

Review Article

Oral Adverse effects of Radiotherapy: A Review

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ABSTRACT

Oral cancer now-a-days is a major health issue in developing countries like India which is caused mainly due to tobacco dependence. It is among the 10 most common cancers worldwide, and is especially seen in disadvantaged elderly males. Treatment of Oral Cancer plays a vital role in dentistry which includes Radiotherapy, chemotherapy, surgery or a combination of any of these treatment modalities. Radiotherapy is the use of a certain type of energy called ionizing radiation to kill cancer cells and shrink tumors. Radiotherapy may result in several adverse effects that manifest either during or after the treatment which includes Xerostomia, dental caries, mucositis, Dysgeusia, ageusia, osteoradionecrosis, infection, and trismus. These effects can be eradicated or controlled with proper treatment. This paper aims to review the effects of ionizing radiation on the oral cavity.

Key words: Radiotherapy, mucositis, ageusia, osteoradionecrosis.

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Introduction

Radiotherapy alone or in combination of other treatment modalities plays a vital role in the treatment of Oral Cancer. It is the use of a certain type of ionizing radiation to kill cancer cells and shrink tumors. Radiation injures or destroys cells in the area being treated (the "target tissue") by damaging their genetic material, making it impossible for these cells to continue to grow and divide. Although radiation damages both cancer cells and normal cells, most normal cells can recover from the effects of radiation and function properly.¹

High-energy radiation damages genetic material (deoxyribonucleic acid, DNA) of cells and thus blocking their ability to divide and proliferate further.² Although radiation damages both normal cells as well as cancer cells, the goal of radiation therapy is to maximize the radiation dose to abnormal cancer cells while minimizing exposure to normal cells, which is adjacent to cancer cells or in the path of radiation. Normal cells usually can repair

themselves at a faster rate and retain its normal function status than the cancer cells. Cancer cells in general are not as efficient as normal cells in repairing the damage caused by radiation treatment resulting in differential cancer cell killing. Various adverse effects are caused by the ionizing radiations. These effects are related to the, the age of the patient, dose of radiation, the field of irradiation, the degree of hypovascularity or hypocellularity of tissues.³

Classification of Adverse Effects

Based on the time of occurrence and the amount of effect caused the adverse effects can be divided into early and late effects. Early effects are the one noticed during or shortly after treatment mostly affecting the oral mucosa, taste buds and salivary glands and late effects are developed at the end or years after the treatment, affecting dentition, bone, muscles and skin^{4,5} as explained in the Table 1

Table 1: Adverse effects of Radiotherapy

Early effects	Late effects
Mucositis	Dentition
Taste dysfunction	Soft tissue necrosis
Bacterial, Viral & Fungal Infections	Osteoradionecrosis
Salivary gland dysfunction	Mucosal fibrosis and Atrophy
	Trismus

Mucositis

Radiotherapy induced Mucositis is the most common early adverse effect experienced by patients undergoing treatment of Oral Cancer. Decreased cell renewal in the epithelium causes damage to the oral mucous membrane leading mucosal atrophy and ulcerations.^{4,5} Signs & symptoms of oral mucositis includes burning sensation, inflammation, erythema, sloughing, mucosal atrophy, ulcers, infections. This is accompanied by pain, burning and discomfort, which are greatly aggravated by contact with highly spicy foods. When the irradiation field involves the pharyngeal mucosa, it may produce difficulties in swallowing and speech.⁶

Scales have been given for assessing the severity of Mucositis by National Cancer Institute and the World Health Organization⁷

Table 2: Scale for rating mucositis severity

Grades	WHO Criteria
0	No symptoms
1	No ulcers or asymptomatic ulcers, erythema or Sore mouth,
2	Painful erythema or ulcers; Patient can eat solid food.
3	Painful erythema, edema or ulcers; patient cannot eat solid food Liquid diet only
4	Patient is unable to eat or drink; Requires parenteral or enteral support (such as gastric feeding tube) to provide nutrition

Salivary gland dysfunction

Radiotherapy leads to the damage to the salivary glands, either by changing the salivary composition or by altering the salivary flow rate. After radiotherapy many mechanisms leads to the salivary gland dysfunction.⁸ Early changes result from damage to the plasma membrane of acinar cells or disturbances in intracellular signalling; late damage results due to lack of proper cell renewal because of damage to the DNA of progenitor cells and stem cells. The extent of salivary gland dysfunction depends on the dose of radiation, the volume of irradiated gland tissue.^{9,10} Radiotherapy also leads to the changes in the composition of saliva, alterations in the buffering capacity, concentration of electrolytes, making

it more viscous and changing its nonimmune and immune antibacterial systems.^{8,11,12} Several salivary substitutes are advised to increase the salivary flow rate and overcome the discomfort caused due to salivary dysfunction.¹³

Taste Buds dysfunction

Taste buds are extremely sensitive to radiation. Doses in the therapeutic range cause extensive degeneration of the normal histology architecture of taste buds. Dysgeusia, hypogeusia or ageusia is often noticed by the patient during the second or third week of radiotherapy. Bitter and acid flavors are more severely affected when the posterior two thirds of the tongue is irradiated, and salt and sweet when the anterior third of the tongue is irradiated. Taste acuity usually decreases by a factor of 1000 to 10,000 during the course of radiotherapy. Alterations in the saliva may account partly for this reduction, which may proceed to a state of virtual insensitivity, with recovery to near-normal levels some 60 to 120 days after irradiation.^{14,15} These alterations can lead to reduction in the intake of food and nutritional deficits, resulting in weight loss and, in severe cases, weakness, cachexia, malnutrition and susceptibility to infection

Infections

The decrease in salivary flow rate due to radiotherapy further results in a shift in the oral microflora, with a increase of cariogenic microorganisms. *Streptococcus mutans*, *Lactobacillus*, and *Candida albicans* are increased whereas, *Streptococcus sanguinis*, *Neisseria*, and *Fusobacterium* are decreased. This shift in oral microflora is an aggravating factor for developing oral mucositis. Candidiasis is the most common infection affecting the oral cavity during radiotherapy.^{16,17} Bacterial infections may occur during the initial stages of radiotherapy. Herpes virus infections may also occur in patients who are seropositive prior to Oral cancer treatment by radiation due to virus re-activation.

Late effects

During the radiotherapy, increased sensitivity to all the hot and cold food is experienced by the patients due to loss of protective layer of saliva.¹⁸

Radiation Caries

Changes in the chemical composition of saliva and increased amounts of cariogenic oral bacteria result in rapid decalcification of dental enamel. Radiation caries is not caused directly by irradiation, but results from the sequelae of xerostomia: decrease of pH, decreased buffering capacity, and increased viscosity.¹⁹ Clinically it's a form of rampant caries, and tends to spread to all the surfaces of teeth, altering the color. As a result of this decay, friability is increased leading to the breakdown of tooth structure.²⁰

Osteoradionecrosis

Osteoradionecrosis, is one of the most serious adverse effect of radiotherapy. It is an inflammatory condition resultant of the bone ionizing radiation. Radiation

damages the osteocytes and the microvascular system, with a progressive decrease of the microvascularization. The tissue becomes hypovascular, hypocellular and hypoxic. All these features avoid the bone healing, and it can proceed to a necrosis with or without infection. These changes in bone result from injury to their modeling system, causing atrophy, osteoradionecrosis and pathological fractures^{13,21}. The mandible is much more susceptible to osteoradionecrosis than the maxilla, because its vascularization is poor and bone density is high. This adverse effect usually occurs within one year of therapy. Radiologic features include ill-defined cortical destruction with or without sequestration²². Clinical features may include pain, oral fistulas, exposed necrotic bone, pathologic fracture and suppuration. The patient may present clinical signs and symptoms of ulceration or necrosis on the mucosa, with exposure of necrotic bone for longer than 3 months. Radiographically, irregular bone destruction is observed and the mandible is most frequently involved. The progression of this process can lead to pathologic fracture and intraoral or extraoral fistula²³

Trismus

During radiotherapy, if masticatory muscles or the temporomandibular joint (TMJ) comes in the path of radiation, trismus can occur. Muscular fibrosis or TMJ ligaments fibrosis, pterygo-mandibular raphe can scar in response to radiation injury. Oral hygiene, speech, nutritional intake of the patient is compromised due to limited jaw opening interferes. Trismus develops in most patients within 3-6 months after radiotherapy and frequently becomes a long lasting problem.²⁴

Conclusion

Radiotherapy plays a major role in treatment of Oral cancer. As a result of which it causes various adverse effects on oral cavity and hence affects the patients quality of life. Larger prospective trials that include the treatment of ionizing radiation-induced damage to oral tissues are needed to improve management and enhance better prognosis.

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