OPEN PEER REVIEW

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Peer Review Report for "Hypothalamic-Pituitary-Adrenal Axis Recovery Following the 1-mg Overnight Dexamethasone Suppression Test in Healthy Volunteers"

Author(s): Adlyne Reena Asirvatham, Karthik Balachandran, Shriraam Mahadevan, Satish Kumar Balasubramaniam

Review Timeline:

Submit Date: 3 Jun 2019
Revised Date: 7 Apr 2020
Accepted Date: 12 Apr 2020

Revision (0)

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

Farhad Hosseinpanah: Reviewer | Revision (0) 25 Oct 2019

Dear AE,
In this study, the investigators assessed the pattern and time of recovery of HPA axis following 1 mg ODST in 10 healthy subjects. The research question is interesting. However there are some important concerns that need to be addressed by the authors.
1) There is no comments regarding the statistics. How did they analyze data?
2) How did they calculate the sample size?
3) Baseline characteristics of the participants such as age and BMI should be provided?
4) In order to obtain accurate results, it would be better to measure serum level of dexamethasone.
5) Table 1, the variables have no unit of measurements and mode of data expression.
6) While reporting pattern of changes across times, a figure is more appropriate than table. please insert a figure in this regard
7) Case number ten had a serum cortisol equal to 3.4 µr/dl. Are you sure that, she was healthy?
Thanks.

REFEREE: Reviewer | **Revision** (0) 14 Dec 2019

Dear AE,
About the manuscript entitled " Hypothalamo-Pituitary-Adrenal (HPA) axis recovery following 1 mg
overnight dexamethasone suppression test in healthy volunteers" that investigate HPA axis recovery after usual screening test for Cushing's syndrome.
That is interesting but need more explanation about methodology especially sample size calculation.
Regards,

REFEREE: Associate Editor | **Revision** (0) 14 Dec 2019

Dear EIC,
The manuscript has interesting research question but some methodological aspect need more explanation. Also data presentation in results section need some change.
Regards,

REFEREE: EIC | **Revision** (0) 15 Dec 2019

Dear Author,
The reviewers' comments are mentioned. Please correct the details as mentioned above carefully according to reviewers' request.
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.

Author's reply

Reviewer 1

In this study, the investigators assessed the pattern and time of recovery of HPA axis following 1 mg ODST in 10 healthy subjects. The research question is interesting. However there are some important concerns that need to be addressed.

1) There is no comments regarding the statistics. How did they analyze data?

Reply :1 Since the data was small we used only descriptive statistics.

2) How did they calculate the sample size?

Reply : 2 Since it was a pilot study and there was no previous study done with 1 mg dexamethasone, we were not able to accurately calculate sample size. In addition due to financial constraints and the inclusion of healthy volunteers, we took ten subjects for this present study. However, we are planning to do this study in a larger number once we get an approval for a study grant.

3) Baseline characteristics of the participants such as age and BMI should be provided?

Reply : 3 We have included the baseline characteristics in Table:1 as recommended.

4) In order to obtain accurate results, it would be better to measure serum level of dexamethasone.

Reply : 4 We completely agree with the reviewers that dexamethasone levels would have added value to the study, but could not be done in this study due to financial constraints. This has been mentioned in the limitations of the study.

5) Table 1, the variables have no unit of measurements and mode of data expression.

Reply : 5 We have made the necessary changes as suggested by the reviewers.

6) While reporting pattern of changes across times, a figure is more appropriate than table. please insert a figure in this regard

Reply : 6 We agree with the reviewers and Figure:1 depicts the pattern of ACTH and Cortisol levels across times.

7) Case number ten had a serum cortisol equal to 3.4 µr/dl. Are you sure that, she was healthy?

Reply : 6 Case number ten was a normal healthy lady with no history of steroid use and no clinical evidence of adrenal insufficiency.

Reviewer 2:
Dear associate editor,
About the manuscript entitled " Hypothalamo-Pituitary-Adrenal (HPA) axis recovery following 1 mg overnight dexamethasone suppression test in healthy volunteers" that investigate HPA axis recovery after usual screening test for Cushing's syndrome.
That is interesting but need more explanation about methodology especially sample size calculation.

Reply : Thank you for the valuable comments and we appreciate your review of our study.

Since it was a pilot study and there was no previous study done with 1 mg dexamethasone, we were not able to accurately calculate sample size. In addition due to financial constraints and the inclusion of healthy volunteers, we took ten subjects for this present study. However, we are planning to do this study in a larger number once we get an approval for a study grant.

Thank you once again.

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.

Farhad Hosseinpanah: Reviewer | **Revision (1)** 23 Mar 2020

Dear AE,
I have no further comment. It can be accepted as a brief report.
Thanks.

Majid Valizadeh: Associate Editor | **Revision (1)** 29 Mar 2020

Dear EIC,
All of the reviewer comments were responded. Now, it is ready for publication as a brief report.
Regards

REFEREE: EIC | **Revision (1)** 4 Apr 2020

Dear Author,
The revised manuscript has significantly improved; however, minor amendments are needed:
1) Everywhere in the manuscript mean value has been reported, SD should also be mentioned (mean±SD).
2) Number of subjects should be included in the legends of both figures; D1, D2 and D3 should be defined in the footnote of Figure 1. Citation to Figure 2 and its description in the main text need to be more comprehensive.
3) During submission of the revised manuscript, the article type should be changed to "brief report".
Thanks.

OPEN PEER REVIEW

Revision (2)

Reply to Reviewers

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

Reply to EIC

S.No	EIC recommendations	Author's reply	Reference for modification
1.	Everywhere in the manuscript mean value has been reported, SD should also be mentioned (mean±SD).	We agree with the EIC and the SD has been mentioned	Page 3
2.	Number of subjects should be included in the legends of both figures;	The number of subjects has been included in the legends of both figures as per EIC recommendation.	Legends of figures
3.	D1, D2 and D3 should be defined in the footnote of Figure 1.	We agree and D1, D2 and D3 have been defined in the footnote.	Figure 1
4.	Citation to Figure 2 and its description in the main text need to be more comprehensive.	Description of figure 2 has been modified as per the suggestion	Page 3
5.	During submission of the revised manuscript, the article type should be changed to "brief report".	Yes. We agree.	

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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.

REFEREE: EIC | **Revision** (2) 12 Apr 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.