OPEN PEER REVIEW

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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

- More transparency, constructiveness and tactful comments of the peer review process: leads to an increase in the quality of reviews
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- 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://brieflands.com/briefland/knowledgebase/category/tree.html#opr.html

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Peer Review Report for "Relationship Between Salivary Nitric Oxide Concentration and Dental Caries in Children: A Systematic Review and Meta-analysis"

Author(s): Nadia Elyassi Gorji, Ali Malekzadeh Shafaroudi, Pegah Nasiri, Mahmood Moosazadeh, Azam Nahvi

Review Timeline:

Submit Date:	6 Jul 2020
Revised Date:	19 Aug 2020
Accepted Date:	24 Aug 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) 22 Jul 2020

Dear AE,
The current version of the manuscript has many issues that need to be revised.
Abstract:
Line 12: " In four studies, the mean salivary NO…": This sentence conflicts with table 1 (Check the column titles/header in the table1)
Introduction:
1- Paragraph 1, line 3-5: Please cite reference for the definition of ECC and S-ECC.
2- Paragraph 1, line 9: Reference #3 is not a good reference for this paragraph. Please cite the appropriate reference.
3- Paragraph 1, line 11: It should be 1-12% according to reference #5.
4- Paragraph 1, line 13-14: It is better to write this sentence in a more appropriate format and avoid reusing consequences. Also, Reference #7 is not an appropriate reference to this explanation. This article is about the Relationship between Sever Early Childhood Caries

and BMI, and they found that there is no relationship between BMI and ECC.
5- Paragraph 1, line 17: Reference #9 is not a good reference for this paragraph. Please cite the appropriate reference.
6- Paragraph 2: Samaranayake is correct.
7- Paragraph 2: Reference #22 is suggested that an increase in NO production contributes to lower the caries occurrence in children. In reference #23: The mean nitrite levels of the control groups (healthy) were much higher when compared with the study groups (rampant or ECC). But you said that the concentration of NO is more in dental caries and this value is less in caries-free. SO you cite the wrong references for this statement!
***I suggest you reconsider the choice of references in the introduction section.
8- Paragraph 3: Briefly explain the importance of this systematic review.
Method:
9- The inclusion and exclusion criteria," P signifies children with dental caries": Be specified in more detail. (For example: children without systemic disease).
Result:
10- Please cite references of these seven studies Before inserting table 1.
11- Table 1: It is best to arrange table 1 by time or type of study.
12- Why is reference 31 numbered before reference 30 in the manuscript? You need to put the reference number in the table based on the text. So please cite references of seven studies in the first paragraph of the result section.
13- In table1, in three studies (18, 29, 31), cases with caries have lower mean NO concentration compared to the control group! Table and text are in conflict (Check the column titles/header in the table1)
Discussion:
14- Please cite reference for " Leukocytes of the oral cavity consist of 90% of monoclonal leukocytes (PMNs and neutrophils) and 10% of mononuclear cells, and 80% of neutrophils in the oral cavity are viable and functional". Reference 44 does not address this issue .
References
15- Please correct the reference #54 in the references section
Thanks

REFEREE: Reviewer | **Revision** (0) 26 Jul 2020

Dear AE,
The writing of this article is very good, but the question is for me: With this small number of articles (n=7), is the result of the review reliable?
- The reference page did not exist in the file.
Thanks

REFEREE: Associate Editor | **Revision** (0) 28 Jul 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)** 30 Jul 2020

Dear Authors,

Thank you for submitting your manuscript to Iran J Pediatr. Your manuscript has now been reviewed by three reviewers and an Associate Editor. I now have the reports of the Referees, which suggest that your manuscript might be suitable for publication following a number of revisions. I attach some reviewer comments and invite you to submit a revised version of your manuscript addressing the points made.

Regards

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.

Reviewer 1

Title: …….

Abstract

(6, 7).

Also, there are more than 700 types of microorganisms in saliva that are associated with systemic and oral diseases (13)

Samaranay,

In this regard, the effect of confounders, if any, can be explained by the performance of a meta-analysis.

List of abbreviations:

DMFT: Decay-Missing-Filled Teeth (for Permanent Teeth)

refrence list

Reviewer 2

According to the American Academy of Dentistry, early childhood caries (ECC) is defined as the presence of one or more decayed, missing, or filled tooth surfaces in any primary tooth in children less than 6 years of age. Moreover, severe early childhood caries (S-ECC) is any sign of smooth-surface caries in a child younger than three years of age. Not only this disorder presents a dental problem but it also stunts Children's growth due to insufficient food intake to meet developmental and metabolic needs. Therefore, children are arguably among the most vulnerable groups in the early years of life (2, 3).. Its prevalence has been reported as 10-12% and 70% in developed and less developed countries, respectively (5). The consequences of ECC affect the quality of life of children and their families and can have adverse socio-economic consequences (6, 7). In addition to microbial etiology, various factors, such as a diet containing

fermentable carbohydrates, genetical, immunological, behavioral, and environmental factors (e.g., social, economic, and cultural) can also influence the prevalence of caries (8, 9).

Samaranay, Studies have demonstrated that the concentration of NO in children with dental caries is more than 50 µm, while this value was reported as less than 40 µm in caries-free children(22, 23).

Therefore, in the light of the abovementioned facts and existing contradictions

children with dental caries, I which represents " Intervention" does not apply since the study was observational,

I2 test and the random effect model was used to estimate the standardized difference of the mean

seven studies in which the mean salivary NO concentration in children with caries was compared with the control group (Table 1).

Table 1-Characteristics of primary studies included to meta-analysis

Score of quality assessment

(18, 29, 31)the mean of this index in children with caries was higher, as compared to the control group and the observed differences were statistically significant in two of these studies(18, 29). In other words, in four studies, the mean salivary NO concentration in children with dental caries was lower than that in the control group and the observed differences were statistically significant in all four studies (22, 24, 30, 32).

Leukocytes of the oral cavity consist of 90% of monoclonal leukocytes (PMNs and neutrophils) and 10% of mononuclear cells, and 80% of neutrophils in the oral cavity are viable and functional.

(54, 55).

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OPEN PEER REVIEW

Revision (1)

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REFEREE: Reviewer | **Revision** (1) 13 Aug 2020

Dear AE,
The comments are as below:
1. There is no need to abstract nitric oxide in the title. Please remove NO.
2. In reply to this reviewer's comment “It is proposed that the authors use the article entitled Evaluation of the Prevalence of Clinical Consequences of Untreated Dental Caries Using PUFA/pufa Index in a Group of Iranian Children Published in the same journal to discuss the consequences of untreated dental caries”
The authors' response is this: Commented [N7R7]: References were revised according. But citation to this paper isn’t found in the text, nor in the reference list.
Thanks

REFEREE: Reviewer | **Revision** (1) 15 Aug 2020

Dear AE,
1- In the results section, you should have corrected the table column titles, not changed the text of the article. In references 24 and 25: The NO levels were higher in high dfs groups. But you said " In these studies, the mean of this index in children with caries was lower, as compared to the control group" ! or in reference 18: This study indicated a significant increase in salivary NO levels in caries-free children as compared to children with caries. but you said "the mean salivary NO concentration in children with dental caries was higher than that in the control group" .So please re-check all the references in table 1 and correct the text and table. Therefore, the abstract of the article also needs to be corrected.
2- Please change nitrous oxide to nitric oxide in the limitation section.
Thanks

REFEREE: Associate Editor | **Revision** (1) 15 Aug 2020

Dear EIC
The reviewer(s) have recommended publication, but also suggest some minor revisions to the manuscript. Therefore, I invite the author to respond to the reviewer(s)' comments and revise his manuscript.
Kind regards,

REFEREE: EIC | **Revision (1)** 16 Aug 2020

Dear Authors,

The second round of peer review of your manuscript is completed. I now have the reports of the Referees, which suggest that your manuscript needs some more correction.

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.

Reviewer 1

1- In the results section, you should have corrected the table column titles, not changed the text of the article. In references 24 and 25: The NO levels were higher in high dfs groups. But you said '' In these studies, the mean of this index in children with caries was lower, as compared to the control group''! Or in reference 18: This study indicated a significant increase in salivary NO levels in caries-free children as compared to children with caries. But you said ''the mean salivary NO concentration in children with dental caries was higher than that in the control group'' .So please re-check all the references in table 1 and correct the text and table. Therefore, the abstract of the article also needs to be corrected.

Reply: this part was revised and corrected.

2- Please change nitrous oxide to nitric oxide in limitation section

Reply: it was corrected.

Reviewer 2

1. There is no need to abstract nitric oxide in the title. Please remove NO.

2. In reply to this reviewer comment “It is proposed that the authors use the article entitled Evaluation of the Prevalence of Clinical Consequences of Untreated Dental Caries Using PUFA/pufa Index in a Group of Iranian Children Published in the same journal to discuss the consequences of untreated dental caries”

The authors response is this: Commented [N7R7]: References were revised according. But citation to this paper isn’t found in the text, nor in the reference list.

Reply: it was corrected.

Reviewer 3

With this small number of articles (n=7), is the result of the review reliable?

Reply: yes it is reliable.

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) 22 Aug 2020

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

REFEREE: Reviewer | **Revision** (2) 23 Aug 2020

Dear AE,
The authors addressed all questions and revised the manuscript properly. I would suggest the publication of this paper in the Iranian Journal of Pediatrics.
Thanks

REFEREE: Associate Editor | **Revision** (2) 23 Aug 2020

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

REFEREE: EIC | **Revision** (2) 24 Aug 2020

Dear Authors,
The third round of peer review of your manuscript has been completed, and I am pleased to inform you that your manuscript has now been accepted for publication in our journal.
Thanks