The effect of cetylpyridinium chloride-containing mouth rinses as adjuncts to toothbrushing on plaque and parameters of gingival inflammation: a systematic review

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CRD summary
This review concluded that cetylpyridinium chloride-containing mouth rinses, when used as an adjunct to toothbrushing, provided a small but significant reduction in plaque and gingival inflammation, when compared with toothbrushing alone or toothbrushing followed by a placebo rinse. The reported heterogeneity limits robust conclusions and the results should be interpreted with some caution.

Authors’ objectives
To determine the effectiveness of cetylpyridinium chloride-containing mouth rinses as adjuncts to toothbrushing in the prevention of dental plaque and gingival inflammation.

Searching
MEDLINE and the Cochrane Central Register of Controlled Trials were searched up to and including January 2008 for English language studies. Search terms were reported. References of relevant articles were also scanned.

Study selection
Randomised controlled trials (RCTs) and controlled trials, of at least four weeks duration, comparing cetylpyridinium chloride-mouth rinses and toothbrushing with toothbrushing alone or in combination with a placebo rinse, were eligible for inclusion. Participants had to be healthy and aged at least 18 years. Outcomes of interest were level of plaque, bleeding and gingivitis. Only formulations that met the American Dental Association's safety criteria of cetylpyridinium chloride concentrations were included (between 0.045% and 0.10%).

Various brands of mouth rinses were included in the trials, with different formulations and concentrations of cetylpyridinium chloride (0.01% to 0.10%). Two studies reported using formulations with highly biovariable cetylpyridinium chloride (72 to 77%), similar information was not provided by the remaining trials. A baseline prophylaxis was given in half of the trials. Oral hygiene (including rinsing) was performed unsupervised in most trials. Outcome measures (plaque, bleeding and gingivitis) varied across trials. Where given, the age of participants ranged from 18 to 66 years. One trial enrolled only male participants. Another trial enrolled only individuals who had previously participated in dental clinical studies.

Two reviewers independently selected papers for inclusion in the review and any disagreements were resolved by discussion.

Assessment of study quality
The quality of the included trials was evaluated based on the following criteria: method of randomisation and allocation concealment, blindness of examiners, and completeness of follow-up.

The authors did not state how many reviewers performed the quality assessment.

Data extraction
Mean values and standard deviations were extracted. In trials that only reported the standard error of the mean, the standard deviation was calculated, where possible, based on the sample size. Differences between baseline and end-of-trial scores were calculated for each trial and descriptive comparisons were presented for each outcome.

Two reviewers performed the data extraction.
Methods of synthesis
Where possible, studies were also pooled in a meta-analysis using a random-effects model. Summary estimates were reported as weighted mean differences with their associated 95% confidence intervals. Baseline and end-of-trial assessments were analysed separately for each outcome. Subgroup analysis for evaluation period was performed. Statistical heterogeneity was assessed using the $I^2$ statistic.

Results of the review
Eight RCTs were included in the review (n=approximately 867 participants; the number of participants was estimated by the review authors in one trial). Two RCTs compared cetylpyridinium chloride-containing mouth rinses plus toothbrushing with toothbrushing alone. Six RCTs compared cetylpyridinium chloride-containing mouth rinses plus toothbrushing with toothbrushing followed by a placebo rinse. Randomisation was reported in all but one trial. Adequate allocation concealment was reported in only one trial. Five trials were reported to be double-blinded; two trials a single blind (operator) design. Duration of follow-up ranged from four weeks to six months.

Trials of at least four weeks duration: Two trials found a significant reduction in plaque (weighted mean difference -0.35, 95% confidence interval (CI): -0.47 to -0.24) and gingival levels (weighted mean difference -0.15, 95% CI: -0.23 to -0.07) with cetylpyridinium chloride-containing mouth rinses plus toothbrushing compared with toothbrushing alone or toothbrushing followed by a placebo rinse for plaque.

Trials less than six months duration: One trial found a significant reduction in plaque with cetylpyridinium chloride-containing mouth rinses plus toothbrushing compared with toothbrushing alone or toothbrushing followed by a placebo rinse for plaque (weighted mean difference -0.25, 95% CI: -0.47 to -0.03).

Trials of at least six months duration: One trial found a significant reduction in plaque with cetylpyridinium chloride-containing mouth rinses plus toothbrushing compared with toothbrushing alone or toothbrushing followed by a placebo rinse for plaque (weighted mean difference -0.42, 95% CI: -0.53 to -0.31).

Evidence of significant statistical heterogeneity was found in all analyses.

No significant between group differences were found in all pooled analyses for baseline scores.

Authors' conclusions
Cetylpyridinium chloride-containing mouth rinses provided a small but significant reduction in plaque and gingival inflammation, when used as an adjunct to either supervised or unsupervised oral hygiene, compared with toothbrushing alone or toothbrushing followed by a placebo rinse.

CRD commentary
The research question was supported with clear inclusion criteria. Two databases were searched, restricted by language, with no attempt made to systematically locate unpublished studies, introducing the possibility of language and publication bias. The selection of studies for inclusion in the review was conducted in duplicate. It was unclear whether similar methods to avoid error and bias were employed during data extraction or quality assessment. Appropriate criteria were used to assess study quality; the authors did not appear to have used results to inform the synthesis. Given the substantial heterogeneity amongst the included trials, a meta-analysis may not have been an appropriate method of synthesis. As acknowledged by the authors, the results are based on individuals with good to moderate gingival health and should not be generalised beyond this population. The reported heterogeneity limits robust conclusions and the results should be interpreted with some caution.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that further research is needed to establish whether cetylpyridinium chloride-containing mouth rinses have additional efficacy in individuals suffering from periodontitis.
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