Pilocarpine for radiation-induced xerostomia in head and neck cancer

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Authors' objectives
To examine the use of pilocarpine hydrochloride for radiation-induced xerostomia in patients with head and neck cancer.

Searching
The following databases were searched for studies published in the English language: MEDLINE from 1966 to 1999; CINAHL from 1982 to 1999; and Cancerlit from 1982 to 1999. The reference lists from the identified studies were also searched manually. Abstracts and review articles were not considered, and the authors of the included studies were not contacted for additional information.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) with more than 10 patients were eligible for inclusion.

Specific interventions included in the review
Systemic or topical pilocarpine. Topical pilocarpine was used as a mouthwash. Systemic pilocarpine was used in doses ranging from 2.5 to 10 mg, three times a day.

Participants included in the review
Head and neck cancer patients with post-radiation xerostomia of at least 2 months' duration. Studies using pilocarpine for xerostomia in patients with advanced cancer and other medical conditions, not necessarily radiation-induced xerostomia, were excluded. Where given, the participants' ages ranged from 16 to 82 years.

Outcomes assessed in the review
The authors did not define any a priori inclusion or exclusion criteria relating to the outcomes. The outcome measures used in the included studies were both objective and subjective. The objective evaluations were of parotid and whole saliva flows. The subjective outcomes included feelings of oral dryness, oral comfort, speaking and chewing; these were assessed by patients' diaries, questionnaires, and visual analogue scores.

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

Assessment of study quality
Studies were scored for methodological quality on a range from 0 to 5, using a modified 3-item scale taken from Jadad et al. (see Other Publications of Related Interest). The authors do not state how the papers were assessed for quality, or how many of the reviewers performed the quality assessment.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.

Data were extracted for the following categories: author, year, sample frame, sample size, age range, study design, outcome measures, and results.
Methods of synthesis
How were the studies combined?
A qualitative narrative synthesis was undertaken. Publication bias was not assessed.

How were differences between studies investigated?
Differences between the studies were investigated within the text of the review.

Results of the review
Four RCTs involving 401 participants were included. Two of these RCTs employed a crossover design (32 participants).

Quality assessment.
The quality score was 3 for two of the studies, and 5 for the other two studies. Methodological limitations of the studies included small sample sizes, non-probability sampling and sparse quantitative data.

All studies reported statistically-significant differences in favour of pilocarpine-stimulated treatment groups. The patients reported improvements in a number of areas, e.g. oral dryness, oral comfort, chewing, and the ability to speak without requiring liquids. There was an apparent time-dependent drug-related benefit noted in two studies, with patients reporting increased improvements after several weeks of pilocarpine treatment.

All studies reported adverse side-effects from pilocarpine, but none were severe. Sixteen per cent of the patients withdrew from the studies. Sweating and urinary frequency were the most common side-effects noted, but headache, rhinitis and abdominal cramping were also reported. In two studies, doses over 5 mg appeared to produce increased side-effects.

When considering both the side-effects and the efficacy of pilocarpine, all studies advocated 5 mg three times a day to be the optimum dose. The data supplied were insufficient to draw any conclusions as to the efficacy of systemic pilocarpine over topical usage.

Publication bias was not assessed, but the authors noted that there was an inherent potential for publication bias.

Authors' conclusions
The persistent findings of symptomatic improvement following pilocarpine use merit consideration. However, there is insufficient evidence from these studies alone to generalise results to the wider population.

CRD commentary
The review question was clearly stated and was well supported by the inclusion and exclusion criteria. The literature search was adequate, although it was restricted to published studies and English language papers only. Relevant studies may therefore have been omitted and, as the authors acknowledged, publication bias may be present. In addition, the search terms were not given.

The quality of the included studies was assessed appropriately. Details of the studies were provided in both the text and in a table; however, information concerning the comparator used was not given for all of the studies. The data were synthesised narratively in the text of the review, but publication bias was not assessed. Details of the review process were lacking: no information was provided on how the primary studies were selected, how quality was judged, or how the data were extracted.

The authors’ conclusions appear to follow from the results, but should be treated with caution given the limitations highlighted.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice. Research: The authors state that further research is required to determine the efficacy of systemic pilocarpine over topical application, or vice versa. Clarification is also needed regarding any time-related drug-benefit relationship. Larger studies conducted over a longer period of time could help determine the nature of any time-related drug benefit relationship.

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**Other publications of related interest**

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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.