Oral and Dental Management Related to Radiation Therapy for Head and Neck Cancer

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Abstract

The clinical management of squamous cell carcinoma of the head and neck causes oral sequelae that can compromise patients' quality of life and necessitate abandonment or reduction of optimal therapeutic regimens, which in turn reduces the odds of long-term survival. Such sequelae can be prevented or at least better managed if dental and medical health care providers work together. It is therefore essential that dentists have an understanding of cancer therapy and a sound working knowledge of the prevention and management options for the oral sequelae of cancer treatment. This paper offers the dental team an overview of the consequences associated with radiotherapy, as well as a systematic overview of preventing or managing acute and chronic conditions before and during radiotherapy. In addition, it reviews considerations for continued treatment needs during the patient's lifetime.

MeSH Key Words: *cranial irradiation/adverse effects; osteoradionecrosis/prevention & control; stomatitis/prevention & control; xerostomia/prevention & control*

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Surgery, chemotherapy and radiotherapy are the options for treatment of head and neck cancers. Each modality is associated with a number of considerations related to treatment of the cancer and quality of life of the patient. When the oral cavity and salivary glands are exposed to high doses of radiation, there can be dramatic effects on the patient's oral health. This paper offers the dental team an overview of the consequences associated with radiotherapy to facilitate collaboration with the patient's medical team[1,2] (summarized in **Table 1**).

Oral Assessment before Treatment

To a significant degree, the oral problems associated with radiation therapy can be prevented or minimized through optimal management. The acute effects of radiation therapy include mucositis, altered salivary gland function and risk of mucosal infection. The long-term effects are due to changes in the vascularity and cellularity of soft tissue and bone, damage to the salivary glands and increased collagen synthesis resulting in fibrosis. These changes lead to hypovascularity, hypocellularity and hypoxia of the tissues. The affected bone and soft tissue have a reduced capacity to remodel and may be at increased risk of infection and necrosis.

A consultation with a dental team experienced in caring for patients undergoing treatment for head and neck cancer should be completed before the start of therapy.[3,4] Many oral conditions, such as poor oral hygiene, broken teeth, defective restorations and periodontal disease, are likely to precipitate complications during and after a course of radiation therapy (**Table 1**).

In addition to the clinical examination, a thorough radiographic examination is crucial to determine the presence of inflammatory periapical abnormalities, periodontal status, other dental disease and tumour invasion of bone. A panoramic radiograph plus selective periapical or bitewing films (or both) should be available for preradiotherapy dental assessments. Consultation with the patient's physician on the timing, nature (external beam radiotherapy or radioactive implant) and features (location and size of treatment fields, radiotherapy fractionation and total dose) of the radiotherapy is essential for overall risk assessment and scheduling of any required dental intervention.

Table 1 **Strategies for oral and dental management in relation to radiotherapy for head and neck cancer**

Component of care	Notes
Before radiotherapy	
Definitive diagnosis	Tumour size and type
Medical history	Prior cancer history, risk factors
Dental knowledge	Past and current dental care
Oral hygiene	Current practices
Complete dental examination	Mucosa, dentition, periodontium, TMJ
Radiographic examination	Panoramic, selected periapical, bitewing
Whole salivary flow rates	Resting (> 0.1 mL/minute), stimulated (> 1.0 mL/minute)
Adjunctive tests as indicated	Pulp tests, specific cultures (fungal, viral, bacterial)
Prognosis (cure or palliation)	
Proposed radiation therapy	Timing, dose, fields
During radiotherapy	
Maintenance of good oral hygiene	Brushing 2 to 4 times daily with soft-bristled brush; flossing daily
Daily topical fluoride	Custom trays, brush-on prescription-strength fluoride
Frequent saline rinses	
Lip moisturizer (non-petroleum based)	
Passive jaw-opening exercises to reduce trismus	
After radiotherapy	
Complete dental work that was deferred during radiotherapy	
Maintain integrity of teeth	Especially those in radiation fields
Frequent follow-up appointments	Check for oral hygiene, xerostomia, decalcification, decay, ORN, metastatic disease, recurrent disease, new malignant disease

TMJ = temporomandibular joint, ORN = osteoradionecrosis

Table 2 **Criteria for preradiotherapy extractions**

Caries (nonrestorable)
Active periapical disease (symptomatic teeth)
Moderate to severe periodontal disease
Lack of opposing teeth, compromised hygiene
Partial impaction or incomplete eruption
Extensive periapical lesions (if not chronic or well localized)

All teeth, but especially those located within the radiation fields, should be closely evaluated. A UK study found that only 11.2% of patients who reported regular visits with a general dentist before a diagnosis of oral cancer were considered to have no dental conditions that required treatment before radiation therapy.[5] The criteria used for dental extractions before radiation therapy are not universally accepted and are subject to clinical judgement. However, teeth in the high-dose radiation field should be considered for extraction before radiotherapy if they are nonrestorable; if they require significant restorative, periodontal or endodontic intervention or if they have moderate to severe periodontal disease (pockets of 5 mm or more).[6]

Factors to consider when assessing preradiotherapy dental status include the overall condition of the patient's dentition (caries, periapical status, inflammatory periapical abnormalities), previous dental care, current oral hygiene, the urgency of the cancer treatment, the planned therapy (radiation fields and dose) and the prognosis of the cancer therapy (cure or palliation). A more aggressive dental management strategy should be considered for patients with limited previous dental care, poor oral hygiene and evidence of past dental or periodontal disease (**Table 2**).

During Therapy

Monitoring of the oral cavity should be increased during radiation therapy in an effort to decrease the severity of side effects. Systematically applied oral hygiene protocols may reduce the incidence, severity and duration of oral complications.[7] This, in turn, reduces the odds that patients' optimal therapeutic course will need to be modified, which thereby increases patients' odds of survival. Therefore, it is imperative that patients continue their oral hygiene regimen throughout their course of cancer therapy.[8] The patient's self-care procedures should include frequent brushing with a soft-bristled toothbrush and fluoride toothpaste or gel to help prevent plaque accumulation and demineralization or caries of the teeth.[3]

Side Effects of Radiation

The oral tissues directly affected by head and neck radiation therapy include the salivary glands, the mucosal membranes, the jaw muscles and bone. Dry mouth (xerostomia) is a common and significant consequence of head and neck radiotherapy. Because of the loss of saliva, patients with xerostomia are more susceptible to

periodontal disease, rampant caries, and oral fungal and bacterial infections. Mucositis, characterized by inflammation and ulceration of the oral mucosa, is the most significant acute side effect reported by patients and is a potential source of life-threatening infection. Almost all patients undergoing head and neck radiation therapy experience confluent mucositis by approximately the third week of treatment.[9,10]

Another potential consequence of radiotherapy to the oral cavity is fibrosis around the muscles of mastication, leading to trismus. It is believed that jaw exercises may limit the severity of trismus, but they will not mobilize fibrosis once it has occurred.[11,12] Bone exposed to high levels of radiation undergoes irreversible physiologic changes including narrowing of the vascular channels (endarteritis), which diminishes blood flow to the area, and loss of osteocytes. The bone essentially becomes nonvital, which leads to limited remodelling of bone and limited healing potential.

Xerostomia

Systemic sialagogues may increase the production of natural saliva from functional glands. There is no optimal substitute for saliva that can be used when glands are nonfunctional. Pilocarpine (Salagen) has shown promising effects in increasing saliva but is only effective for salivary glands with residual function.[13] Cevimeline (Evoxac), a new sialagogue approved for use in the United States for Sjogren's disease, may increase salivary flow in patients undergoing head and neck radiotherapy. Two alternative medications that may be beneficial in stimulating salivary glands include anethole trithione (Sialor) and bethanechol (Urecholine)[14] (**Table 3**).

Although saliva replacements such as UniMist (Westons Health), Mouth Kote (Parnell Pharmaceuticals) and Oral Balance Gel (Laclede Pharmaceuticals) are poor salivary substitutes, as they primarily attempt to mimic the texture of saliva but do not simulate the rheologic properties, the antimicrobial factors (e.g., antibodies, antimicrobial proteins) and other components of saliva, patients may find that they offer some relief. Oral Balance Gel may be the best accepted by patients because of its extended duration of effect.[15,16] Sugarless gum or lozenges may stimulate salivary secretion in patients with residual salivary gland function. Sugar-free popsicles, plain ice cubes or ice water may be used to keep the mouth cool and moist. Eating foods high in ascorbic acid, malic acid or citric acid will stimulate the glands to increase salivary flow, but this measure is not recommended in dentate patients because the acidity can further irritate oral tissues and contribute to the demineralization of teeth.

For the prevention of rampant dental demineralization and caries, patients should apply a 1.1% neutral sodium fluoride gel daily (for at least 5 minutes), using a custom-fitted vinyl tray if possible.[3,11,17] This practice may be started on the first day of radiation therapy and continued daily as long as salivary flow rates are low and the mouth remains dry. High-potency fluoride brush-on gels and dentifrices may be considered in those who are unable or unwilling to comply with the use of fluoride trays.

Oral Infection

Health care providers should be concerned about preventing local and systemic infections in addition to managing oral symptoms. Treating infections as soon as they are detected will help to reduce pain, as well as the spread of infection. A fungal, bacterial or viral culture is recommended if infection is suspected.

In patients undergoing head and neck radiotherapy, *Candida* colonization tends to increase throughout the course of treatment and remains increased if xerostomia occurs.[18,19] Nystatin rinses are the most widely prescribed treatment for oral fungal infections, despite a lack of proven efficacy. Nystatin has an unpleasant flavour and may cause nausea and vomiting,[17] and its high sucrose content is a major concern in dentate patients. For more severe infections, the use of a systemic antifungal medication such as fluconazole (Diflucan) or amphotericin B is recommended.[3] Systemic amphotericin B must be used with caution because of its potential to cause liver toxicity[4] (**Table 3**). Topical antifungals to consider include clotrimazole, ketoconazole and chlorhexidine.

Chlorhexidine gluconate (0.12%; Peridex), an antimicrobial rinse, has both antifungal and antibacterial properties in addition to antiplaque effects; however, its value is still unconfirmed. Its tendency to stain teeth and its alcohol content, which can irritate inflamed tissues, are drawbacks.[18] If chlorhexidine is used, it is important to note that nystatin and chlorhexidine should *not* be used concurrently, because chlorhexidine binds to nystatin, rendering both ineffective;[17] furthermore, chlorhexidine should be used at least 30 minutes before or after the use of any other topical agents with which it may bind.

For cancer patients with viral infections, such as Herpes simplex 1, acyclovir (Zovirax, GlaxoSmithKline) or derivatives are recommended for both prophylaxis and treatment.[3,20] Penciclovir (Denavir, GlaxoSmithKline), a newer topical antiviral with increased tissue penetration, is now available.

Oral Mucositis

Maintaining a self-care regimen may decrease the incidence of mucositis.[17] While many products and combined product rinses have been suggested for clinical use, they have not been studied in randomized controlled trials and should be used with caution. Among the concerns with the use of combinations of rinses are the risks that some products may interfere with the action of others,

Table 3 **Therapies to deal with specific problems associated with head and neck radiotherapy**

Therapy	Dose	Contraindications
Systemic sialogogue		
Pilocarpine (Salagen[a]), 5 mg	3–6 tabs daily	Asthma, glaucoma, liver dysfunction
Bethanechol (Urecholine), 25 mg	1 tab 3 times daily	Asthma, peptic ulcer, bladder inflammation
Anethole dithiolethione (Sialor),[b] 25 mg	1 tab 3 times daily	Hypersensitivity
Cevimeline (Evoxac),[c] 30 mg	1 tab 3 times daily	Asthma, glaucoma, liver dysfunction, cardiovascular disease
Antifungal agents		
Systemic		
Fluconazole (Diflucan), 100 mg	1 tab once daily	Liver or renal dysfunction, coumadin, warfarin
Amphotericin B, 0.1 mg/mL (compounded)	5 mL, rinse > 1 minute, then spit (3 times daily)	Hypersensitivity to drug class
Topical		
Nystatin suspension, 100,000 U/mL	5–10 mL, rinse, then spit (3 times daily)	Other topical medications; do not use in dentate patients
Nystatin cream or ointment, 100,000 U/g	Apply to dry denture surface 3 times daily	Hypersensitivity to drug class
Clotrimazole cream, 1%	Apply to dry denture surface 3 times daily	Hypersensitivity to drug class
Clotrimazole troches, 10 mg	Dissolve in mouth, 5 times daily for 14 days	Hypersensitivity to drug class, liver dysfunction
Ketoconazole, 200 mg	1 or 2 tabs by mouth 4 times daily	Liver dysfunction
Chlorhexidine rinse (Peridex), 0.12%	5–10 mL, rinse > 1 minute, then spit (3 times daily)	Hypersensitivity to drug class
Mucosal coating agents		
Milk of magnesia/Maalox	15–30 mL by mouth 4 times daily as needed	Hypersensitivity to drug class, renal dysfunction
Diphenhydramine liquid (Benadryl), 12.5 mg/5 mL	5–10 mL, rinse > 1 minute, then spit (4 times daily)	Asthma, glaucoma, cardiovascular disease, pulmonary disease
Sucralfate, 1 g /10 mL	5–10 mL, rinse > 1 minute, then spit (4 times daily)	Hypersensitivity to drug class, renal dysfunction
Topical anesthetics or analgesics		
Benzydamine hydrochloride (Tantum)	5 mL, rinse > 1 minute, then spit (as needed)	Hypersensitivity to drug class
Viscous lidocaine, 4%	5 mL, rinse >1 minute, then spit (as needed)	Hypersensitivity to drug class, liver dysfunction
Doxepin suspension, 0.5% (compounded)	5 mL, rinse > 1 minute, then spit (4 times daily)	Hypersensitivity to drug class, glaucoma, urinary retention
Benzocaine, 20% in Orajel	Apply topically to areas of pain	Hypersensitivity to drug class
Sucralfate, 1 g/10 mL	5–10 mL, rinse > 1 minute, then spit or swallow (4 times daily)	Hypersensitivity to drug class, renal dysfunction

[a]*Brand names are included only as examples and not to promote any one product. The manufacturers are as follows: Salagen, Pharmacia; Urecholine, Merck; Sialor, Paladin; Evoxac, SnowBrand Pharmaceuticals; Diflucan, Pfizer; Fungizone, Bristol-Myers Squibb Canada Inc.; Peridex, Zila Pharmaceuticals; Maalox, Novartis Consumer Health; Benadryl, Pfizer Consumer Healthcare; Tantum, 3M Pharmaceuticals; Orajel, Del Laboratories.*
[b]*Over the counter; not available in the United States.*
[c]*Not available in Canada.*

and compounding may result in dilution of the individual products to levels that may be ineffective.

The use of a common oral rinse, such as isotonic saline or sodium bicarbonate, is often suggested, but no studies have confirmed any beneficial effect upon mucositis.[3] It has been suggested that patients begin prophylactic rinses with chlorhexidine to prevent the onset of microbial infection, gum inflammation and bleeding, and to reduce the risk of caries. While some authors report that a chlorhexidine oral rinse has potential effects on mucositis, others report no effects,[9] and no effects have been reported for radiation-induced mucositis to date. Use of other oral rinses, including commercial alcohol-based mouthwashes and hydrogen peroxide rinses, should be discontinued because of their drying and irritating effects on the oral mucosa.

The discomfort of mucositis can be reduced with coating agents, topical anesthetics and analgesics, although systemic analgesics are frequently needed.[3] Aluminum

hydroxide/magnesium hydroxide (milk of magnesia-Maalox) and sucralfate have been suggested as coating agents for the oral mucosa. Sucralfate suspension may also be helpful in the treatment of oral pain, although the effect on mucositis has not been clearly documented[21–25] (**Table 3**).

Topical anesthetics used in rinse form may result in intense but short-term anesthesia. However, the localized anesthesia can increase the risk of aspiration, and their systemic absorption can cause cardiac effects. When oral mucosal pain is present, benzydamine hydrochloride (Tantum), doxepin suspension 0.5% or an antihistamine such as diphenhydramine can be prescribed.[10,26] Benzydamine is the only medication available that has been shown in multicentre, double-blind controlled studies to reduce mucositis and pain in patients with head and neck cancer.[10,26] Topical anesthetics, such as benzocaine, viscous lidocaine and topical benzocaine can be applied locally to sites of pain with a swab or a soft vinyl mouth guard[3] (**Table 3**).

Of all available mouth rinses that can be used as treatments for mucositis, the least costly and easiest for patients to prepare is a simple mouthwash comprising a teaspoon (10 mL) of salt and a teaspoon (10 mL) of baking soda (sodium bicarbonate) in 8 ounces (250 mL) of water. A comparison among salt and soda mouthwashes, mouthwashes prepared from lidocaine and diphenhydramine with Maalox, and mouthwashes of 0.12% chlorhexidine gluconate found that the 3 options were equally effective in the treatment of chemotherapy-induced mucositis.[27] Although chlorhexidine may also decrease oral *Candida* counts and bacterial levels, studies on radiotherapy patients have shown no effect on mucositis. According to the current literature, good oral hygiene, topical fluorides for caries prevention and benzydamine offer the greatest benefits.

After Therapy

After the completion of radiation therapy, acute oral complications usually begin to resolve. Patients should continue to follow an oral health self-care regimen to keep the teeth and gums healthy and to facilitate repair of any residual oral damage. Oral exercises should be continued or introduced to reduce the risk and severity of trismus. Additional dietary counselling sessions may be appropriate for patients who must make long-term dietary adaptations to accommodate permanent changes to their oral cavity produced by surgery and radiation. The referral of patients to support groups may also be a useful adjunct to patients' return to optimal functioning.

Long-term management and close follow-up of patients after radiation therapy is mandatory. It is critical to remember that patients at highest risk for a new or recurrent cancer are those previously treated for cancer of the upper aerodigestive tract. Therefore, careful examination to detect signs of recurrence or new primary malignant lesions is essential. Close follow-up will facilitate the management of any chronic complications that may occur, such as xerostomia, mucosal sensitivity, increased risk of cavities, candidiasis and persisting risk of osteoradionecrosis (ORN).

The period after completion of cancer therapy is an excellent time for patients to resolve any oral concerns that were previously deemed not medically necessary and for which care had been deferred. Since patients with cancer are more likely to experience a recurrence or a new cancer and require further therapy, resolution of any deferred dental care should be a top priority.

Osteoradionecrosis

ORN is irreversible, progressive devitalization of irradiated bone. The condition is characterized by necrotic soft tissue and bone that fails to heal spontaneously. Most cases of ORN occur in the mandible, where vascularization is poor and bone density is high. Clinical manifestations of ORN may include pain, orofacial fistulas, exposed necrotic bone, pathologic fracture and suppuration.[28–30] One-third of ORN cases occur spontaneously. Among cases where ORN has been initiated by trauma the majority result from extraction of teeth. The incidence of ORN is twice as high in dentate patients as it is among edentulous patients. Poor oral hygiene and continued use of alcohol and tobacco may also lead to rapid onset of ORN.[31]

Over the years, ORN has been treated by numerous methods with variable success.[28] Hyperbaric oxygen therapy is considered an adjunctive treatment for ORN, often used in conjunction with surgery, and has been associated with better success rates than surgery alone.[29,30,32,33]

Conclusions

The complications of radiotherapy must be considered thoroughly so that every effort is undertaken to minimize the oral morbidity of these patients before, during and after cancer treatment and throughout the patient's lifetime. ◆

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