

ORAL CARE STUDY GROUP

ISOO/MASCC/ASCO Guideline:

Salivary Gland Hypofunction and/or Xerostomia Induced by Nonsurgical Cancer Therapies

Citation:

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Abstract:

Purpose: To provide evidence-based recommendations for prevention and management of salivary gland hypofunction and xerostomia induced by nonsurgical cancer therapies.

Methods: Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO) and ASCO convened a multidisciplinary Expert Panel to evaluate the evidence and formulate recommendations. PubMed, EMBASE, and Cochrane Library were searched for randomized controlled trials published between January 2009 and June 2020. The guideline also incorporated two previous systematic reviews conducted by MASCC/ISOO, which included studies published from 1990 through 2008.

Results: A total of 58 publications were identified: 46 addressed preventive interventions and 12 addressed therapeutic interventions. A majority of the evidence focused on the setting of radiation therapy for head and neck cancer. For the prevention of salivary gland hypofunction and/or xerostomia in patients with head and neck cancer, there is high-quality evidence for tissue-sparing radiation modalities. Evidence is weaker or insufficient for other interventions. For the management of salivary gland hypofunction and/or xerostomia, intermediate quality evidence supports the use of topical mucosal lubricants, saliva substitutes, and agents that stimulate the salivary reflex.

Guideline Question

What are the most effective interventions to prevent, minimize, and manage salivary gland hypofunction and xerostomia in the oncology patient receiving nonsurgical cancer therapy?

Clinical question 1.

What is the efficacy of available pharmacologic and nonpharmacologic interventions (including the effects of radiation dose, type, and regimen) for the prevention of salivary gland hypofunction and/or xerostomia induced by nonsurgical cancer therapies?

Recommendation 1.1.

Intensity-modulated radiation therapy should be used to spare major and minor salivary glands from a higher dose of radiation to reduce the risk of salivary gland hypofunction and xerostomia in patients with head and neck cancer

type: evidence-based; evidence quality: high; strength of recommendation: strong

Recommendation 1.2.

Other radiation modalities that limit cumulative dose to and irradiated volume of major and minor salivary glands as or more effectively than intensity-modulated radiation therapy may be offered to reduce salivary gland hypofunction and xerostomia

type: informal consensus; evidence quality: low; strength of recommendation: strong

Recommendation 1.3.

Acupuncture may be offered during radiation therapy for head and neck cancer to reduce the risk of developing xerostomia

type: evidence-based; evidence quality: intermediate; strength of recommendation: moderate

Recommendation 1.4.

Systemic administration of the sialogogue bethanechol may be offered during radiation therapy for head and neck cancer to reduce the risk of salivary gland hypofunction and xerostomia

type: evidence-based; evidence quality: low; strength of recommendation: weak

Recommendation 1.5.

Vitamin E or other antioxidants should not be used to reduce the risk of radiation-induced salivary gland hypofunction and xerostomia because of the potential adverse impact on cancer-related outcomes and the lack of evidence of benefit

type: informal consensus; evidence quality: low; strength of recommendation: weak

Recommendation 1.6.

Evidence remains insufficient for a recommendation for or against the use of submandibular gland transfer administered before head and neck cancer treatment to reduce the risk of salivary gland hypofunction and xerostomia because of insufficient evidence with contemporary radiation modalities.

Recommendation 1.7.

Evidence remains insufficient for a recommendation for or against the use of the following interventions

during radiation therapy for head and neck cancer: Oral pilocarpine, amifostine (with contemporary radiation modalities), or low-level laser therapy.

Recommendation 1.8.

Evidence remains insufficient for a recommendation for or against the use of the following interventions to reduce the risk of salivary gland hypofunction or xerostomia in patients with head and neck cancer: n-acetylcysteine oral rinse, traditional Chinese medicine–based herbal mouthwash, local clonidine, concurrent chemotherapy with nedaplatin, boost radiation therapy, hyperfractionated or hypofractionated radiation therapy, intra-arterial chemoradiation, minocycline, melatonin, nimotuzumab, zinc sulfate, propolis, viscosity-reducing mouth spray, transcutaneous electrical nerve stimulation (TENS), parotid gland massage, thyme honey, and human epidermal growth factor.

Clinical question 2.

What is the efficacy of available pharmacologic and nonpharmacologic interventions for the management of salivary gland hypofunction and/or xerostomia induced by nonsurgical cancer therapies?

Recommendation 2.1.

Topical mucosal lubricants or saliva substitutes (agents directed at ameliorating xerostomia and other salivary gland hypofunction-related symptoms) may be offered to improve xerostomia induced by nonsurgical cancer therapies

type: evidence-based; evidence quality: intermediate; strength of recommendation: strong

Recommendation 2.2.

Gustatory and masticatory salivary reflex stimulation by sugar-free lozenges, acidic (nonerosive and sugar-free special preparation if dentate patients) candies, or sugar-free, nonacidic chewing gum may be offered to produce transitory increased saliva flow rate and transitory relief from xerostomia by stimulating residual capacity of salivary gland tissue

type: evidence-based; evidence quality: intermediate; strength of recommendation: moderate

Recommendation 2.3.

Oral pilocarpine, and cevimeline where available, may be offered after radiation therapy in patients with head and neck cancer for transitory improvement of xerostomia and salivary gland hypofunction by stimulating residual capacity of salivary gland tissue. However, improvement of salivary gland hypofunction may be limited

type: evidence-based; evidence quality: high; strength of recommendation: strong

Recommendation 2.4.

Acupuncture may be offered after radiation therapy in patients with head and neck cancer for improvement of xerostomia

type: evidence-based; evidence quality: low; strength of recommendation: weak

Recommendation 2.5.

Transcutaneous electrostimulation or acupuncture-like transcutaneous electrostimulation of the salivary glands may be offered after radiation therapy in patients with head and neck cancer for improvement of salivary gland hypofunction and xerostomia

type: evidence-based; evidence quality: low; strength of recommendation: weak

Recommendation 2.6.

Evidence remains insufficient for a recommendation for or against the use of the following interventions for improvement of salivary gland hypofunction and xerostomia: Extract of ginger and mesenchymal stem cell therapy.

Grading of Recommendations and Levels of Evidence

Types of recommendations	
Evidence - based	There was sufficient evidence from published studies to inform a recommendation to guide clinical practice.
Formal consensus	The available evidence was deemed insufficient to inform a recommendation to guide clinical practice. Therefore, the Expert Panel used a formal consensus process to reach this recommendation, which is considered the best current guidance for practice. The results of the formal consensus process are summarized in the guideline and reported in the Data Supplement.
Informal consensus	The available evidence was deemed insufficient to inform a recommendation to guide clinical practice. The recommendation is considered the best current guidance for practice, based on informal consensus of the Expert Panel. The Panel agreed that a formal consensus process was not necessary for reasons described in the literature review and discussion.
No recommendation	There is insufficient evidence, confidence, or agreement to provide a recommendation to guide clinical practice at this time. The Panel deemed the available evidence as insufficient and concluded it was unlikely that a formal consensus process would achieve the level of agreement needed for a recommendation.
Quality of the evidence	
High	High confidence that the available evidence reflects the true magnitude and direction of the net effect (i.e., balance of benefits v harms) and that further research is very unlikely to change either the magnitude or direction of this net effect.

Intermediate	Moderate confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research is unlikely to alter the direction of the net effect; however, it might alter the magnitude of the net effect.
Low	Low confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research may change either the magnitude and/or direction this net effect.
Insufficient	Evidence is insufficient to discern the true magnitude and direction of the net effect. Further research may better inform the topic. The use of the consensus opinion of experts is reasonable to inform outcomes related to the topic.
Strength of the recommendation	
Strong	There is high confidence that the recommendation reflects best practice. This is based on (1) strong evidence for a true net effect (eg, benefits exceed harms); (2) consistent results, with no or minor exceptions; (3) minor or no concerns about study quality; and/or (4) the extent of panelists' agreement.
Moderate	There is moderate confidence that the recommendation reflects best practice. This is based on (1) good evidence for a true net effect (eg, benefits exceed harms); (2) consistent results, with minor and/or few exceptions; (3) minor and/or few concerns about study quality; and/or (4) the extent of panelists' agreement.
Weak	There is some confidence that the recommendation offers the best current guidance for practice. This is based on (1) limited evidence for a true net effect (eg, benefits exceed harms); (2) consistent results, but with important exceptions; (3) concerns about study quality; and/or (4) the extent of panelists' agreement.