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OPEN PEER REVIEW

A Prospective Cross-Sectional Study on Exhaled Nitric Oxide and Sensitivity to Indoor Inhaled Aeroallergens in Patients with Rhinosinusitis with Nasal Polyps

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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

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1 Original submission

3 comments · 4 Apr 2020 – 7 Apr 2020

Referee 1 Reviewer

MAJOR REVISION 4 Apr 2020

Comments:
1) Capitalize the first character of each keyword.
2) The background needs to be expanded to include existing evidence on nitric oxide and sensitivity to indoor inhaler aeroallergens in patients with rhinosinusitis.
3) You should add some new references published in Jundishapur Journal of Chronic Disease Care.
4) Sample size: I would like to know how many participants are in this study.
5) The table should be modified.
6) Please highlight your study's strengths and limitations.
7) The references should be revised based on the journal's style.

Associate Editor

MAJOR REVISION 7 Apr 2020

Dear Author,
This manuscript is interesting but needs some revisions before publication.
Thanks

Editor-in-Chief

MAJOR REVISION 7 Apr 2020

Dear Author,
Thank you for submitting your manuscript. Based on our reviewers' comments, your manuscript needs some revision in all parts. I recommend that you resubmit your revisions as soon as possible.
Thanks.

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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.

Reviewers' Comments:

Reviewer 1:
You raised a very good and important issue. The manuscript has major drawbacks, especially in the method section. Other points are mentioned in the text of the article. Good luck

Answer: we revised the mentioned section the changes are made by red.
Reviewer 2:
Comments:
1) Capitalize the first character of each keyword.

Answer: we capitalized the first character of each keyword.
2) The background needs to be expanded to include existing evidence of nitric oxide and sensitivity to indoor inhaler Aeroallergens in patients with Rhinosinusitis.

Answer: we added this item in the background
3) should add some new references published in Jundishapur Journal of Chronic Disease Care.
4) Sample size: I would like How many participants are in this study?

Answer: 72
5) table should be modifying.

Answer: we modified the tables
6) Please highlight your study's strengths and limitations.

Answer: we highlighted the main points n highlight section
7) The references should be revised based on style journal.

Answer: we referenced according to the journal style

2 Revision 1

2 comments · 27 Apr 2020 – 27 Apr 2020

Associate Editor

MINOR REVISION 27 Apr 2020

Dear Author,
Please pay attention to all comments and resubmit.
Thanks.

Editor-in-Chief

MINOR REVISION 27 Apr 2020

Dear Author,
As you know, your manuscript needs to be revised based on our reviewers' comments. Our reviewers want to see your revised manuscript. Please pay attention to all reviewers' comments.
Thanks

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Revision 2

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.

Reviewers' Comments:

Reviewer 1:
You raised a very good and important issue. The manuscript has major drawbacks, especially in the method section. Other points are mentioned in the text of the article. Good luck

Answer: we revised the mentioned section the changes are made by red.

The section we added: **Method of prick skin test**

A skin prick test, also called a puncture or scratch test, checks for immediate allergic reactions to as many as 50 different substances at once. This test is usually done to identify allergies to pollen, mold, pet dander, dust mites and foods. In adults, the test is usually done on the forearm. Children may be tested on the upper back.

After cleaning the test site with alcohol, the nurse draws small marks on the skin and applies a drop of allergen extract next to each mark. He or she then uses a lancet to prick the extracts into the skin's surface. A new lancet is used for each allergen.

To see if the skin is reacting normally, two additional substances are scratched into the skin's surface:

- **Histamine.** In most people, this substance causes a skin response. If you don't react to histamine, your allergy skin test may not reveal an allergy even if you have one.
- **Glycerin or saline.** In most people, these substances don't cause any reaction. If you do react to glycerin or saline, you may have sensitive skin. Test results will need to be interpreted cautiously to avoid a false allergy diagnosis.

About 15 minutes after the skin pricks, the nurse observes your skin for signs of allergic reactions. If you are allergic to one of the substances tested, you'll develop a raised, red, itchy bump (wheal) that may look like a mosquito bite. The nurse will then measure the bump's size and record the results. Next, he or she will clean your skin with alcohol to remove the marks.

A positive skin test means that you may be allergic to a particular substance. Bigger wheals usually indicate a greater degree of sensitivity. A negative skin test means that you probably aren't allergic to a particular allergen.

Method of FeNO measurement

Exhaled NO measured by device NObreath device.

NObreath device

We used FeNO testing with the Bedfont® NObreath® device. The Bedfont® NObreath® is a simple to use, battery-powered handheld monitor that measures

Fractional exhaled Nitric Oxide (FeNO) in the breath. The device has been designed for use in almost any clinical setting and can be used to test children as well as adults. An adult patient blows into the NObreath® for 12 seconds giving an instant result for FeNO in ppb (parts per billion). The higher the FeNO reading the greater the inflammation in the airways.

Reviewer 2:
Comments:
1) Capitalize the first character of each keyword.

Answer: we capitalized the first character of each keyword.

The chnge we made: Chronic rhinosinusitis; Allergens; Skin prick tests; Inhalation allergen challenge; Allergy; Asthma; Allergic rhinitit
2) The background needs to be expanded to include existing evidence of nitric oxide and sensitivity to indoor inhaler Aeroallergens in patients with Rhinosinusitis.

Answer: one point to mention is that we have vocabulary limitation then we discuss it in the text and by the way we added this item in the background

Rhinosinusitis is a nasal and para-nasal sinuses infection. Chronic infection and allergies are two major causes of nasal polyps formation. Generally, the initial phase of nasal polyposis may appear with increased exudation of the vessels, lamina propria edema and nasal mucosa contractionIn this study we examine the relationship between NO and the aeroallergen to determine the relation between Expiratory Nitric Oxide Level and Sensitivity to aeroallergen in chronic rhinosinusitis with nasal polyps (CRSwNP) patients referring to Hazrat Rasool Hospital in Tehran from December 2016 to May 2017
3) should add some new references published in Jundishapur Journal of Chronic Disease Care.

We searched the journal but unfortunately we did not find relevant papers to use.
4) Sample size: I would like How many participants are in this study?

Answer: 72
5) table should be modifying.

Answer: we modified the tables
6) Please highlight your study's strengths and limitations.

Answer: we highlighted the main points n highlight section
7) The references should be revised based on style journal.

Answer: we referenced according to the journal style

3 Revision 2

2 comments · 17 Jun 2020 – 17 Jun 2020

Associate Editor

MINOR REVISION 17 Jun 2020

Dear Author,
You should address all comments.
with the best.

Editor-in-Chief

MINOR REVISION 17 Jun 2020

Dear Author,
You should make the minor revisions requested by the reviewers.
With the best.

4

Revision 3

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.

Reviewer 1:
With many thanks for the responses, there are left just few questions to be answered:
1. The method part is better to be started with pointing out to the design.

Answer: dear reviewer we start the method with the opinion of the design.
2. How do you defend of this design? It seems to be a cross sectional study than a cohort one!
[It could be just as an answer to me not adding in the manuscript]. Y

Answer: you are right we changed the word cohort to cross sectional cause it beliongs to a limited time and place.
3. Is it a bigger Cohort Study with a specific code? What about the protocol of study? Has it been published before?

Answer: yes there are similar studies in other countries we mentioned in the method: According to a previous study, and according to the prick skin test that was positive in 73% of patients with chronic rhinosinusitis and also considering to the error level of α 5%, and the accuracy of 0.1 final sample size was counted 76 patients by WinPepi software (14).
Best regards

4 Revision 3

2 comments · 7 Jul 2020 – 7 Jul 2020

Associate Editor

MINOR REVISION 7 Jul 2020

Dear Author,
Please see one of the articles currently published in JJCDC. As you know, our criteria for accepting a manuscript are based on our guidelines, and the methodology should describe dosing, sampling, inclusion and exclusion criteria, instruments and their validity and reliability, and ethical considerations (code of ethics). Please revise your manuscript again based on one reviewer's feedback, organize your manuscript as I have indicated, and resubmit. I apologize for this extra revision because I have to adhere to the new journal guidelines.
Thank you very much indeed.

Editor-in-Chief

MAJOR REVISION 7 Jul 2020

Dear Author,
Please pay attention to all reviewers' comments. You wrote prospective cross-sectional study?
In the abstract, you should explain more about your method.
You should write about ethical considerations (code of ethics).
Please carefully look at a current original research article published in JJCDC.
Thank you very much.

5

Revision 4

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.

Reviewer 1:
The method part is better to be started with pointing out to the design.

Answer: dear reviewer we started the method with the study design according to your comment. The change is made by RED.Reviewer 2:To the respected Editor-in-Chief of the journal, The article is suitable for publication in the journal. Respectfully, it is suggested that 1. in the Methods part of the abstract, the sample size, sampling method and the instrument used be stated specifically. Write here what you did. The Methods is incomplete.

1. *The change was applied according to your suggestion. The Methods was stated briefly.2. Write the keywords based on MeSH (Mesh).*
2. *The terms were selected according to MeSH.3. In the Introduction, statistics and figures related to rhinosinusitis in dear Iran have not been mentioned.*
3. *According to the studies, the statistics of Iran have been reported in a scattered way, and we added the latest statistics of one province as an example.4. At the end of the Introduction, the results of similar studies should be briefly mentioned so that the gap that the study covers becomes clear. Divide the Introduction into paragraphs.*
4. *Similar studies have been reported in the Discussion, and adding them again would cause repetition. The Introduction was divided into paragraphs.*
   5. Sentences should be written in the passive voice, that is, the word "we" should be removed.
5. *Active sentences are more tangible and do not create a problem in writing the article, and many academic writings are written in this way; therefore, this change is not applied.6. In the Methods, first the type of study should be written. Then the method of determining the sample size and the sampling method should be explained.*
6. *The Methods was corrected; the sample size is mentioned both in the abstract and at the beginning of the Methods. The sampling method has also been mentioned; please read carefully. The inclusion and exclusion criteria and the name of the device and the tests have been fully mentioned.7. The validity and reliability of the instrument used should be mentioned.*
7. *The name of the instrument has been mentioned8. Summarise the method, but write it in such a way that it is reproducible if other researchers wish to conduct a similar study.*
8. *The method had been written briefly; in the previous revision we were asked to write it in detail.9. Ethical considerations should be mentioned. The ethics code should be mentioned.*
9. *The ethics code has been included; please pay attention10. Divide the findings into paragraphs to make them clearer.*
10. *The findings were divided into paragraphs.11. In the Discussion, only the results of the present study and the studies of others are stated, but no comparison has been made and the opinions of the respected authors have not been mentioned.*

11. *This matter is in the form of a discussion, and comparing the findings is not appropriate given the regions where the studies were conducted.12. The Discussion should be divided into paragraphs to make it clearer.*
12. *The Discussion was divided into paragraphs.13. The limitations of the study and suggestions have not been mentioned.*
13. *Limitations were added14. The references are old; they should be updated.*
14. *The references have been included according to similar works 15. In the Acknowledgements section, the Vice-Chancellery for Research of the university of medical sciences where the study was conducted should be thanked*
15. *Added.Stay healthy and successful*

5 Revision 4

3 comments · 25 Jul 2020 – 15 Aug 2020

Elham Rajaei Reviewer — ACCEPT 25 Jul 2020

dear author
The revision was appropriate, and your manuscript is ready for publication.

Associate Editor — ACCEPT 15 Aug 2020

Dear Author,
Your manuscript in the current format is acceptable.
Thanks

Editor-in-Chief — ACCEPT 15 Aug 2020

Dear Author,
Your manuscript in its current format is acceptable. Please check your proof on our journal site for any additional comments. Thanks