Mucositis incidence, severity and associated outcomes in patients with head and neck cancer receiving radiotherapy with or without chemotherapy: a systematic literature review


CRD summary
This well-conducted review examined the incidence of mucositis in patients treated with radiotherapy for head and neck cancer. The authors concluded that mucositis occurs frequently and severely, but that its overall impact on treatment outcomes has not been adequately investigated. The authors’ conclusions are appropriate considering the paucity of evidence found for many relevant treatment outcomes.

Authors' objectives
To determine the frequency of mucositis and associated outcomes in patients receiving radiotherapy (RT) for head and neck cancer.

Searching
MEDLINE and Current Contents were searched from January 1996 to December 1999; some search terms were given. In addition, references were reviewed to identify further studies.

Study selection
Study designs of evaluations included in the review
The inclusion criteria were randomised controlled trials (RCTs) with at least 10 patients.

Specific interventions included in the review
The inclusion criteria were RT with or without chemotherapy. Studies of both altered fractionation radiotherapy (AF-RT) and conventional RT were included in the review. Some studies also included surgery as an adjuvant procedure.

Participants included in the review
The inclusion criteria were patients with head and neck cancer. Eighty-one per cent of the participants included in the review were male and 68% of the patients were aged 55 years or older. The patients included in the review had primary tumours at sites such as the oral cavity, oropharynx, larynx, hypopharynx, paranasal tissues and nasopharynx. Tumour stages ranged from I to IV.

Outcomes assessed in the review
The inclusion criteria were: pain; dysphagia; weight loss; interruptions in, or modifications to RT and/or chemotherapy, including delays or reductions in dose; hospitalisation; incidence of feeding tube insertions; use of opioids; quality of life; tumour response; and survival.

How were decisions on the relevance of primary studies made?
Two reviewers screened both abstracts and full papers to select studies for inclusion in the review. It was not stated whether the reviewers performed the selection independently.

Assessment of study quality
The validity of the primary studies was assessed using the Jadad scale, which assesses randomisation, blinding and handling of withdrawals (see Other Publications of Related Interest no.1). Level of evidence was further assessed using the methods of Cook et al. (see Other Publications of Related Interest no.2). The authors did not state how the papers were assessed for validity, or how many reviewers performed the validity assessment.
Data extraction
One reviewer performed the data extraction, which was then checked by another reviewer. Data were extracted on study treatment, patient characteristics and outcomes. Intention-to-treat analyses were extracted where available.

Methods of synthesis
How were the studies combined?
The studies were combined in a narrative.

How were differences between studies investigated?
The studies were grouped by the outcomes reported and intervention(s) used. Other differences were discussed in the text.

Results of the review
Thirty-three studies with 6,181 patients were included in the review.

Three studies (n=405) reported on the incidence of oral pain. Of these, two studies used mixed AF-RT and conventional RT while the other used conventional RT. Sixty-nine per cent of patients experienced oral pain. Twenty-three per cent of patients in these studies experienced grade 3 to 4 mucositis.

Four studies (n=660) reported dysphagia. The incidence of dysphagia was 56%. Three of these studies involved interventions to reduce mucositis. Two of these intervention studies reported significant reductions in dysphagia in the intervention group (polymixin, tobramycin and amphotericin, P=0.006; amifostine, P=0.001), while one (suclral) found no effect.

One study (n=30), using combined RT and chemotherapy, reported on opioid use. Opioids were administered to 53% of patients, and 33% of patients had grade 3 to 4 mucositis.

Ten studies (n not stated) reported a mean weight loss ranging from 3.0 to 6.7 kg (6 to 12% of body weight). Eight studies (n=880) reported the incidence of weight loss; 34% of patients lost weight in these studies. In the 3 studies (n=485) that reported losses of 10% or more of body weight, 17% of the patients lost at least 10% of their body weight.

One study (n not stated) reported quality of life, but without reference to the incidence or severity of mucositis.

Three studies (n=932) reported planned treatment interruptions for grade 3 to 4 mucositis. Two studies compared AF-RT with AF-RT plus chemotherapy, with interrupted treatment planned only for the groups receiving chemotherapy. The rates in one study (n not given) were 75% for AF-RT and 76% for AF-RT plus chemotherapy. In the other study (n not given), the rates were 16% for AF-RT and 38% for AF-RT plus chemotherapy. A third study (n=253) compared AF-RT with conventional RT, with interrupted treatment planned only for the group receiving AF-RT, and found rates of 49% for conventional RT and 65% for AF-RT.

Eighteen studies (n=3,852) reported unplanned interruptions or modifications to treatment. Eleven per cent (n=424) of patients had a deviation from their treatment plan. Five studies (n=1,267) reported unplanned interruptions or modifications to RT due to mucositis. In these studies, 11% of modifications resulted from mucositis (range: 8 to 27%).

Three studies (n=700) reported hospitalisation due to mucositis with an overall incidence of 16%. A higher proportion of those receiving AF-RT (32%) had mucositis than those receiving conventional RT (5%).

Five studies (n=819) reported feeding tube insertion, with a mean frequency of 19%.

Authors' conclusions
Mucositis is a frequent and severe toxicity, which may lead to hospitalisation and interruptions to treatment, in patients treated with RT for cancer of the head and neck. The overall impact of mucositis on treatment outcomes has not been adequately investigated.
CRD commentary
The review question and the inclusion criteria were clear. The search was adequate, although the restriction to studies published in English might have led to the introduction of language and publication biases. No tests for publication bias were conducted. The authors reported using procedures to minimise bias and error in the study selection and data extraction processes, but not when conducting the validity assessment. The method used to assess validity was, however, appropriate. The decision to use a thorough narrative synthesis of the results appears appropriate, although the authors did not provide clear evidence tables to support this synthesis. The authors' conclusions were appropriate in light of the heterogeneous nature of the studies included in the review, and the paucity of evidence found for many outcomes.

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

Research: The authors stated that the CTC toxicity criteria should be adopted as a single 'yardstick' for clinical trials. They stated that oral pain, dysphagia, weight loss, interruptions to treatment, opioid use, hospitalisation, feeding tube use, and mucositis-associated costs should be included as end points in future intervention trials for mucositis secondary to RT for head and neck cancer.

Bibliographic details

PubMedID
12742264

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Adolescent; Adult; Aged; Aged, 80 and over; Antineoplastic Agents /therapeutic use; Combined Modality Therapy; Female; Head and Neck Neoplasms /drug therapy /radiotherapy; Humans; Incidence; Male; Middle Aged; Mouth Mucosa /drug effects /radiation effects; Outcome Assessment (Health Care); Quality of Life; Radiation Injuries /classification /epidemiology /etiology; Randomized Controlled Trials as Topic; Stomatitis /classification /epidemiology /etiology

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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.