, there was less than 5% of plagiarism detected in the manuscript, which is I an acceptable range.

• The Materials & Methods part of the manuscript is clear and it is easy to understand what the author exactly measured. Moreover, considering the type of study, the applied measures for data analysis are relevant and of an appropriate choice.

• The observation made and reported is not something new; however, it reproduces previously made observations in detail.

• The presentation of the obtained study data is adequate. There is important information outlined and explained in detail.

• The citations and references seem to be correctly mentioned in the manuscript and the references part.

• The submitted paper is a clear and concise manuscript. In addition, the study appears to be sound, and the manuscript is well written. All parts of the manuscript are written accurately. Editing by a native English speaker or professional translator is not required.

• The title of the paper is appealing, because it clearly conveys the topic, and the writing is strong.

• The discussion part reflects what the data in the article reports. In addition, necessary conjecture or founded conclusions that are based on the evidence are presented. Besides, a possible strength of this approach is mentioned.

Dear Reviewer 1,

I highly appreciate your comments on the manuscript and I am glad that the previously-made revisions and the current manuscript are approved by your side.

Reviewer 2:

Thank you for submitting the revised manuscript.

1. I suggest this sentence for background: Acute mania causes many problems for the patient and others. Therefore, it is very important to eliminate the symptoms quickly. This part is revised according to your valuable comment.

2. In introduction: The second sentence of the introduction needs to be edited. I suggest this sentence: A series of recent studies demonstrated in eleven different European, American and Asian countries that prevalence of Bipolar I disorder as about 0.6%. This part is revised according to your valuable comment.

3. Did patients have any medical or drug history? If yes, how did you eliminate these confounding factors? Many thanks for your notes. The study inclusion criteria included being inpatients hospitalized in the acute ward who were admitted to the hospital following the aggravation of symptoms induced by discontinuing pharmacotherapy since at least four weeks prior to hospitalization, as well as the lack of a medical history or undergoing pharmacotherapy for physical conditions. (This part is now amended in the manuscript.)

Reviewer 3:

Most of the comments have been answered completely , but comment No 4 (page 3 paragraph 3 line 7, sodium valproate is classified as an anticonvulsant drug not antipsychotic drug) have not been applied in the manuscript yet! The manuscript can be published in the "Iranian Journal of Psychiatry and Behavioral Sciences" only when the complete answer to the mention comment raised. We have revised this part in the manuscript according to your precise point.

Associate Editor's Comments:

Associate Editor 1:

Dear author

Many thanks for revising ” A Comparison of Adjunctive Quetiapine Versus Adjunctive Haloperidol in Combination with Sodium Valproate for Treatment of Patients with Mania or Mixed Feature Bipolar I Disorder". I received comments from reviewers believed that some of necessary revisions have been done but some of them identified concerns and think that the manuscript needs some other revisions (some of the comments were also mentioned previously). Therefore, I conclude the manuscript has the potential of consideration for publication after satisfactorily addressing reviewers concerns. Thus, I invite you to reply to all of the reviewers' comments and resubmit your revised manuscript for further review. (Also, please mention DOI and PMID of the articles in the references part.) If you choose to revise your submission please upload your revised manuscript and an annotated list addressing the reviewers comments and highlighting where changes have been made to the paper.

My decision: minor revision

sincerely yours

Dear Associate Editor,

I highly appreciate your valuable comments on the manuscript. I would like to inform you that the references are revised according to the associate editor’s comment and all available DOI & PMID are mentioned. However, for example, the reference number 3 is a text book without such information accessible.

Kind regards,

Gita Sadighi, MD

OPEN PEER REVIEW

Revision (2)

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

REFEREE: Reviewer | **Revision** (2) 18 May 2020

Dear AE,
The authors answered well to my comment.
Thanks.

Elaheh Ahounbar: Reviewer | **Revision** (2) 8 Jun 2020

Dear AE,
After checking the document with a relevant tool, there was no plagiarism detected (not more than five percent of the whole text, which is acceptable).
- The authors have clarified several of the questions I raised in my previous review. All of the major and minor problems have been addressed by this revision. As I stated in my previous review, I deem it likely that all those issues could be solved merely by a few changes in some parts. Thus, there are no fundamental concerns with the experimental design and, most critically, with the analysis. This means the strong conclusions put forward by this manuscript are warranted and I can approve the manuscript in this form.
- I think this paper is excellent and is an important addition to the literature. The results are illustrating the concept and findings; and therefore, facilitate understanding the findings of the research.
- This manuscript does an excellent job demonstrating citations and references, and no revisions are required in these sections.
- The manuscript is precise and well written; no further edition is necessary for terms of the English language or the format.
- I think the manuscript is well designed, all the previously mentioned review comments have been observed and the required revisions are made; therefore, I believe the manuscript is now ready for publication in the Iranian Journal of Psychiatry and Behavioral Sciences.
Best regards

REFEREE: Reviewer | **Revision** (2) 7 Oct 2020

Dear AE,
Thanks for revising the points. I think necessary revisions have been done and the

manuscript could be published in the journal.
My decision: accept
Best regards

REFEREE: Associate Editor | **Revision (2)** 7 Oct 2020

Dear EIC,
Many thanks for revising "A Comparison of Adjunctive Quetiapine Versus Adjunctive Haloperidol in Combination with Sodium Valproate for Treatment of Patients with Mania or Mixed Feature Bipolar I Disorder". I received comments from reviewers who believed that necessary revisions have been done. Therefore, I think the manuscript could be published in the Iranian journal of psychiatry and behavioral sciences.
My decision: accept
sincerely yours

REFEREE: EIC | **Revision (2)** 21 Nov 2020

Dear Authors,
We have completed our review of your manuscript and are pleased to inform you that it is considered for publication in the IJPBS. Note that the publication of your article will only be finalized upon your cooperation with the editorial processing.
Thank you for your fine contribution. On behalf of the Editors of IJPBS, we look forward to your continued contributions to the Journal.
Thanks.