The effectiveness of commonly used mouthwashes for the prevention of chemotherapy-induced oral mucositis: a systematic review


CRD summary
The review investigated whether medicated mouthwashes are effective in the prevention or amelioration of oral mucositis among patients undergoing chemotherapy. The results did not support the use of chlorhexidine or other mouthwashes for this purpose. Given the limited search strategy and poor reporting of the review methods, the authors’ conclusions should be interpreted with caution.

Authors’ objectives
To assess the effectiveness of mouthwashes in the prevention or amelioration of oral mucositis among patients undergoing cytostatic chemotherapy.

Searching
MEDLINE and CINAHL were searched from 1992 to Autumn 2004. Search terms were reported. It was not clear whether a language restriction was applied to the search.

Study selection
Randomised controlled trials (RCTs) on the use of mouthwashes for the treatment oral mucositis in adult participants undergoing chemotherapy were eligible for inclusion.

Included studies were required to assess the severity of oral mucositis as an outcome measure. The severity of mucositis was scored using a World Health Organization (WHO) instrument (or an adaptation of this scale), the Oral Assessment Guide scale and a purpose-developed scale. Severity was assessed daily, weekly or less often.

In the included studies: the mean age of patients was 56.3 years; 72% of patients had received chemotherapy; 6% had a haematopoietic stem cell transplant (HSCT); and for 22% of patients treatment was unknown. The active ingredients in the mouthwashes were chlorhexidine (0.12 to 0.3%), nystatin (100,000 U/ml), lidocaine (0.5%) with diphenhydramine hydrochloride (0.25 mL) and aluminium hydroxide (14.75 mL), chamomile solution (20 drops in 100 mL water) and povidone-iodine. The instructions for use ranged from a 20 second rinse twice daily to a one minute rinse four times daily. The intervention mouthwashes were salt solution (with or without soda), mouthwash without the active ingredient (chlorhexidine or chamomile), amine-stannous fluoride or water.

Two authors independently performed the study selection. Disagreements were resolved through discussion with a third reviewer.

Assessment of study quality
A validity assessment was performed by assessing whether each study had adequately used the following methods: randomisation, blinding and the use of intention-to-treat analysis.

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

Data extraction
The weighted mean difference (WMD) of change in oral muscositis severity was extracted. The authors did not state many reviewers performed the data extraction.

Methods of synthesis
Trials of chlorhexidine mouthwashes were combined using a fixed-effect meta-analysis. A χ2 test of homogeneity was used to investigate differences between studies. Studies of other mouthwashes were described individually.
**Results of the review**

Seven RCTs (721 patients) were included in the review. The trial quality varied, with double blinding used in five trials and intention-to-treat analysis used in four trials. None of the trials reported a power calculation.

Compliance was assessed in three trials and was moderately good, although in one trial, patients using the intervention mouthwash were less compliant than those using the control mouthwash.

In five trials (n=500), chlorhexidine mouthwash was not found to be more effective than control, WMD 0.22, 95% CI -0.20, 0.63, P=0.31. There was no evidence of statistical heterogeneity (P=0.94).

In one study (n=164) of chamomile mouthwash, no difference in incidence or severity of mucositis was found comparing intervention to control.

In one study (n=40), iodine mouthwash was associated with less severe (30% lower) and shorter duration of mucositis than control, although the results could have been due to chance.

**Authors’ conclusions**

The results do not support the use of chlorhexidine mouthwash in the prevention or amelioration of oral mucositis.

**CRD commentary**

The review addressed a clearly stated research question, and inclusion criteria for design, participants, intervention and outcome were clearly stated. The search strategy appears somewhat limited, although the authors stated that the date limit on their database search was to restrict included studies to those relevant to current oncology care. No attempt was made to locate unpublished studies and it is unclear whether the search was restricted by language. Therefore, it is possible that some studies were missed, and the review may be affected by publication bias. The authors attempted to minimise bias and errors during the selection of studies for the review, but it is not reported whether similar methods were used for data extraction or quality assessment. Factors which might have affected the results of the review, including the quality of the included studies and the compliance of the participants in the included studies, were described by the authors. Where the data were synthesised quantitatively, standard meta-analytic methods were used and statistical heterogeneity was assessed. Given the limited search strategy and the poor reporting of the review methods, it is difficult to assess the reliability of the results of the review, therefore the authors’ conclusions should be interpreted with caution.

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

Practice: The authors recommended the use of sterile water, 0.9% saline solution or sodium bicarbonate rather than chlorhexidine mouthwash for the prevention or amelioration of oral mucositis associated with chemotherapy.

Research: The authors stated that the use of iodine solution for the prevention or amelioration of oral mucositis associated with chemotherapy should be further investigated.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.