Peer Review File

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First Round External Peer Review

Reviewer A

Dear, despite periapical radiography being the ideal technique for the daily routine of dental clinics around the world, especially for endodontic and periodontal evaluation, we cannot forget that even using the parallelism technique and its positioners we cannot guarantee that, when performing of 328 radiographs, the vertical and horizontal angulations were respected in all images obtained. That is why in this type of research we have the obligation to at least compare, in the same sample, with the gold standard imaging exam, tomography. In this way, the methodology employed does not add, unfortunately, to the results obtained, any reliable information, at the present time, in relation to the proposed objective. *Reply*:

You noted a great point. Because of the nature of in vivo studies, we didn't have a gold standard to compare our results. Intending to compare with a gold standard, we should apply a CBCT or an exploring surgery for detecting the accurate location of the mental foramen, but ethical limitations didn't permit us to do that.

I wish future studies, especially in vitro research will consider this problem by adding such factors to the methodology.

We are thankful to you for reviewing our work and your precious recommend.

I hope my manuscript deserves your publication criteria.

Truly yours

Reviewer B

I would like to congratulate the authors for the study. Studies involving radiographic anatomy are always very important for the development of science, especially in the field of surgery and diagnosis.

Below are my suggestions about the article:

In the introduction, in lines 77 and 78: "In different populations, the location of the foramens can vary due to geographical and ethnic factors" – I suggest the inclusion of data on ethnicities, showing how the frequency occurs in the ethnicities already studied.

Reply 1:

Thank you for your careful review and constructive comments. Your comments are responded in the following paragraphs.

Yes, it was a delicate point. I try to explain completely in the following sentences.

Changes in the text: "In different populations, the location of the foramen can vary due to geographical and ethnic factors (3).

In previous studies, some results show us how ethnicity can make differences in normal anatomical variations. For example, the prevalence of accessory mental foramen is noted like that: 2.6% in French; 1.4% in American Whites; 5.7% in American Blacks; 3.3% in Greeks; 1.5% in Russians; 3.0% in Hungarians; 9.7% in Melanesians; and 3.6% in Egyptians (4). On the other hand, a high frequency was reported at 6.7-12.5% in the Japanese population (5). In the other comparison, mental foramen location was reported between the first and second premolar in Caucasoids and Sri Lankan populations, but in Turkish and Mongoloid populations, results showed mental foramen in line with the second premolar axis. Mental foramen was detected between the second premolar and first molar in the Japanese and Tanzanian populations (6), (7), (8). This outcome reveals how ethnicity, race, and geographic factors can vary in location, shape, and number of mental foramen."

In the methodology, in lines 128-149: I suggest creating a scheme to represent horizontal positioning 1,2,3,4,6 and vertical positioning A,B,C. If possible, make a scheme (drawing) and associate it with the periapical radiographs that made up the sample, with arrows indicating each classification.

Reply 2: I added a scheme as your explanation; I wish it were suitable.

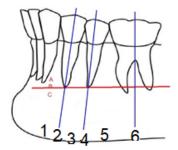


Figure 1. vertical axis of premolars and molar teeth are shown with blue lines. Redline presents a line that connected two apexes of premolars



Figure 2. blue and red lines of figure 1 are shown in the periapical radiography.

On line 125: "The study was approved by the ethics committee of Birjand University of Medical Sciences (IR.BUMS.REC.1398.416)." – I consider it appropriate to relocate this sentence to the beginning of the methodology.

Reply 3:

I relocated that to the beginning of the methodology.

In the results, table 1 and table 2, in table 1 the first column is named "Frequency (percent)" and in table 2 the first column is named "percent" only, I suggest standardizing the terms. *Reply 4:*

It has been corrected.

In the discussion, I suggest the construction of a first paragraph defending the method chosen for this study, that is, periapical radiography. Therefore, the authors should discuss why the chosen method is suitable for the study.

Reply 5:

Your point was explained in the paragraph and added.

Changes in the text: "Despite the wide usage of advanced modalities for dental purposes, periapical radiography is the most popular and available method worldwide.

Compared with panoramic radiography, distortions in size and shape are at the minimum amount in periapical radiography, and the position of the object has the most negligible effect on the movement of the image.

In addition, navigating the instruments to avoid critical anatomical landmarks injury always is in concern for all clinical operations. So, the present study aimed to plan and classify the normal variations in a particular population."

Reviewer C

The authors evaluated the location of the mental foramen and its relationship with the roots of the mandibular premolar on intraoral radiographs. The study performed well. However, I think that the study has insufficient impact on publication in an international journal because the location of the mental foramen can be more accurately determined by 3-dimentional imaging such as CT and CBCT. In intraoral radiography, the positional relationship between molar(s) and mental foramen is changeable by the difference in exposure angle because they are not located in the same sagittal plane.

Reply 1:

Thank you for your careful review and constructive comments. Your comments are responded in the following paragraphs.

You noted a great point. Because of the nature of in vivo studies, we didn't have a gold standard to compare our results. Intending to compare with a gold standard, we should apply a CBCT or an exploring surgery for detecting the accurate location of the mental foramen, but ethical limitations didn't permit us to do that.

I wish future studies, especially in vitro research will consider this problem by adding such factors to the methodology.

We are thankful to you for reviewing our work and your precious recommend.

Additionally, I found some issues as follows:

1. Inclusion and exclusion criteria should be shown.

Reply 2: Inclusion and exclusion criteria are shown in the paragraph.

Changes in the text: "All images were taken with a perpendicular angle to the contact between the first and second molar. Researchers repeated radiography with digital artifacts and other distorting factors. Patients with the malocclusion class II, III (upper and lower molar relationship) and any history of surgery on the mandible body were removed from the study. In addition, patients who performed orthodontic treatment or extraction of mandibular premolars and first molar in the past were excluded from the study. The images were taken with an excessive vertical angle that causes elongation or foreshortening were deleted."

2. When a patient has malocclusion such as severe class 3, did you include the patient? *Reply 3:*

No, we examined mandible and maxillary first molar relationship then we excluded class 2 and 3 malocclusion cases.

3. The description of the orientation of mental foramens toward premolar roots should be rechecked. I thought following correction is needed: 1. Mesial toward mandibular first "pre"molar, 2. Along vertical axis of mandibular first "pre"molar, 3. Between the mandibular first and second premolars, 4. Along the mandibular second premolar, 5. "Between" mandibular second premolar and first molar, 6. Along the mandibular first molar. Additionally, criteria of the vertical and horizontal positions of mental foramen should be explained with actual radiographs or figures.

Reply 4:

Yes, you are right, thank you. I corrected that as you noted.

I explained that classification in the figure.

Changes in the text:

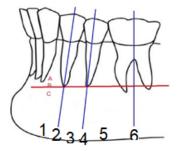


Figure 3. vertical axis of premolars and molar teeth are shown with blue lines. Redline presents a line that connected two apexes of premolars



Figure 4. blue and red lines of figure 1 are shown in the periapical radiography.

4. How many observers did this study employ? Inter- and intra-observer agreement is needed for the study with image interpretation.

Reply 5:

We had two observer (two oral and radiologists).

Changes in the text: "the inter-examiner and intra-examiner reliability were determined by comparing two repeated measurements at 20 (1.22%) randomly chosen images one month later, with 95% limits of agreement extended by a 95% confidence interval for differences between the means (using the Kappa coefficient). "

5. The authors should change the order of the columns in the tables.

Reply 6:

It has been corrected.

Study limitations should be described in the discussion section.

Reply 7:

Limitations and recommendations of the study were added into the discussion section.

Changes in the text: So, the present study aimed to plan and classify the normal variations in a particular population. Although we used periapical radiography as the most common for determining the location of the mental foramen, advanced modalities like CBCT are recommended for future studies.

In this in vivo study, applying a gold standard for accurate locating, such as more CBCT examination or exploring surgery, was not possible; all these preparations can suggest an in vitro study."

6. There are several abbreviations in the text and abstract. They should be clearly defined in the text where firstly used.

Reply 8:

All abbreviations were defined in first used.

8. A reference list should be described in accordance with the instruction for authors.

Reply 9:

Reference list is revised as the instruction for authors.

Reviewer D

This manuscript investigated the horizonal and vertical relationships between mandibular premolars and mental foramen in patients with different ages and genders, and found that the most common locations for mental foramen are at the vertical axis of second premolars or between the roots of the first and second premolars and below the line connecting the apices of the two premolars. No age or gender related difference was identified in the locations of mental foramen.

This is a straightforward study with the methods and results clearly presented.

Comments

1. The observations were made on intraoral periapical radiographs. Although paralleling technique was utilized, the variations in horizontal and vertical angulations of x-ray cannot be fully prevented among the radiographs, which could affect the relative location of mental foramen in the radiographs. Please elaborate this in the "Discussion" section.

Reply 1:

Thank you for your careful review and constructive comments. Your comments are responded in the following paragraphs.

Your point was explained in the paragraph and added to the discussion.

Changes in the text: "Compared with panoramic radiography, distortions in size and shape are at the minimum amount in periapical radiography, and the position of the object has the most negligible effect on the movement of the image.

In addition, navigating the instruments to avoid critical anatomical landmarks injury always is in concern for all clinical operations. The present study aimed to plan and classify the normal variations in a particular population. Although we used periapical radiography as the most common for determining the location of the mental foramen, advanced modalities like CBCT are recommended for future studies.

In this in vivo study, applying a gold standard for accurate locating, such as more CBCT examination or exploring surgery, was not possible; all these preparations can suggest an in vitro study. "

2. It is not clear from the "Material and Method" section what is the selection criteria for the patients, if all the patients have two premolars and first molar present in the mandible, or if the patients had orthodontic treatment before, since ortho may change relation position of the teeth vs. mental foramen. Please detail the selection criteria for the study.

Reply 2:

Inclusion and exclusion criteria are shown in the paragraph.

Changes in the text: "All images were taken with a perpendicular angle to the contact between the first and second molar. Researchers repeated radiography with digital artifacts and other distorting factors. Patients with the malocclusion class II, III (upper and lower molar relationship) and any history of surgery on the mandible body were removed from the study. In addition, patients who performed orthodontic treatment or extraction of mandibular premolars and first molar in the past were excluded from the study. The images were taken with an excessive vertical angle that causes elongation or foreshortening were deleted."

3. There are grammatical errors and typos in the manuscript. A careful proofread is strongly recommended.

Reply 3:

We checked and corrected all over the manuscript in Grammarly software version of premium.

Second Round External Peer Review

Original Reviewer D

This manuscript has been improved by incorporation of the revisions suggested by the reviewers.

Comment

- 1. On line 182, it states "Although we used periapical radiography as the most common for determining the ...". Please add "method" between "periapical radiography" and "as the most common..."
- 2. Suggest more grammatical corrections before publication.