Preventive intervention possibilities in radiotherapy- and chemotherapy-induced oral mucositis: results of meta-analyses  

CRD summary  
This review assessed the efficacy of interventions for the prevention of head and neck radiotherapy- and/or chemotherapy-induced oral mucositis. The authors concluded that no individual intervention is capable of preventing oral mucositis completely. Given a number of issues with the review methodology and reporting, it is not possible to determine the reliability of this conclusion.

Authors’ objectives  
To evaluate the effectiveness of interventions for the prevention of oral mucositis in cancer patients treated with head and neck radiotherapy and/or chemotherapy.

Searching  
MEDLINE, EMBASE and CINAHL were searched from January 1966 to December 2004; the search terms were reported. In addition, reference lists were checked. Only studies reported in English were eligible for inclusion.

Study selection  
Study designs of evaluations included in the review  
Randomised controlled trials (RCTs) were eligible for inclusion in the review.

Specific interventions included in the review  
Studies of any intervention, the aim of which was to prevent mucositis in patients undergoing head and neck radiation, chemotherapy or chemoradiation, were eligible for inclusion. Eligible studies used a control group treated with placebo, no intervention, or an alternative intervention. The studies included in the review included the following classes of intervention: basic oral care; antiseptic and antimicrobial agents; anti-inflammatory agents; cytokines and/or growth factors; locally applied non-pharmacological methods; mouth-coating agents; radical scavengers; amino acids; antioxidants; antineoplastic agent antagonists; immunomodulatory drugs; and anticholinergic agents. The majority of the included studies used a placebo or a no intervention control group.

Participants included in the review  
Studies of patients undergoing head and neck radiation and/or chemotherapy were eligible for inclusion. No further participant details were provided.

Outcomes assessed in the review  
Studies which reported the outcome of mucositis using the World Health Organization score, the National Cancer Institute-Common Toxicity Criteria (NCI-CTC) score, the presence or absence of ulcerations, or the presence or absence of grade 3 and 4 mucositis were eligible for inclusion. Studies reporting inadequate data on this outcome were excluded from the review.

How were decisions on the relevance of primary studies made?  
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality  
The authors did not state that they assessed validity.

Data extraction  
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. Data on the interventions employed and the outcomes for the treatment groups were extracted. Odds ratios (ORs) were calculated, and studies reporting zero or infinite ORs were excluded.
Methods of synthesis

How were the studies combined?
The authors stated that the studies were combined in meta-analyses using a Mantel-Haenszel fixed-effect model, unless statistically significant heterogeneity was detected, in which case a DerSimonian-Laird random-effects model was used. However, it was not clear whether the results presented were derived from a fixed-effect or random-effects model. Where meta-analysis was not possible, a brief narrative synthesis was provided.

How were differences between studies investigated?
The authors stated that statistical heterogeneity between the studies was examined, but provide neither details of nor results from these analyses. The studies were grouped by the intervention employed and studies with insufficient appropriate data, or a unique intervention, were excluded from meta-analyses.

Results of the review

Sixty-two studies were included in the review, of which 17 included unique interventions. Thus, 45 studies were included in the meta-analyses (n=4,115).

Basic oral care (2 studies).

In both RCTs additional oral care had a positive attenuation effect on the development of mucositis compared with standard care, although due to the limited data in one study no meta-analysis was performed.

Topical antiseptic and antimicrobial agents (16 studies).

Chlorhexidine (7 studies): there was no significant difference between groups treated with chlorhexidine and control groups (OR 0.70, 95% confidence interval, CI: 0.43, 1.12).

Providone-iodine (1 study): Mucositis was significantly decreased in radiotherapy patients treated with providone-iodine mouthrinse than the control group.

Iseganan (3 studies): a meta-analysis of 2 RCTs showed no effect of iseganan in the prevention of ulcerations (OR 0.75, 95% CI:0.55, 1.02); the third study also found no significant benefit of iseganan.

Combination antimicrobials (5 studies): there was a significant benefit for radiotherapy patients of combination antimicrobials in the prevention of ulcerations (OR 0.61, 95% CI: 0.39, 0.96), but no significant impact on the prevention of mucositis.

Anti-inflammatory agents (3 studies).

Benzydamine (1 study): patients treated with benzydamine had a higher incidence of ulcer-free outcomes and lower incidence of ulceration and erythema than controls.

Prostaglandins (1 study): conflicting outcomes were reported for this study.

Corticosteroids (1 study): there were no significant differences between the corticosteroid and control groups.

Cytokines and/or growth factors (13 studies).

Ten studies were included in the meta-analyses.

Systemic intervention (6 studies): there was a significant benefit of cytokines and/or growth factors compared with control in preventing mucositis (OR 0.53, 95% CI: 0.33, 0.87).

Topical intervention (4 studies): there was no significant difference between the groups in the incidence of mucositis (OR 0.32, 95% CI 0.06, 1.67).

Locally applied non-pharmacological methods (5 studies).
Oral cooling (2 studies): chemotherapy patients given oral cooling showed a significantly lower incidence of mucositis than those in the control group (OR 0.3, 95% CI: 0.16, 0.56).

Low-energy helium-neon laser (3 studies): all 3 studies reported significantly reduced severity and duration of oral mucositis in radiotherapy and chemotherapy patients.

Mouth-coating agents (sucralfate) (13 studies).

Nine studies were included in the meta-analysis. There were no significant differences between the groups in occurrence of mucositis and ulcerations (OR 0.82, 95% CI: 0.05, 1.33).

Radical scavengers (amifostine) (9 studies).

Seven studies were included in the meta-analysis. There was a significantly lower incidence of grades 3 and 4 mucositis in patients treated with amifostine than in the control groups (OR 0.37, 95% CI: 0.15, 0.89).

Amino acids (glutamine) (5 studies).

Two studies were included in the meta-analysis. There was no difference between groups of radiotherapy and chemotherapy patients treated with glutamine and control groups in the incidence of mucositis (OR 1.25, 95% CI: 0.61, 2.59).

Antioxidants (3 studies).

Antioxidants such as azelastine hydrochloride, vitamin E and zinc sulphate appear to be interesting interventions for the prevention of mucositis.

Antineoplastic agent antagonists (allopurinol) (1 study).

There were no significant differences in mucositis between the allopurinol and placebo groups.

Immunomodulatory drugs (pentoxifylline) (2 studies).

Neither trial found a significant difference between the pentoxifylline and the control group in the incidence of mucositis in chemotherapy patients.

Anticholinergic agents (1 study).

One crossover trial showed a significant decrease in the development of chemotherapy-induced mucositis with pilocarpine hydrochloride.

Miscellaneous (5 studies).

Traumeel mouthwash (1 study): Traumeel mouthwash significantly reduced the severity and duration of mucositis in chemotherapy patients compared with placebo.

Honey (1 study): a significant reduction in grade 3 and 4 mucositis was found in radiotherapy patients treated with honey compared with the control group.

Calcium phosphate mouthrinse (1 study): patients treated with mouthrinse had a lesser duration and severity of mucositis than those in the control group.

Aloe vera gel (1 study): there were no significant differences between the aloe vera gel and control groups.

Chamomile mouthwash (1 study): there were no significant differences between the chamomile mouthwash and control groups.
Authors' conclusions
No single intervention is capable of preventing oral mucositis completely.

CRD commentary
The review question and the inclusion criteria were clear. The search was adequate, although the restriction to studies reported in English and the fact that the authors did not report searching for unpublished studies might have increased the possibility that some relevant studies were not included in the review. The authors did not report using methods to minimise bias and errors when selecting studies for the review or extracting the data, nor did they report having assessed validity. In addition, details of studies not included in the meta-analyses were not reported. It was therefore difficult to assess the appropriateness of the decision to employ meta-analyses. For these reasons, it is not possible to determine the reliability of the authors' conclusions.

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

Research: The authors stated that future studies should evaluate a combination of interventions for the prevention of oral mucositis. In addition, research is required to develop novel therapies that may be capable of completely preventing oral mucositis.

Funding
Not stated.

Bibliographic details

PubMedID
16861284

Original Paper URL
http://jdr.iadrjournals.org/

Indexing Status
Subject indexing assigned by NLM

MeSH
Amifostine /therapeutic use; Anti-Bacterial Agents /therapeutic use; Antineoplastic Agents /adverse effects; Colony-Stimulating Factors /therapeutic use; Cranial Irradiation /adverse effects; Cryotherapy; Drug Combinations; Head and Neck Neoplasms /drug therapy /radiotherapy; Humans; Mouth Mucosa /drug effects /radiation effects; Mucositis /etiologic factors /prevention & control; Radiation-Protective Agents /therapeutic use; Stomatitis /etiologic factors /prevention & control

AccessionNumber
12006008490

Date bibliographic record published
03/05/2007

Date abstract record published
09/08/2008

Record Status
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.