Reviewer’s report

Title: Evaluation of chemiluminescence, toluidine blue and histopathology for detection of high risk oral precancerous lesions: a cross-sectional study

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Reviewer: P Guneri

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Frankly, the authors have done a lot and presented a not-very-well-known statistical analysis method (Hui and Walter’s multinomial latent class model). Unfortunately, the manuscript had some shortcomings, which are mentioned below:

ABSTRACT
1. Background: Please clarify what you mean with “… technical…” in the second sentence.
2. Methods:
   a) Histopathology is not a screening method or tool. The authors should rephrase this sentence, i.e., “…the screening performance of chemiluminescence and toluidine blue, using histopathology as the reference standard”.
   b) In the 5th line, please correct the term “histopathological”.
3. Results: Please state the sensitivity and specificity of the screening methods clearly.
4. Conclusion: This part needs to be written in a more academic language and style.

INTRODUCTION
The main reason to conduct this study is not reasonable. The authors state that “…if the histopathological evaluation is itself subject to errors then the estimates of the sensitivity and specificity of the light-based protocols can be expected to be biased.” If we consider this statement true, then this approach can be proposed for every conventional or novel screening method. Unfortunately, in order to have scientific validity, we need to have a reference standard in such studies –even though the reference itself has pitfalls. In order to overcome this problem, a panel of pathologists which would provide an agreed histopathological decision for each lesion is suggested. So, this “purpose” is not suitable or appropriate to conduct the present research.

PATIENTS AND METHODS
As far as I understand, the authors have used 2 screening methods: chemiluminescence and toluidine blue. On the other hand, on the last paragraph of this section, they have written that “..Therefore this model can be used only if there are at least three tests (number of parameters to be estimated = 7 and”
degrees of freedom = 7).” The authors have classified the lesions according to their toluidine blue staining degree. Dark staining lesions were considered positive, faint were considered equivocal, and unstained ones were negative. 1) TBLU group: positive if the lesions were dark stained, negative if the result was either equivocal or negative. 2) TBEQ group: positive if dark or equivocal, negative if unstained. 3) CHTB group: positive if the lesion was both CHEM-positive and TBLU-positive, negative if otherwise. Here, we have 2 screening tests, no matter how the authors classified the results. Also, what had happened to “CHEM-positive and TBEQ positive lesions” in the authors’ subgrouping process?

The authors state that “…Histopathologic evaluation was done by two senior Oral Pathologists blinded to the clinical findings. The first pathologist evaluated each specimen at two time points.” However, there is not information about the second pathologist. In cases when there is a disagreement, what have the pathologists done to reach to a consensus?

The interevaluation agreement between 2 pathologists for each category of the classification was not clearly explained in the manuscript, and this part needs further clarification. The authors have presented the data analysis results of one pathologist in page 10: “..there was neither a bias in the histopathologist’s two evaluations nor a significant departure from variability at each time point as indicated by the Pitman’s test. Despite this, however, the Pearson’s correlation coefficient for scores at two time points by the same histopathologist was only 0.28.” Unfortunately, I have not received any information regarding the second histopathologist. These should be mentioned not only within the figure legends of Figure 2, but also within the text, as well.

DISCUSSION

The authors declared that “Additionally, there is a need for an objective and more accurate diagnostic method when evaluating the histopathological specimens”. This is not one of the purposes of this study, and actually, I do not understand what the authors mean by “accurate diagnostic method for evaluation of histopathological specimens”.

Level of interest: An article of insufficient interest to warrant publication in a scientific/medical journal

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests.