The effect of hexetidine mouthwash on the prevention of plaque and gingival inflammation: a systematic review

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CRD summary
The authors concluded that hexetidine mouthwash reduced plaque accumulation compared to placebo but may not be a suitable alternative to chlorhexidine mouthwash. However, variation between trials precluded strong conclusions. Given the limitations of the evidence and potential for missed data, the authors' suggestion that no strong conclusions could be drawn seems appropriate as the evidence may not be reliable.

Authors' objectives
To assess the effectiveness of hexetidine-containing mouthwash in the prevention of dental plaque and gingivitis.

Searching
MEDLINE/PubMed and Cochrane CENTRAL were searched up to January 2010 for publications in English. Search terms were reported. Reference lists of relevant studies were screened manually.

Study selection
Eligible studies were randomised controlled trials (RCTs) or controlled clinical trials (CCTs) in populations in good general health and aged at least 16 years. Trials were required to compare the effectiveness of hexetidine mouthwash alone or in combination with tooth brushing versus a control mouthwash (placebo or chlorhexidine). Outcomes of interest were plaque (measured at any time point) and bleeding or gingivitis measured in the long term (≥4 weeks).

Included trials were published between 1974 and 2005. Mean ages, where reported, ranged from 28 to 36.4 years (range 16 to 66 years). Most participants were female. One trial was in participants with aphthous ulcerations. Trials compared various brands of hexetidine (0.1 to 0.2%) versus chlorhexidine (0.1 to 0.2%) mouthwash, saline or placebo with or without normal oral hygiene practice. Where reported, rinsing time ranged from 30 seconds to one minute and occurred twice or three times daily. Only one trial incorporated supervised rinsing during week days. Different tools were used to measure outcomes.

Adverse effects (including tooth staining and sensitivity) were recorded.

Two reviewers independently screened studies for inclusion; disagreements were resolved through referral to a third reviewer.

Assessment of study quality
Two reviewers assessed the methodological quality of trials according to various previously published criteria; internal and external validity and statistical methods. Trials were considered to be at low risk of bias if they reported on random allocation, defined inclusion/exclusion criteria, blinded both patients and examiners, included similar comparator groups, and reported follow-up criteria. Trials were considered to be at moderate risk of bias if they did not report on one of the aforementioned criteria and at high risk of bias if the did not report on two or more criteria.

Data extraction
Two reviewers extracted or calculated baseline and final follow-up means and standard deviations. Where overall data for crossover trials were not reported, data were used from initial treatment only.

Methods of synthesis
Due to clinical and methodological heterogeneity, data were presented in tables and as a narrative synthesis.

Results of the review
Five RCTs (312 patients analysed) and one CCT (24 patients analysed) were included in the review. Three RCTs were crossover double-blind, two RCTs were parallel double-blind and the CCT was parallel single-blind. Follow-up ranged
from four days to six weeks. Two RCTs were considered low risk of bias, two moderate and one high risk of bias. The CCT was considered to be at high risk of bias.

**Plaque (six trials):** Two trials (one moderate and one high risk of bias) showed that hexetidine statistically significantly reduced plaque in the short term (<4 weeks) compared to placebo or saline but was less effective or of equal effectiveness when compared to chlorhexidine mouthwash.

Two trials that reported long-term effects (≥4 weeks) showed conflicting results when comparing the effectiveness of hexetidine versus placebo on plaque. One trial was at moderate and one at low risk of bias. The trial at low risk of bias compared the effects of hexetidine versus chlorhexidine on plaque accumulation and reported no statistically significant differences.

**Other outcomes (two trials; one moderate and one low risk of bias):** The two trials that assessed gingivitis and bleeding showed no statistically significant differences between treatments in the long term.

Higher concentrations of hexetidine resulted in more adverse effects compared to lower concentrations. Other results on adverse effects were reported in the review.

**Authors’ conclusions**
The evidence suggested that hexetidine mouthwash reduced levels of plaque compared to placebo mouthwashes but did not appear to be a suitable alternative to chlorhexidine mouthwash. However, variation in studies precluded strong conclusions.

**CRD commentary**
The review question and supporting inclusion criteria were stated clearly. The search for relevant literature was somewhat limited (only two databases). The search was restricted by language and did not appear to attempt to locate unpublished data so potentially relevant data may have been missed. Trial quality was assessed using previously published criteria; only two trials were considered to be a low risk of bias. Each stage of the review process was performed in duplicate, thereby minimising potential for reviewer error and bias.

Details on study and participant characteristics were not always well reported in the individual trials. The authors acknowledged the heterogeneity between trials and a narrative synthesis was appropriate. The evidence base was limited with only a small number of trials and small sample sizes. It was unclear how the authors defined whether or not differences between treatments were significant.

Given the limitations of the evidence and potential for missed data, the authors’ suggestion that no strong conclusions could be drawn seems appropriate as the evidence may not be reliable.

**Implications of the review for practice and research**

**Practice:** The authors stated that higher concentrations of hexetidine resulted in more side effects and should not be used routinely in a mouthwash.

**Research:** The authors did not state any implications for research.

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