Associazione Italiana
Radioterapia Oncologica
Gruppo Interregionale
Lazio/Abruzzo/Molise

Le terapie di supporto in Radioterapia:

Verso una Guida Pratica

Lunedì 4 Dicembre 2017
Centro Studi Cardello
Via del Cardello 24 – Roma

Tossicità nei trattamenti del distretto Testa-Collo

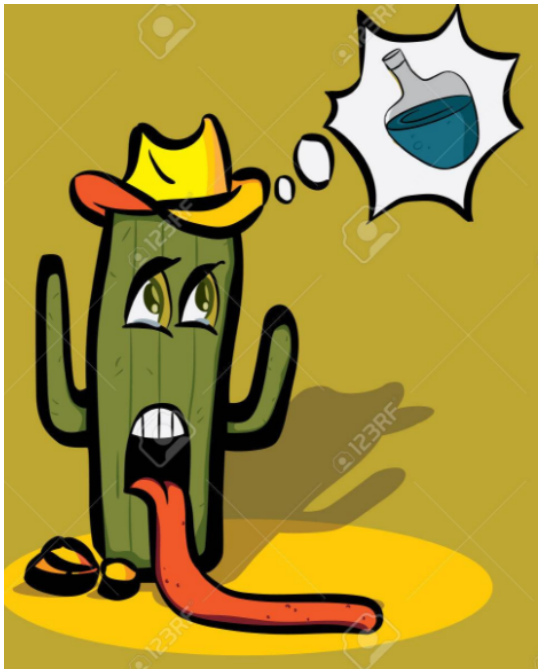
Xerostomia

Presidi di prevenzione e trattamento delle tossicità

F. Miccichè

ESTRO Institutional member 2017

Gemelli ART Advanced Radiation Therapy



- **Cause**
- **Stato dell'Arte**
- **Presidi di prevenzione**
  - ***Dose dipendente***
  - ***Farmaco-dipendente***
- **Presidi di terapia**
  - ***Farmaco-dipendente***

Fattori predisponenti

Fattori RT correlati

Dose per frazione
Dose Totale
Volume irradiato
Organi a rischio prossimi al Target

Comorbidità

Patologie/insufficienze d'organo
Malattie metaboliche
Malattie vascolari

Associazione con Farmaci

Chemioterapia concomitante
Radiosensibilizzanti
Target Therapies

Manuale di Cure di Supporto in Oncologia, 1° Ediz. 2015 SEU

Xerostomia-Stato dell'arte

Xerostomia [4]

Prevenzione e cura delle complicanze

- Igiene del cavo orale (spazzolino, filo interdentale, sciacqui con fluoruri topici).
- Prevenzione della demineralizzazione dei denti (gel e dentifricio).
- Terapia delle infezioni della cavità orale e delle ghiandole salivari.
- Amifostina somministrata durante la radioterapia può ridurre il rischio di xerostomia, tuttavia per i suoi effetti collaterali il suo impiego non può essere considerato routinario.

Terapia medica

- Se residua funzione secretoria salivare→ stimolazione:
  - prodotti senza zucchero (chewing gum, compresse) contenenti acido ascorbico, acido citrico, acido malico;
  - pilocarpina (agonista muscarinico): 5-10 mg x 3/die.
- Se residua funzione secretoria insufficiente→ sostituti salivari:
  - Soluzioni ioniche acquose,composti a base di mucina, composti a base di metilcellulosa, gel contenenti enzimi, prodotti contenenti glicoproteine).

Manuale di Cure di Supporto in Oncologia, 1° Ediz. 2015 SEU

Presidi di Prevenzione -Dose dipendente-

Parotid-sparing intensity modulated versus conventional radiotherapy in head and neck cancer (PARSPORT): a phase 3 multicentre randomised controlled trial

*Christopher M Nutting, James P Morden, Kevin J Harrington, Teresa Guerrero Urbano, Shreerang A Bhide, Catharine Clark, Elizabeth A Miles, Aisha B Miah, Kate Newbold, MaryAnne Tanay, Fawzi Adab, Sarah J Jefferies, Christopher Scrase, Beng K Yap, Roger P A'Hern, Mark A Sydenham, Marie Emson, Emma Hall, on behalf of the PARSPORT trial management group**

Summary

Background Xerostomia is the most common late side-effect of radiotherapy to the head and neck. Compared with conventional radiotherapy, intensity-modulated radiotherapy (IMRT) can reduce irradiation of the parotid glands. We assessed the hypothesis that parotid-sparing IMRT reduces the incidence of severe xerostomia.

Methods We undertook a randomised controlled trial between Jan 21, 2003, and Dec 7, 2007, that compared conventional radiotherapy (control) with parotid-sparing IMRT. We randomly assigned patients with histologically confirmed pharyngeal squamous-cell carcinoma (T1–4, N0–3, M0) at six UK radiotherapy centres between the two radiotherapy techniques (1:1 ratio). A dose of 60 or 65 Gy was prescribed in 30 daily fractions given Monday to Friday. Treatment was not masked. Randomisation was by computer-generated permuted blocks and was stratified by centre and tumour site. Our primary endpoint was the proportion of patients with grade 2 or worse xerostomia at 12 months, as assessed by the Late Effects of Normal Tissue (LENT SOMA) scale. Analyses were done on an intention-to-treat basis, with all patients who had assessments included. Long-term follow-up of patients is ongoing. This study is registered with the International Standard Randomised Controlled Trial register, number ISRCTN48243537.

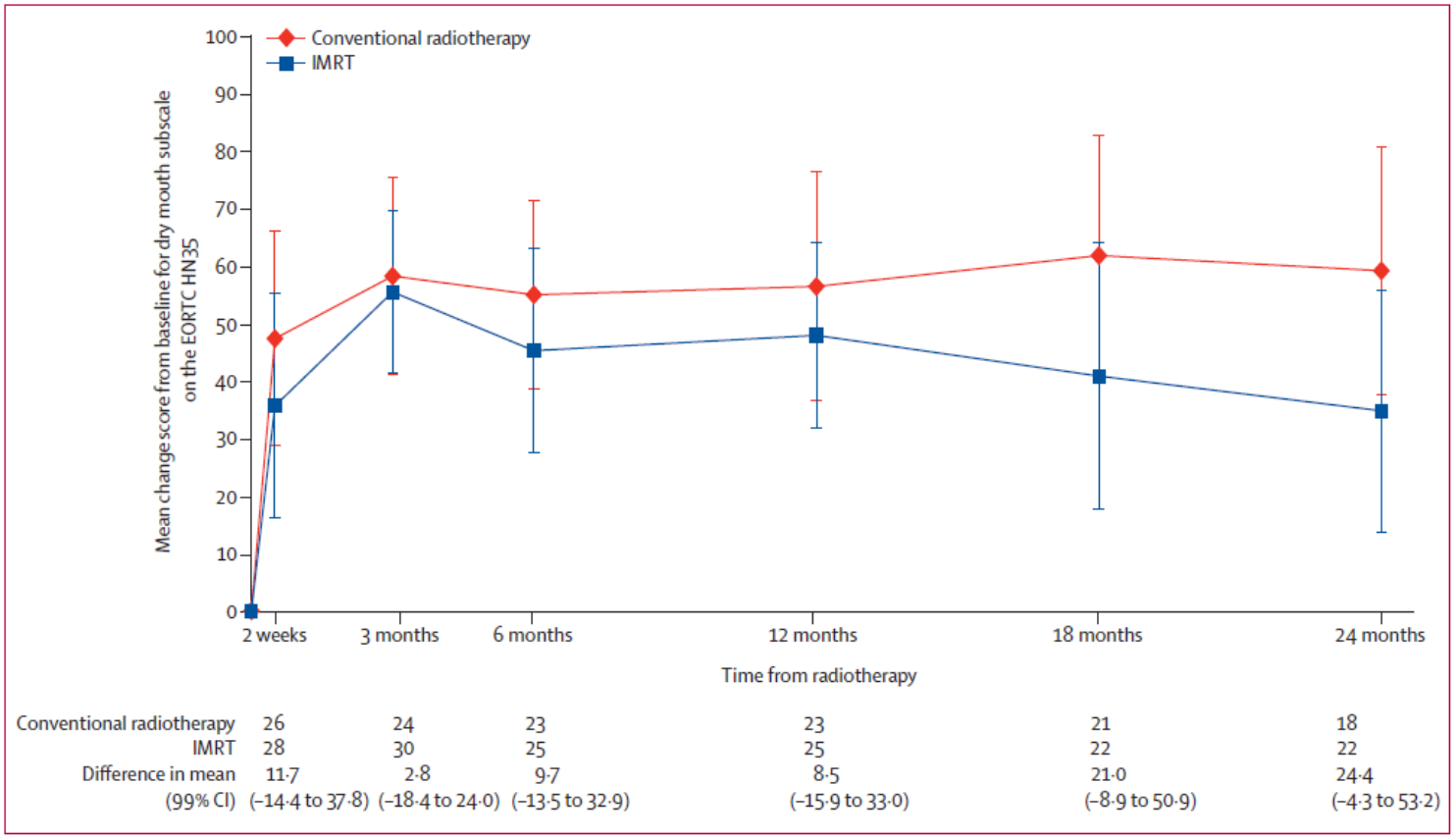
Findings 47 patients were assigned to each treatment arm. Median follow-up was 44·0 months (IQR 30·0–59·7). Six patients from each group died before 12 months and seven patients from the conventional radiotherapy and two from the IMRT group were not assessed at 12 months. At 12 months xerostomia side-effects were reported in 73 of 82 alive patients; grade 2 or worse xerostomia at 12 months was significantly lower in the IMRT group than in the conventional radiotherapy group (25 [74%; 95% CI 56–87] of 34 patients given conventional radiotherapy *vs* 15 [38%; 23–55] of 39 given IMRT, p=0·0027). The only recorded acute adverse event of grade 2 or worse that differed significantly between the treatment groups was fatigue, which was more prevalent in the IMRT group (18 [41%; 99% CI 23–61] of 44 patients given conventional radiotherapy *vs* 35 [74%; 55–89] of 47 given IMRT, p=0·0015). At 24 months, grade 2 or worse xerostomia was significantly less common with IMRT than with conventional radiotherapy (20 [83%; 95% CI 63–95] of 24 patients given conventional radiotherapy *vs* nine [29%; 14–48] of 31 given IMRT; p<0·0001). At 12 and 24 months, significant benefits were seen in recovery of saliva secretion with IMRT compared with conventional radiotherapy, as were clinically significant improvements in dry-mouth-specific and global quality of life scores. At 24 months, no significant differences were seen between randomised groups in non-xerostomia late toxicities, locoregional control, or overall survival.

Interpretation Sparing the parotid glands with IMRT significantly reduces the incidence of xerostomia and leads to recovery of saliva secretion and improvements in associated quality of life, and thus strongly supports a role for IMRT in squamous-cell carcinoma of the head and neck.

- 6 centri UK
- 94 pts: 47 CRT vs 47 parotid sparing IMRT
- FUP mediano 44 mesi
- *Xerostomia ≥ G2* a 12 mesi SOMA LENT
  - 38% vs 75%a 12 mesi, p= 0.0027 a 12 m.
  - 29% vs 83%a 24 mesi, p< 0.0001 a 24 m.

Nutting CM et Al, 2011 The Lancet Oncology

Presidi di Prevenzione -Dose dipendente-



Conventional radiotherapy	26	24	23	23	21	18
IMRT	28	30	25	25	22	22
Difference in mean (99% CI)	11·7 (−14·4 to 37·8)	2·8 (−18·4 to 24·0)	9·7 (−13·5 to 32·9)	8·5 (−15·9 to 33·0)	21·0 (−8·9 to 50·9)	24·4 (−4·3 to 53·2)

Figure 3: **Mean EORTC HN35 dry mouth subscale score changes from baseline**
IMRT=intensity-modulated radiotherapy. EORTC HN35=European Organization for Research and Treatment of Cancer head and neck specific module HN35.

Nutting CM et Al, 2011 The Lancet Oncology

Presidi di Prevenzione -Dose dipendente-

HEAD & NECK
JOURNAL OF THE SCIENCES AND SPECIALTIES OF THE HEAD AND NECK

ORIGINAL ARTICLE

FUNCTIONAL OUTCOMES RELATED TO THE PREVENTION OF RADIATION-INDUCED XEROSTOMIA: ORAL PILOCARPINE VERSUS SUBMANDIBULAR SALIVARY GLAND TRANSFER

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Accepted 22 October 2010
Published online 17 March 2011 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/hed.21682

Rieger JM et Al, 2012 Head Neck

Presidi di Prevenzione
-Dose dipendente-

BACKGROUND: Xerostomia has a devastating impact on oral function and quality of life in patients who receive radiation treatment for head and neck cancer. The purpose of this study was to examine functional outcomes related to 2 saliva-sparing treatments: (1) oral pilocarpine during radiotherapy; or (2) the submandibular salivary gland transfer (SGT) before radiotherapy.

METHODS: Sixty-nine patients were recruited (SGT = 36; pilocarpine = 33). Speech intelligibility, swallowing outcomes, and quality of life were assessed at 4 points in time (pretreatment, and 1 month, 6 months, and 12 months after the pretreatment assessment).

RESULTS: There were no differences between groups in speech outcomes; however, significant between-group differences existed in swallowing and quality of life outcomes. In all cases, patients who received the SGT procedure had better swallowing outcomes and quality of life scores than the patients who received oral pilocarpine.

CONCLUSION: The SGT should be the treatment of choice between the 2 treatments offered to prevent xerostomia in the present study.

Rieger JM et Al, 2012 Head Neck

Livello Raccomandazione Prevenzione Xerostomia

TABELLA II – Grado delle raccomandazioni SIGN e descrittori
A. Almeno una meta-analisi o revisione sistematica o RCT valutato 1++ e i cui risultati sono direttamente applicabili alla popolazione target. Il corpo delle evidenze disponibili consiste principalmente in studi valutati 1+, direttamente applicabili alla popolazione target. I risultati dei vari studi dovrebbero essere coerenti sia per direzione sia per dimensione dell'effetto del trattamento.
B. Il corpo delle evidenze include studi valutati 2++ con risultati applicabili direttamente alla popolazione target e con risultati coerenti sia per direzione sia per dimensione dell'effetto. Evidenze estrapolate da studi valutati 1++ o 1+.
C. Il corpo delle evidenze include studi valutati 2+ con risultati applicabili direttamente alla popolazione target e con risultati coerenti per direzione e dimensione dell'effetto. Evidenze estrapolate da studi valutati 2++.
D. Evidenze di livello 3 o 4. Evidenze estrapolate da studi valutati 2+.

Forza Raccomandazione Prevenzione Xerostomia

Forza della raccomandazione	Descrizione	Esempio esplicativo
Positiva forte	La maggior parte dei pazienti con le caratteristiche descritte devono essere invitati a considerare l'intervento in oggetto; il bilancio tra beneficio e danno è nettamente a favore del beneficio	Nei pazienti X con le caratteristiche Y, il trattamento Z deve essere somministrato
Positiva debole	pazienti con le caratteristiche descritte devono essere informati sull'esistenza di un trattamento che potrebbe avere degli effetti positivi, tuttavia il bilancio tra beneficio e danno del trattamento è carico di incertezza. Il medico deve tenere conto dei valori e delle preferenze del paziente	Nei pazienti X con le caratteristiche Y, il trattamento Z dovrebbe essere somministrato
Negativa debole	A fronte di una piccola probabilità di beneficio dovuto al trattamento, il bilancio beneficio/ danno tende a dimostrare più eventi dannosi e le evidenze sono cariche di incertezza. Il medico deve tenere conto dei valori e delle preferenze del paziente	Nei pazienti X con le caratteristiche Y, il trattamento Z non dovrebbe essere somministrato
Negativa forte	I pazienti non devono essere sottoposti all'intervento in oggetto perché il bilancio beneficio/ danno è a favore del danno con un buon margine di certezza	Nei pazienti X con le caratteristiche Y, il trattamento Z non deve essere somministrato

Presidi di Prevenzione -Farmaco dipendente-

Effect of Amifostine in Head and Neck Cancer Patients Treated with Radiotherapy: A Systematic Review and Meta-Analysis Based on Randomized Controlled Trials

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Abstract

Background: Amifostine is the most clinical used chemical radioprotector, but its effect in patients treated with radiation is not consistent.

Methods: By searching Medline, CENTRAL, EMBASE, ASCO, ESMO, and CNKI databases, the published randomized controlled trials (RCTs) about the efficacy of amifostine in HNSCC patients treated with radiotherapy were collected. The pooled efficacy and side effects of this drug were calculated by RevMan software.

Results: Seventeen trials including a total of 1167 patients (604 and 563 each arm) were analyzed in the meta-analysis. The pooled data showed that the use of amifostine significantly reduce the risk of developing Grade3–4 mucositis (relative risk [RR],0.72; 95% confidence interval [CI],0.54–0.95; $p<0.00001$), Grade 2–4 acute xerostomia (RR,0.70; 95%CI,0.52–0.96; $p=0.02$), or late xerostomia (RR,0.60; 95%CI,0.49–0.74; $p<0.00001$) and Grade 3–4 dysphagia (RR,0.39; 95%CI,0.17–0.92; $p=0.03$). However, subgroup analysis demonstrated that no statistically significant reduction of Grade3–4 mucositis (RR,0.97; 95% CI,0.74–1.26; $p=0.80$), Grade 2–4 acute xerostomia (RR,0.35; 95%CI,0.02–5.44; $p=0.45$), or late xerostomia (RR,0.40; 95%CI,0.13–1.24; $p=0.11$) and Grade 3–4 dysphagia (RR,0.23; 95%CI,0.01–4.78; $p=0.35$) was observed in patients treated with concomitant chemoradiotherapy. Compared with placebo or observation, amifostine does not show tumor protective effect in complete response (RR,1.02; 95%CI,0.89–1.17; $p=0.76$) and partial response (RR,0.90; 95%CI, 0.56–1.44; $p=0.66$). For the hematologic side effect, no statistical difference of Grade 3–4 leucopenia (RR,0.60; 95%CI,0.35–1.05; $p=0.07$), anemia (RR,0.80; 95%CI, 0.42–1.53; $p=0.50$) and thrombocytopenia (RR,0.43; 95%CI,0.16–1.15; $p=0.09$) were found between amifostine and control groups. The most common amifostine related side effects were nausea, emesis, hypotension and allergic with an average incidence rate (Grade 3–4) of 5%, 6%, 4% and 4% respectively.

Conclusion: This systematic review showed that amifostine significantly reduce the serious mucositis, acute/late xerastomia and dysphagia without protection of the tumor in HNSCC patients treated with radiotherapy. And the toxicities of amifostine were generally acceptable.

Gu J et Al, Plos One 2014

Presidi di Prevenzione -Farmaco dipendente-

17 Trials
1167 pts

Table 2. Subgroup analysis of radiation induced side effects according to treatment strategy.

Subgroups	Mucositis		p	Acute xerostomia		p	Late xerostomia		p	Dysphagia		p
	RR	95%CI		RR	95%CI		RR	95%CI		RR	95%CI	
Treatment												
Chemradiation	0.97	0.74–1.26	0.80	0.35	0.02–5.44	0.45	0.40	0.13–1.24	0.11	0.23	0.01–4.78	0.35
Radiation only	0.49	0.30–0.78	0.03	0.69	0.52–0.93	0.02	0.64	0.45–0.91	0.01	0.32	0.17–0.61	0.0004
Administration												
IV	0.52	0.34–0.78	0.002	0,73	0.54–0.97	0.03	0.60	0.49–0.74	0.00001	0.39	0.17–0.92	0.03
IH	1.09	0.94–1.27	0.24	0.08	0–1.34	0.08						

doi:10.1371/journal.pone.0095968.t002

Gu J et Al, Plos One 2014

Presidi di Trattamento

Int J Radiat Oncol Biol Phys. 2016 Mar 1;94(3):503-11. doi: 10.1016/j.ijrobp.2015.11.012. Epub 2015 Nov 10.

Is Pilocarpine Effective in Preventing Radiation-Induced Xerostomia? A Systematic Review and Meta-analysis.

Yang WF[1], Liao GQ[1], Hakim SG[2], Ouyang DQ[1], Ringash J[3], Su YX[4].

Author information

Abstract

PURPOSE: To evaluate the efficacy of concomitant administration of pilocarpine on radiation-induced xerostomia in patients with head and neck cancers.

METHODS AND MATERIALS: The PubMed, Web of Science, Cochrane Library, and ClinicalTrials were searched to identify randomized, controlled trials studying the effect of concomitant administration of pilocarpine for radiation-induced xerostomia. Included trials were systematically reviewed, and quantifiable outcomes were pooled for meta-analysis. Outcomes of interest included salivary flow, clinician-rated xerostomia grade, patient-reported xerostomia scoring, quality of life, and adverse effects.

RESULTS: Six prospective, randomized, controlled trials in 8 articles were included in this systematic review. The total number of patients was 369 in the pilocarpine group and 367 in the control group. Concomitant administration of pilocarpine during radiation could increase the unstimulated salivary flow rate in a period of 3 to 6 months after treatment, and also reduce the clinician-rated xerostomia grade. Patient-reported xerostomia was not significantly impacted by pilocarpine in the initial 3 months but was superior at 6 months. No significant difference of stimulated salivary flow rate could be confirmed between the 2 arms. Adverse effects of pilocarpine were mild and tolerable.

CONCLUSIONS: The concomitant administration of pilocarpine during radiation increases unstimulated salivary flow rate and reduces clinician-rated xerostomia grade after radiation. It also relieves patients' xerostomia at 6 months and possibly at 12 months. However, pilocarpine has no effect on stimulated salivary flow rate.

PMID: 26867879 DOI: 10.1016/j.ijrobp.2015.11.012

Yang WF et Al, IJROBP 2016

Presidi di Trattamento

Oral Oncol. 2017 Mar;66:64-74. doi: 10.1016/j.oraloncology.2016.12.031. Epub 2017 Jan 19.

Interventions for the management of radiotherapy-induced xerostomia and hyposalivation: A systematic review and meta-analysis.

Mercadante V[1], Al Hamad A[2], Lodi G[3], Porter S[4], Fedele S[5].

Author information

Abstract

INTRODUCTION: Salivary gland hypofunction is a common and permanent adverse effect of radiotherapy to the head and neck. Randomised trials of available treatment modalities have produced unclear results and offer little reliable guidance for clinicians to inform evidence-based therapy. We have undertaken this systematic review and meta-analysis to estimate the effectiveness of available interventions for radiotherapy-induced xerostomia and hyposalivation.

METHODS: We searched MEDLINE, Cochrane Central, EMBASE, AMED, and CINAHL database through July 2016 for randomised controlled trials comparing any topical or systemic intervention to active and/or non-active controls for the treatment of radiotherapy-induced xerostomia. The results of clinically and statistically homogenous studies were pooled and meta-analyzed.

RESULTS: 1732 patients from twenty studies were included in the systematic review. Interventions included systemic or topical pilocarpine, systemic cevimeline, saliva substitutes/mouthcare systems, hyperthermic humidification, acupuncture, acupuncture-like transcutaneous electrical nerve stimulation, low-level laser therapy and herbal medicine. Results from the meta-analysis, which included six studies, suggest that both cevimeline and pilocarpine can reduce xerostomia symptoms and increase salivary flow compared to placebo, although some aspects of the relevant effect size, duration of the benefit, and clinical meaningfulness remain unclear. With regard to interventions not included in the meta-analysis, we found no evidence, or very weak evidence, that they can reduce xerostomia symptoms or increase salivary flow in this population.

CONCLUSIONS: Pilocarpine and cevimeline should represent the first line of therapy in head and neck cancer survivors with radiotherapy-induced xerostomia and hyposalivation. The use of other treatment modalities cannot be supported on the basis of current evidence.

Mercadante V et Al. Oral Oncol 2017

39 controlled trials
3520 pts

Cochrane Database Syst Rev. 2017 Jul 31;7:CD012744. doi: 10.1002/14651858.CD012744.

Pharmacological interventions for preventing dry mouth and salivary gland dysfunction following radiotherapy.

Riley P[1], Glenny AM, Hua F, Worthington HV.

Author information

Abstract

BACKGROUND: Salivary gland dysfunction is an 'umbrella' term for the presence of either xerostomia (subjective sensation of dryness), or salivary gland hypofunction (reduction in saliva production). It is a predictable side effect of radiotherapy to the head and neck region, and is associated with a significant impairment of quality of life. A wide range of pharmacological interventions, with varying mechanisms of action, have been used for the prevention of radiation-induced salivary gland dysfunction.

OBJECTIVES: To assess the effects of pharmacological interventions for the prevention of radiation-induced salivary gland dysfunction.

SEARCH METHODS: Cochrane Oral Health's Information Specialist searched the following databases: Cochrane Oral Health's Trials Register (to 14 September 2016); the Cochrane Central Register of Controlled Trials (CENTRAL; 2016, Issue 8) in the Cochrane Library (searched 14 September 2016); MEDLINE Ovid (1946 to 14 September 2016); Embase Ovid (1980 to 14 September 2016); CINAHL EBSCO (Cumulative Index to Nursing and Allied Health Literature; 1937 to 14 September 2016); LILACS BIREME Virtual Health Library (Latin American and Caribbean Health Science Information database; 1982 to 14 September 2016); Zetoc Conference Proceedings (1993 to 14 September 2016); and OpenGrey (1997 to 14 September 2016). We searched the US National Institutes of Health Ongoing Trials Register (ClinicalTrials.gov) and the World Health Organization International Clinical Trials Registry Platform for ongoing trials. No restrictions were placed on the language or date of publication when searching the electronic databases.

SELECTION CRITERIA: We included randomised controlled trials, irrespective of their language of publication or publication status. Trials included participants of all ages, ethnic origin and gender, scheduled to receive radiotherapy on its own or in addition to chemotherapy to the head and neck region. Participants could be outpatients or inpatients. We included trials comparing any pharmacological agent regimen, prescribed prophylactically for salivary gland dysfunction prior to or during radiotherapy, with placebo, no intervention or an alternative pharmacological intervention. Comparisons of radiation techniques were excluded.

DATA COLLECTION AND ANALYSIS: We used standard methodological procedures expected by Cochrane.

MAIN RESULTS: We included 39 studies that randomised 3520 participants, the number of participants analysed varied by outcome and time point. The studies were ordered into 14 separate comparisons with meta-analysis only being possible in three of those.We found low-quality evidence to show that amifostine, when compared to a placebo or no treatment control, might reduce the risk of moderate to severe xerostomia (grade 2 or higher on a 0 to 4 scale) at the end of radiotherapy (risk ratio (RR) 0.35, 95% confidence interval (CI) 0.19 to 0.67; P = 0.001, 3 studies, 119 participants), and up to three months after radiotherapy (RR 0.66, 95% CI 0.48 to 0.92; P = 0.01, 5 studies, 687 participants), but there is insufficient evidence that the effect is sustained up to 12 months after radiotherapy (RR 0.70, 95% CI 0.40 to 1.23; P = 0.21, 7 studies, 682 participants). We found very low-quality evidence that amifostine increased unstimulated salivary flow rate up to 12 months after radiotherapy, both in terms of mg of saliva per 5 minutes (mean difference (MD) 0.32, 95% CI 0.09 to 0.55; P = 0.006, 1 study, 27 participants), and incidence of producing greater than 0.1 g of saliva over 5 minutes (RR 1.45, 95% CI 1.13 to 1.86; P = 0.004, 1 study, 175 participants). However, there was insufficient evidence to show a difference when looking at stimulated salivary flow rates. There was quality evidence that amifostine is associated with increases in: vomiting (RR 4.90, 95% CI 2.87 to 8.38; P < 0.00001, 5 studies, 601 participants); hypotension (RR 9.20, 95% CI 2.84 to 29.83; P = 0.0002, 3 studies, 376 participants); nausea (RR 2.60, 95% CI 1.81 to 3.74; P < 0.00001, 4 studies, 556 participants); and allergic response (RR 7.51, 95% CI 1.40 to 40.39; P = 0.02, 3 studies, 524 participants).We found insufficient evidence (that was of very low quality) to determine whether or not pilocarpine performed better or worse than a placebo or no treatment control for the outcomes: xerostomia, salivary flow rate, survival, and quality of life. There was some low-quality evidence that pilocarpine was associated with an increase in sweating (RR 2.98, 95% CI 1.43 to 6.22; P = 0.004, 5 studies, 389 participants).We found insufficient evidence to determine whether or not palifermin performed better or worse than placebo for: xerostomia (low quality); survival (moderate quality); and any adverse effects.There was also insufficient evidence to determine the effects of the following interventions: biperiden plus pilocarpine, Chinese medicines, bethanechol, artificial saliva, selenium, antiseptic mouthrinse, antimicrobial lozenge, polaprezinc, azulene rinse, and Venalot Depot (coumarin plus troxerutin).

AUTHORS' CONCLUSIONS: There is some low-quality evidence to suggest that amifostine prevents the feeling of dry mouth in people receiving radiotherapy to the head and neck (with or without chemotherapy) in the short- (end of radiotherapy) to medium-term (three months postradiotherapy). However, it is less clear whether or not this effect is sustained to 12 months postradiotherapy. The benefits of amifostine should be weighed against its high cost and side effects. There was insufficient evidence to show that any other intervention is beneficial.

Livello Raccomandazione Trattamento Xerostomia

TABELLA II – Grado delle raccomandazioni SIGN e descrittori
A. Almeno una meta-analisi o revisione sistematica o RCT valutato 1++ e i cui risultati sono direttamente applicabili alla popolazione target. Il corpo delle evidenze disponibili consiste principalmente in studi valutati 1+, direttamente applicabili alla popolazione target. I risultati dei vari studi dovrebbero essere coerenti sia per direzione sia per dimensione dell'effetto del trattamento.
B. Il corpo delle evidenze include studi valutati 2++ con risultati applicabili direttamente alla popolazione target e con risultati coerenti sia per direzione sia per dimensione dell'effetto. Evidenze estrapolate da studi valutati 1++ o 1+.
C. Il corpo delle evidenze include studi valutati 2+ con risultati applicabili direttamente alla popolazione target e con risultati coerenti per direzione e dimensione dell'effetto. Evidenze estrapolate da studi valutati 2++.
D. Evidenze di livello 3 o 4. Evidenze estrapolate da studi valutati 2+.

Forza Raccomandazione Trattamento Xerostomia

Forza della raccomandazione	Descrizione	Esempio esplicativo
Positiva forte	La maggior parte dei pazienti con le caratteristiche descritte devono essere invitati a considerare l'intervento in oggetto; il bilancio tra beneficio e danno è nettamente a favore del beneficio	Nei pazienti X con le caratteristiche Y, il trattamento Z deve essere somministrato
Positiva debole	pazienti con le caratteristiche descritte devono essere informati sull'esistenza di un trattamento che potrebbe avere degli effetti positivi, tuttavia il bilancio tra beneficio e danno del trattamento è carico di incertezza. Il medico deve tenere conto dei valori e delle preferenze del paziente	Nei pazienti X con le caratteristiche Y, il trattamento Z dovrebbe essere somministrato
Negativa debole	A fronte di una piccola probabilità di beneficio dovuto al trattamento, il bilancio beneficio/ danno tende a dimostrare più eventi dannosi e le evidenze sono cariche di incertezza. Il medico deve tenere conto dei valori e delle preferenze del paziente	Nei pazienti X con le caratteristiche Y, il trattamento Z non dovrebbe essere somministrato
Negativa forte	I pazienti non devono essere sottoposti all'intervento in oggetto perché il bilancio beneficio/ danno è a favore del danno con un buon margine di certezza	Nei pazienti X con le caratteristiche Y, il trattamento Z non deve essere somministrato


Grazie