Author’s response to reviews

Title: Diagnostic accuracy of three placement sites for the cold test in subjects amongst different age groups.

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Author’s response to reviews:

LETTER WITH ANSWERS. MANUSCRIPT VERIFIED AND CORRECTED.

Manuscript: "Diagnostic accuracy of three placement sites for the cold test in subjects amongst different age groups." (OHEA-D-18-00196).

All the changes you requested on the manuscript in highlighted in yellow on the document.

Dear Sahng G. Kim (Reviewer 1). Thanks a lot for all your recommendations; we found that all of them are aimed to improve the manuscript.

1. Comment (Results). The authors should present overall diagnostic accuracy (sensitivity, specificity, accuracy, PPV, and NPV) of cold pulp testing in the three placement sites, MTBS, CTBS, and MTLS, respectively.
1. Answer (Results). Thanks for the comment. To report overall diagnostic accuracy, researchers must specify values of sensitivity, specificity, accuracy, positive predictive value and negative predictive value.

We include the overall diagnostic accuracy (sensitivity, specificity, accuracy, PPV, and NPV) of cold pulp testing in the three placement sites, MTBS, CTBS, and MTLS, respectively.

The changes are located on: Results section, page 8

Changes on the manuscript:

The overall diagnostic accuracy in the three placement sites was: 1. MTBS: sensitivity= 0.94, specificity= 0.75, accuracy= 0.85, PPV= 0.80, and NPV= 0.92; 2. CTBS: sensitivity= 0.91, specificity= 0.81, accuracy= 0.86, PPV= 0.84, and NPV= 0.91 and MTLS: sensitivity= 0.96, specificity= 0.72, accuracy= 0.81, PPV= 0.76, and NPV= 0.95.

2. Comment (Results). It is recommended that the results be presented according to anterior vs posterior teeth. It is thought that the tooth type also affects the results when different cold placement sites were used.

2. Answer (Results). Thanks for the recommendations, but unfortunately on this study we cannot present the results according to anterior and posterior teeth for two main reasons:

1.- Sample size.

2.- The frequency of anterior and posterior teeth in the groups.

1.- Sample size.

On this study, subjects were divided into two groups: 1) a female group and 2) a male group. Both groups were subdivided into 4 age groups: 17-27, 28-39, 40-50, and 51-65 years forming a total of eight groups.

The sample size was calculated with the study characteristics:

Calculation of sample size. The sample size was calculated with a two-factor design (two-way ANOVA). One factor (age) consisted of eight experimental groups (17-27, 28-39, 40-50, and 51-65 years). It was determined that 20 subjects per group was the minimum sample size with a power of 0.8 and a significance level of 0.05.

The results show that 258 subjects were included because they met the selection criteria. Subjects were divided into 8 groups: 1) 38 female (27%) from 17-27 years; 2) 37 female (26%)
from 28-39 years; 3) 34 female (24%) from 40-50 years; 4) 31 female (23%) from 51-65 years; 5) 33 male (28%) from 17-27 years; 6) 36 male (30%) from 28-39 years; 7) 29 male (25%) from 40-50 years and 8) 20 male (17%) from 51-65 years.

If we followed your recommendation we would need to form 16 groups;

- 8 groups where we reported the results for anterior teeth and
- 8 groups where we reported the results for posterior teeth; with a total of 320 subjects.

Therefore, with your recommendation we would have to increase 62 subjects to complete the 320 subjects.

2.- Frequency of anterior and posterior teeth.

On table 1 we show teeth with vital and necrotic pulp according to the gold standard and the clinical evaluation in the female and male group from 17 to 65 year olds.

On this table we report the frequencies of anterior and posterior teeth. The different frequencies of said teeth are not enough for us to make diagnostic accuracy calculations (sensitivity, specificity, accuracy, positive predictive value and negative predictive value) of anterior and posterior teeth.

For example:

In the female group from 17-27 years we did not find anterior teeth with vital pulp (frequency=0); therefore, we would not be able to obtain the values for the diagnostic accuracy due to the lack of anterior teeth in this group.

3. Comment (Tables 2, 3 and 4). The authors should present the total values of the results in each column and or row. For example, the results from all ages within the placement sites and genders and the results from all placement sites within the age groups and genders should be added in Table 3. In table 2, diagnostic accuracy values (sensitivity, specificity, PPV, NPV, and accuracy) from all age groups in each placement site should be presented. Similar total values can be presented in Table 4.

3. Answer (Tables 2, 3 and 4). Thanks for the recommendations.

---Table 2.

To report the diagnostic accuracy values, researchers must specify values of sensitivity, specificity, accuracy, positive predictive value and negative predictive value.
The diagnostic accuracy results are reported as proportions, therefore it is not recommended to show total values.

The following is a list of different references that shows result tables of studies related to this topic: Diagnostic tests, on the reports we did not find proportion total values.

List of references.


---Table 3.

On this document we included the changes based on your recommendation (The authors should present the total values of the results in each column and or row).

Changes are located on: Results section, table 3, page 24.

---Table 4.

The reproducibility results are reported as proportions.

On the table 4 correlation of times are reported.

Therefore, it is not recommended to show total values.

4. Comment (Discussion). The authors should compare the diagnostic accuracy values with those of the previous articles or systematic/meta-analysis review papers.

4. Answer (Discussion). On the document we included the changes based on your recommendation. Thanks.

The changes are located on: Discussion section, pages: 11 and 12.

Changes on the manuscript:

The highest diagnostic accuracy including sensitivity (1.00), specificity (0.95), predictive values (PPV= 0.95 and NPV= 1.00) and accuracy (0.97) was identified in the MTBS site of the female group from 40–50 years. The sites with sensitivity, specificity and predictive values ≥ 0.70 and accuracy ≥ 0.75 were observed in all groups. Only in the male group from 51-65 years values of 0.25 to 0.65 were identified in specificity and in positive predictive values. In the accuracy, values from 0.62 to 0.72 were identified. Several authors reported differences between male and female subjects (16, 18, 20). The thicker dentin and larger diameters of the crown in males may...
increase the time of the response to a stimulus to reach the pulpal nerves, resulting in a higher threshold (18). Other variables to consider are: psychological and behavioral factors (apprehension or Hawthorne effect) and biological factors (hormonal levels and neurological differences). On the other hand, researchers did not report differences between genders (16, 25, 26). In terms of age, the sites with predictive values ≥ 0.70 and accuracy ≥ 0.75 were observed in all the age groups, but the highest values of false positives were identified in the male group from 51–65 years (frequency= 15) and the false negatives in the female group from 51–65 years (frequency= 4). Researchers have identified diagnostic accuracy values of the pulp sensibility tests in subjects with different ages. One study evaluated 656 patients from ages 6 to 85 years. The results of pulpal sensibility tests (MTBS site), the tooth number, age, sex, number of restored surfaces, presence or absence of clinical or radiographic caries, and reported recent use of analgesic medications, were recorded. Authors observed that patients from 21–50 years showed a more accurate response to cold testing (accuracy= 0.904; sensitivity= 0.916; specificity= 0.896; positive predictive value= 0.862; and negative predictive value= 0.937) (2). Some authors reported that due to the aging process, a higher frequency of collagenous fibers in the pulp, fewer blood vessels, nerve fiber degeneration, an increase in dentin sclerosis, an increase in the width of the secondary dentin, and a higher incidence of coronal calcifications were observed (2,16, 27-30). When researching the literature, we did not find studies with populations of both genders including different age ranges. The results obtained from these studies could be a possible complement to facilitate the endodontic diagnosis in the clinic.

5. Comment (Background and Discussion). The contents need to be described logically without subheadings in Background and Discussion sections. It is recommended that the subheadings should not be used in these sections.

5. Answer. (Background and Discussion).On the document we included the changes based on your recommendation. Thanks.

The changes are located on: Background, pages: 3-4 and Discussion pages: 10-15.

6. Comment. There are grammatically awkward sentences and typos. For instance, "The true results are correct diagnoses because the cold test obtained the same diagnosis than that of the ideal standard."(page 3 lines 46-49) "Unfortunately, …an external stimulus from of the nervous system." (page 20 lines 19-20)

6. Answer. Thanks for the recommendation. We eliminated the phrases from the document.
7. Comment. Please consider using "gold standard" instead of "ideal standard" throughout the manuscript.

7. Answer. On the document we included the changes based on your recommendation. Thanks.

The changes are located on:

Abstract section.
Page 2

Background section.
Pages: 3 and 4.

Methods section.
Page: 7

Results section.
Pages: 8 and 9.

Discussion section.
Pages: 10, 11 and 14.

8. Comment. (Discussion). It would be more interesting if the authors have tested incisal edge or occlusal surface for cold testing since there are previous studies using these sites. Please discuss it in the discussion section.

8. Answer (Discussion). We included the changes based on your recommendation. Thanks.

The changes are located on: Discussion section, Page 14.

Changes on the manuscript: The incisal edge or occlusal surface are sites that have been analyzed by different studies. Researchers have reported high and low values of sensitivity, specificity, accuracy, positive predictive value and negative predictive value with cold and electric tests (16, 22, 26). On this study we are not evaluating the incisal edge or occlusal surface, since several authors have reported high frequencies of caries, restoration, enamel loss (abrasion) and exposed dentin on those sites (37, 38). All these clinical pathologies are associated with false results when using pulp sensibility tests (7, 22). Therefore, we decided not to include said sites on this study.
9. Comment (Discussion). The following sentence may not be appropriate. "We included teeth with..., but studies in teeth with reversible and irreversible pulpitis are necessary." (page 15, lines 57-58) The reversible pulpitis or irreversible pulpitis may not be confirmed using clinical observation. Furthermore, it is not ethical to do any invasive treatment in teeth with reversible pulpitis. Please revise this sentence.

9. Answer (Discussion). Thanks for the recommendation. We eliminated the phrases from the document.

10. Comment. (Conclusion). The author should present the overall values of each diagnostic accuracy.

10. Answer (Conclusion). On the document we included the changes based on your recommendation. Thanks.

The changes are located on: Conclusion section, page 16.

Changes on the manuscript:

a) Overall, the sites with sensitivity, specificity and predictive values ≥ 0.70 and accuracy ≥ 0.75 were observed in all groups. Only in the male group from 51-65 years, values from 0.25 to 0.65 were identified in specificity and in positive predictive values. As for the accuracy, values from 0.62 to 0.72 were observed


11. Answer (References). We included the changes based on your recommendation. Thanks.

The changes are located on: References.

Reviewer 2 (Reviewer 2): PEER REVIEWER COMMENTS: To view the full report from the academic peer reviewer, please see the attached file.

REVIEWER COMMENTS FROM REPORT: The authors have evaluated different placement sites for cold pulp sensitivity test. The authors have included the age of the patients as a variable in the analysis. The methods demonstrate attention to the details. The results of this study should be clinically relevant.
Comment. REQUESTED REVISIONS:

A major issue with the research is the sample size evaluation. The cross sectional study should have pre test power analysis. In the present study, the sample were divided into eight subgroups depending upon the age and the gender of the patients. Including less sample reduces the power of the study, making the results unreliable. The authors should now perform a reverse power analysis to support their conclusions.

Answer. REQUESTED REVISIONS.

On the document we included the changes based on your recommendation. Thank you.

The changes are located on: Methods section, page 5.

Changes on the manuscript:

Calculation of sample size.

The sample size was calculated with a two-factor design (two-way ANOVA). One factor (age) consisted of eight experimental groups (17-27, 28-39, 40-50, and 51-65 years). It was determined that 20 subjects per group was the minimum sample size with a power of 0.8 and a significance level of 0.05 (18).