Complete Summary

GUIDELINE TITLE

Symptomatic treatment of radiation-induced xerostomia in head and neck cancer patients.

BIBLIOGRAPHIC SOURCE(S)

Head and Neck Cancer Disease Site Group. Hodson DI, Haines T, Berry M. Symptomatic treatment of radiation-induced xerostomia in head and neck cancer patients [full report]. Toronto (ON): Cancer Care Ontario (CCO); 2004 Mar [online update]. 11 p. (Practice guideline report; no. 5-5). [29 references]

GUIDELINE STATUS

This is the current release of the guideline.

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COMPLETE SUMMARY CONTENT

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SCOPE

DISEASE/CONDITION(S)

Radiation-induced xerostomia in head and neck cancer

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Oncology
Otolaryngology
Radiation Oncology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To make recommendations regarding optimum symptomatic management for xerostomic patients following conventionally fractionated radical radiotherapy for head and neck cancer

TARGET POPULATION

Adult head and neck cancer patients with symptomatic xerostomia following radiation therapy

INTERVENTIONS AND PRACTICES CONSIDERED

1. Pilocarpine (tablets or oral solution)
2. Other treatments for radiation-induced xerostomia considered but not recommended: artificial saliva, chewing gum, lozenges, classical acupuncture, Glandosane spray, sodium bicarbonate 1%, xialine, cevimeline, humidification, bethanechol, oral gel, and toothpaste

MAJOR OUTCOMES CONSIDERED

The primary outcome of interest is improvement in patient symptomatology. Toxicity was also considered.

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Original 1998 Guideline

MEDLINE and CANCERLIT searches were performed for the period 1980 to October 1998. Search terms included "radiation", "treatment", "xerostomia", "prevention", "management", "clinical trial", "meta-analysis", and "practice guideline(s)". To locate recent articles that had not yet been indexed in MEDLINE, PREMEDLINE was searched up to October 1998, using the text words "xerostomia" and "radiation." Ongoing trials (actively recruiting or recently closed) were identified from the Physician Data Query (PDQ) database. Articles identified by the search or cited in relevant papers or reviews were retrieved and reviewed.

March 2004 Update

The original literature search has been updated using MEDLINE (through March 2004), EMBASE (through March 2004), the Cochrane Library (Issue 1, 2004), the Physician Data Query database, the Canadian Medical Association Infobase, and the National Guideline Clearinghouse, as well as abstracts published in the proceedings of the meetings of the American Society of Clinical Oncology (1995–2003), the American Society for Therapeutic Radiology and Oncology (2000–2003), and the European Society for Medical Oncology (1998, 2000, 2002). Article bibliographies and personal files were also searched to March 2004 for evidence relevant to this practice guideline report.

Inclusion Criteria

Articles were selected for inclusion in this systematic review of the evidence if they met the following criteria:

1. Randomized controlled trials (RCTs) that measured symptomatic relief of radiation-induced xerostomia in head and neck cancer
2. English language publications

NUMBER OF SOURCE DOCUMENTS

Original 1998 Guideline

Of 65 articles identified by the searches, 11 were deemed appropriate for in-depth review. Five of these were general management overviews. No published guidelines or meta-analyses were found. Five randomized trials (four placebo-controlled trials of oral pilocarpine and one trial comparing artificial saliva with a mouthwash containing pilocarpine) met inclusion criteria. One cohort study was found which addressed some of the Disease Site Group member's concerns about long-term treatment. The four placebo-controlled trials of oral pilocarpine were included in this practice guideline report.

March 2004 Update

An update of the literature identified one systematic review, a paper integrating results of two previously identified trials, ten fully published new randomized trials, and one new trial published as an abstract.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis of Randomized Controlled Trials
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The guideline report was developed by the Cancer Care Ontario Practice Guidelines Initiative (CCOPGI) using the methodology of the Practice Guidelines Development Cycle (see companion document by Browman et al). Evidence was selected and reviewed by two members of the CCOPGI´s Head and Neck Cancer Disease Site Group and methodologists.

Original 1998 Guideline

Synthesizing the evidence: To obtain a more precise overall estimate of the effects of treatment, results were pooled across trials where possible and appropriate using *Metaanalyst*[0.988] software provided by Dr. Joseph Lau (Boston, MA). Pooled results are expressed as risk ratios (RR, the proportion of patients in the treated group reporting improvement over the proportion in the placebo group) with 95% confidence intervals (CI). In this case, risk ratios greater than 1.0 favour the active treatment group. Data were analysed using the more conservative random-effects model. All significance tests are two-sided.

March 2004 Update

The information above remains current.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Original 1998 Guideline

The practice guideline was initially prepared by two members of the Hamilton Regional Cancer Centre Head and Neck Cancer Disease Site Group (DSG). The report was discussed by the Provincial Head and Neck Cancer DSG, and the amended report circulated for critique and comment.

Issues discussed by the Provincial Head and Neck Cancer DSG included the ideal time to start treatment with pilocarpine, the duration of treatment, the duration of

benefit, toxicity, availability and cost, and the target patient population. The DSG members agreed that the ideal time to start treatment with pilocarpine and the duration of treatment remain undefined.

March 2004 Update

The information above remains current.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Original 1998 Guideline

Practitioner feedback was obtained through a mailed survey of 41 practitioners in Ontario (17 radiation oncologists, 7 medical oncologists, 9 surgeons, and 8 otolaryngologists) consisting of nine questions asking for ratings on the quality of draft recommendations and whether the draft recommendations should serve as a practice guideline. Written comments were invited. Follow-up reminders were at two weeks (postcard) and four weeks (complete package mailed again). The Head and Neck Cancer Disease Site Group reviewed the results of the survey. Twenty-four (59%) surveys were returned.

Final approval of the original guideline report was obtained from the Practice Guidelines Coordinating Committee.

March 2004 Update

The guideline authors have reviewed the new evidence from trials of pilocarpine and have concluded that it is consistent with evidence used to inform the original guideline recommendations. No changes to the recommendations are warranted at this time. The remaining randomized trials of novel agents or aids have failed to demonstrate a meaningful difference between treatment and control arms. Again, no changes to the recommendations are warranted at this time.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

- For head and neck cancer patients with symptomatic xerostomia following radiation therapy using conventional fractionation schedules, pilocarpine at 5 mg three times per day is recommended.
- Patients must have evidence of preexisting salivary function and no medical contraindications to pilocarpine therapy.
- The ideal duration of treatment with pilocarpine is undefined. The decision to extend treatment beyond three months can be based only on clinical judgment and not on evidence.
- It is reasonable to use pilocarpine for patients with symptomatic xerostomia following hyperfractionated or accelerated fractionation radiotherapy.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are supported by randomized controlled trials.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Original 1998 Guideline

Pilocarpine at 5 mg to 10 mg orally three times per day produced subjective responses to treatment including improvements in overall xerostomia symptoms (Risk Ratio of improvement [RR], 1.83; 95% confidence interval, 1.34 to 2.49; p = 0.00013), oral dryness (RR, 1.60; 95% confidence interval, 1.17 to 2.19; p = 0.0035), and the need for salivary substitutes (RR, 2.51; 95% confidence interval, 1.51 to 4.15; p = 0.00035).

March 2004 Update

The information above remains current.

POTENTIAL HARMS

1998 Guideline

Adverse events were dose-related. Adverse parasympathetic events were reported by participants in randomized controlled trials, the most frequent and troublesome being increased sweating which occurred in about one-quarter of patients taking 5 mg three times per day and about one-half of patients taking 10 mg. Eighteen percent of patients discontinued treatment because of adverse effects during a 36-month maintenance study. None of the events reported in any of these studies were classified as severe or life threatening.

March 2004 Update

The information above remains current.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Care has been taken in the preparation of the information contained in this document. Nonetheless, any person seeking to apply or consult these guidelines is expected to use independent medical judgment in the context of individual clinical circumstances or seek out the supervision of a qualified clinician. Cancer Care Ontario makes no representation or warranties of any kind whatsoever regarding their content or use or application and disclaims any responsibility for their application or use in any way.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1998 Oct 15 (revised 2004 Mar)

GUIDELINE DEVELOPER(S)

Program in Evidence-based Care - State/Local Government Agency [Non-U.S.]

GUIDELINE DEVELOPER COMMENT

The Practice Guidelines Initiative (PGI) is the main project of the Program in Evidence-based Care (PEBC), a Province of Ontario initiative sponsored by Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care.

SOURCE(S) OF FUNDING

Cancer Care Ontario
Ontario Ministry of Health and Long-Term Care

GUIDELINE COMMITTEE

Provincial Head and Neck Cancer Disease Site Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

For a current list of past and present members, please see the Cancer Care Ontario Web site.

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Members of the Head and Neck Cancer Disease Site Group disclosed potential conflict of interest information.

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GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Symptomatic treatment of radiation-induced xerostomia in head and neck cancer patients. Summary. Toronto (ON): Cancer Care Ontario, 1998 Oct 15 (updated online 2004 Mar). Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.
- Browman GP, Levine MN, Mohide EA, Hayward RS, Pritchard KI, Gafni A, et al. The practice guidelines development cycle: a conceptual tool for practice guidelines development and implementation. J Clin Oncol 1995;13(2):502-12.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on August 19, 1999. The information was verified by the guideline developer as of September 17, 1999. This NGC summary was updated by ECRI on December 17, 2001. The updated information was reviewed by the guideline developer as of January 10, 2002. This NGC summary was updated by ECRI on March 20, 2003. The information was verified by the guideline developer on May 8, 2003. This NGC summary was updated again on June 29, 2004. The information was verified by the guideline developer on July 19, 2004.

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