Author’s response to reviews

Title: Comparing the effect of 0.06 %-, 0.12 % and 0.2 % Chlorhexidine on plaque, bleeding and side effects in an experimental gingivitis model. A parallel group, double masked randomized clinical trial.

Authors:
Maliha Haydari (malihah@student.odont.uio.no)
Ayse Gul Bardakci Bardakci (aysegb@student.odont.uio.no)
Odd Carsten Koldsland Koldsland (oddcko@odont.uio.no)
Anne Merete Aass Aass (a.m.aass@odont.uio.no)
Leiv Sandvik (leiv.sandvik@odont.uio.no)
Hans Preus (hpreus@odont.uio.no)

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Reviewer reports:

Icíar Arteagoitia (Reviewer 1): It is a well-designed, randomized blinded clinical trial. It meets the requirements of CONSORT statement.

The only aspect to point out is that they do not use placebo so they can only compare three different concentrations between each other and the working hypothesis might be clearer

RESPONSE: The issue of placebo has been quite extensively debated in the discussion section. However, this is testing of new commercially available concentrations of CHX (0.06% and 0.12%) against the gold standard of 0.2% CHX. It is not to test the efficacy of CHX as such. We wanted to see if the new solutions were as good as the gold standard (0.2%). However, in the discussion findings are debated against previous studies using water as control. Placebo would also be impossible to make since the different CHX products come in different solutions
regarding osmolality, color, taste, smell, and texture. And for the clinicians, we had to test the commercially available product – that’s what they use, and that’s what they want advice on.
RESPONSE: Working hypothesis has now been included in the introduction. (P3 L 74-80) and discussion on placebo has been added to the discussion (P11 L316 – 321)

Hermann Agis, PhD (Reviewer 2): In their study the authors' objective was to reveal the inhibiting effect of clinically applied products containing 0.2% and 0.12% chlorhexidine and 0.06% chlorhexidine on plaque and gingivitis. The authors performed a clinical study using an experimental gingivitis. Two different treatment protocols were applied whereas on quadrant in each patient received mouthwash alone, the other quadrant was rinsed with mouthwash and oral hygiene treatment was performed mechanically. The patients were observed over 21 days. Based on their results the authors conclude that the mouthwash with 0.2% chlorhexidine prevented dental plaque with better efficiency than than the mouthwash with 0.12% and or 0.06% chlorhexidine. While the study was planned and carried carefully there are issues that need to be resolved before the manuscript can be recommended for publication.

Majour issues:
1) Why did the authors compare commercially available mouthwash at 0.2%, 0.12%, and 0.06% chlorhexidine? What was the rational for including those concentrations? This should be clearly presented.

We thank for this advice and see that we have not explained our intent clearly enough. The clinician does not know what to suggest for his patient unless we test the products as such, and it is of limited value to make our own solutions with the different CHX concentrations. We have changed the wording to make our intention clearer. (P3 L 76-80)

2) The authors presented that there are a variety of studies on the effect of different chlorhexidine concentrations (Background, page 3, line 70-77). It is not entirely clear what the novelty of the study is. This should be clearly presented.

Not a variety, few actually. The introduction describes that most of these studies have been scored with a different scoring system (Quigley and Hine) which may not be relevant to test such remedies. This is also debated in the discussion and mentioned in the introduction.
We have changed the wording to make our claim and novelty clearer. (P3 L 74-81)
3) The authors compared the following mouthwashes: (i) 0.2% chlorhexidine, (ii) 0.12% chlorhexidine with 910 ppm NaF², and (iii) 0.06% chlorhexidine with 250 ppm NaF³. Did the products also differ in other ingredients? Based on the described mouthwashes the differences between the products is not limited to the chlorhexidine concentration. Could this have an impact on the effect of the different mouthwashes in this study? This is an important point. The different products have different ingredients and the reactive CHX may well bind to some of those. Our view is that the more ingredients – the less CHX is available for active “duty”. However, ingredients such as NaF has proven not to interfere with the activity of CHX [ref 27] However, the whole point with the CHX containing mouthwashes is to prevent plaque in times when the patient is not able to brush. Earlier, we had pure products on the market. Nowadays it seems that the manufacturers put all sorts of “effective” ingredients into mouthwashes and market them as actually working – which most are not (except Fluorides and CHX with high enough concentrations).

We have clarified this in the discussion on P 11 L338-341.

4) Several outcome parameters were not presented in the study and were indicated as (data not shown). The authors should at least consider presenting these data as supplementary figures or tables. These data should not be excluded. All data should be presented and accessible.

We have added tables to the manuscript. To the Editor: Please feel free to put table 2 and 3 as supplementary tables 1 and 2 if that suits the journal best.

5) As BMC encourages to present the raw data it is appreciated that the authors provide them in an Excel format. However, the data should be presented in a way that it is clear for the reader what they represent. Currently it is not entirely clear.

Sorry. Not well enough presented. We have presented the data in EXCEL so that anyone could copy this to their own statistical programs (like IBM SPSS). “Sheet” is the original data on all teeth. Sheet 1 describes what the columns in “sheet “ represents. We hope this is satisfactory now. Please do not hesitate to call on us again to make this in a form acceptable for the reviewer and journal.

6) The authors should present future directions for research and the clinical impact of the findings should be discussed and mentioned in the conclusion.

Done on 10 L 279-283, P.11 L 332 – 374.

7) The conclusion should be based on the study and not compare the results to other studies.
Minor issues:

1) Abstract, page 2, line 37: Proved is not the ideal word. Please replace it.
   Done

2) The authors should use the same term and not switch between "commercially available product" and "commercially available mouthwash".
   Done, changed all to “mouthwash(es)"

3) Table 1: The authors should not present findings from other studies in their result section. This should be part of the discussion and not of the table.
   Done

4) The authors should revise the manuscript with the help of a scientifically trained native speaker.
   Done