International Journal of Current Advanced Research
ISSN: O: 2319-6475, ISSN: P: 2319-6505, Impact Factor: 6.614
Available Online at www.journalijcar.org
Volume 7; Issue 7(D); July 2018; Page No. 14131-14135
DOI: http://dx.doi.org/10.24327/ijcar.2018.14135.2551

Research Article

MANAGEMENT OF RADIATION INDUCED TOXICITIES DURING TREATMENT OF HEAD AND NECK CANCERS

Jagmohan.Singh[1]., Vikas Roshan[1*]., Senniandavar.V[1]., P.Bala[2]., Vandhana.D[1]., Abin CV[1] and Rajiv.K.S[1]

[1]Department of Radiation Oncology, Shri Mata Vaishno Devi Narayana Superspeciality Hospital
[2]Department of Emergency Medicine, Shri Mata Vaishno Devi Narayana Superspeciality Hospital

A R T I C L E I N F O

Article History:

Received 5th April, 2018
Received in revised form 24th May, 2018 Accepted 20th June, 2018
Published online 28th July, 2018

Key words:

Mucositis, Xerostomia, skin toxicity, oral candidiasis, Dental caries, ORN, Head and Neck cancers

A B S T R A C T

Of the long-term survivors treated with head and neck radiation therapy, 77% to 100% have mild-to-severe radiation damage of soft tissues and bones.[1,2] The severity of disturbances varies with age, radiation dose and field sizes, and concomitant treatment such as chemotherapy.[1,3] To a large degree, salivary glands, oral mucosa, skin and bones are susceptible to changes that can result in constitutional complications such as dehydration, malnutrition and systemic infections. Implementation of oral care protocols before, during and after radiation therapy and frequent evaluation of lesions during local therapy can prevent incidences and severity of toxicities of treatment

INTRODUCTION

Radiation therapy along with surgery or chemotherapy has increased cure rates in Head and neck cancers. However, this modality of treatment can produce adverse outcomes that manifest during or after the completion of therapy [1-3].

Treatment of Complications

Radiation induced complications generally divided into early (that includes toxicities associated with mucosa, taste and salivary glands) and late toxicities (that include side effects associated with salivary glands, teeth, muscles and skin. The degree, progression, and irreversibility of these changes are related to the radiation dose, the child's age at diagnosis, the irradiation field, the degree of hypovascularity and hypocellularity of tissues, and the healing capacity of the exposed epithelial
cells.[4,5]

Mucositis

Mucositis is the most troubling acute side effect experienced by patients undergoing radiation therapy of the head and neck. Mucosal damage occurs because of decreased cell renewal in the epithelium, which causes mucosal atrophy and ulceration. [4] Sonis describes the 4 successive phases of the development of mucositis as inflammatory-vascular, epithelial, ulcerative-bacteriologic and healing.[6]

Corresponding author:* **Vikas Roshan
Department of Radiation Oncology, Shri Mata Vaishno Devi Narayana Superspeciality Hospital

Each stage is interdependent and is because of cytokines released in response to radiation treatment and direct effect of radiotherapy on epithelium and oral bacterial flora.[6]

Clinically, mucositis presents as erythema, mucosal atrophy, and ulceration with or without pseudomembranes. These changes in the oral mucous membrane become evident during the first week after a 2-Gy daily fractioned radiation therapy program and heal completely 2 to 3 weeks later.[4,7]The primary clinical problem for patients developing oral mucositis is the pain which inturn affects ability to eat, speak and sleep.

Management

The elimination of oral gram-negative bacilli – using lozenges containing polymycin E, tobramycin and amphotericin B – can prevent the onset of severe mucositis and, consequently, other complications such as nasogastric tube feedings and weight loss.[8] Mucositis may be aggravated by the the trauma of ill-fitting dentures, so patients are advised to keep the denture wearing to a minimum during radiotherapy treatment. Meticulous denture care is also required – soaking dentures in a chlorhexidine solution or commercially available denture cleaner is recommended. In addition to oral hygiene practices, consideration must be given to the use of lubricants and anaesthetics. Lubricants are required to clean and moisten lips and keep them intact. The most commonly used lubricants are jelly, Vaseline or mineral oil. Therapeutic mixtures of various topical anaesthetics, analgesics and mucosal coating agents are used routinely for the management of mucositis. Some of the medicaments that have been advocated include

diphenhydramine hydrochloride (Benadryl); Kaopectate and milk of magnesia; Benadryl and Kaopectate; and Xylocaine viscous.

Xerostomia

Radiation treatment of tumours of the head and neck commonly damages the salivary glands, decreasing the salivary flow rate and changing salivary composition.[9] Salivary gland dysfunction is due to effect of radiation on plasma cell membranes of acinar cells as well as disturbance in intracellular signalling.; late damage may be the result of a lack of proper cell renewal because of damage to the DNA of progenitor cells and stem cells.[10]

The damage to salivary functions depends upon the volume of salivary glands irradiated. The functional impairment of salivary glands results in impeded oral functioning, a burning sensation, cracked lips, and increased susceptibility to oral infections and dental caries.[11,12]

The composition, viscosity and ph buffering capacity of saliva changes during radiotherapy.[8,10,11]

Management

Mastication is a normal physiological stimulus for salivation, and vigorous chewing should, therefore, be encouraged. Low-calorie foods such as celery and carrots or sugarless gum are especially suitable. Frequent chewing of sugarless gum over a period of two weeks has been shown to increase parotid salivary output and increase the pH and buffer capacities of parotid and whole saliva. Of the four primary gustatory stimuli, acid is the most potent stimulator of salivary flow. Citric acid, found in selected fruits and sour lozenges, may be employed to stimulate the flow of saliva but its use in dentate individuals is strongly discouraged as it has the potential to erode tooth enamel. The parasympathomimetic drug pilocarpine has been shown to be a potent stimulant of exocrine secretion. Pilocarpine has since been used routinely in the management of glaucoma and has been studied extensively on irradiated patients and Sjogren's syndrome sufferers. Where sialogogues fail, other methods must be employed to moisten oral tissues. The simplest and best practice is to encourage the frequent consumption of water, which is recommended for all xerostomic patients. Patients are encouraged to carry water in a small aerosol spray or plastic water bottles similar to those used by cyclists or athletes. A lactoperoxidase, lysozyme, and lactoferrin-containing product, Biotene, has been developed to address deficiencies in salivary composition in xerostomic patients. The four essential elements of oral hygiene instruction are assessment, brushing, rinsing and flossing. Teaching and reinforcing these oral hygiene practices is necessary before, during and after therapy. Sugar-free gum is preferred, but even sugared gum can be beneficial as sugar-containing gum produces a drop in salivary pH for 20 minutes, despite a stimulated salivary flow, but as the flavour and sweetness leech out of the chewing gum, the salivary flow rate is comparable to chewing gum base alone. It has been suggested that chewing sugared gum after meals which contain fermentable carbohydrate still exerts a pH raising effect, although this is less than the pH-raising impact of sugarless gum.[13-14]

Chewing hard cheese, which is rich in nitrogenous substrates, also elicits a rapid rise in plaque pH following a sucrose rinse. It is believed the proteolysis of cheese proteins such as casein contributes to this pH-elevating effect. Cheese chewing also raises plaque calcium and phosphate levels[15] and facilitates enamel rehardening.[16] Alteration in Taste and associated Malnutrition Patients can develop an altered taste (dysgeusia), partial loss of taste (hypogeusia) or complete loss of taste (ageusia). This alteration of taste is because of direct effect of radiation on fungiform papillae and taste buds. These alterations can lead to an food aversion and reduced intake which leads to reduced intake and results in malnutrition, weakness, cachexia and susceptibility to infection.

Management

Early intervention with a nasogastric feeding tube or parenteral nutrition is required to maintain weight and prevent nutritional deficiencies. Zinc supplements accelerate the recovery of taste sensations in these patients.[18]

Dental Caries Changes in the chemical composition of saliva and increased amounts of cariogenic oral bacteria result in rapid decalcification of dental enamel. Aggressive and extensive caries, commonly known as radiation caries, tends to spread to all dental surfaces, changing their translucency and colour. Tooth decay is not because of radiation directly but results from radiation induced xerostomia and shift in micro flora that leads to breakdown of teeth.

Irradiation may also induce disturbances in odontogenesis. Abnormally small teeth (microdontia), short or blunted roots, small crowns, malocclusion, incomplete calcification, enlarged pulp chambers), premature closure of apices and delayed or arrested development of teeth have been reported.[1,2,] These changes results in malocclusion and affects facial development. To prevent these caries oral hygiene should be maintained, use of topical fluoride is recommended. Patient need intensive home care and mouth rinses to eliminate debris and control micro flora. There is no one universally accepted protocol for the management of radiation caries; however, the importance of fluoride is well recognized. Fluoride has reduced dental extractions after radiotherapy and three-six month dental follow up is the proper way to prevent the development of radiation caries.

Recommended fluoride preparations contain 0.4 percent stannous fluoride, 1.1 percent sodium fluoride, 1.23 percent sodium fluoride or 1.23 percent acidulated phosphate fluoride, which are applied using a brush on technique or in a customized tray. Topical daily application of 1% neutral sodium fluoride gel with custom-made fluoride carriers reduce post radiation caries.[19] Treatment with prophylactic fluoride is initiated at least 1 week before radiation therapy and continued indefinitely. Dietary instructions about non-cariogenic foods should be given.

Brushing with a small soft toothbrush, reaching all the contours and gingival crevices of the teeth, is recommended. Fluoridated toothpaste is preferred. Most toothpastes contain the detergent and foaming ingredient sodium lauryl sulfate (SLS) which may increase the incidence of mucosal irritation and oral ulceration. Their use should be avoided in xerostomic individuals.

Recommendations on the frequency of brushing vary greatly from a minimum of twice daily to four times daily to after meals and four-hourly during waking hours.[20,21,22] Several rinse solutions have been suggested: hydrogen peroxide saline or hydrogen peroxide and water (1:2 or 1:4 mixture); sodium

bicarbonate (one teaspoon in one cup of water or one teaspoon in 500ml water); and half a teaspoon of salt and one teaspoon of baking soda in one litre of water.[22,23] Sodium bicarbonate rinses are used extensively to elevate salivary pH and buffering capacity. Alcohol-containing mouthwashes may irritate or dry the mucosa and are not recommended.[24]Moreover the rapid development of xerostomia in radiotherapy patients deprives the oral epithelium of its usual salivary fluid coating, thereby diminishing the mucosal protective effect of the chlorhexidine. Thus the full range of therapeutic benefits of chlorhexidine is denied to these xerostomic patients. Patients should be cautioned that a greater emphasis needs to be placed on these factors. For example, over time, high carbohydrate consumption may lead to sub-surface decalcification, while the surface, which has a lower solubility, remains intact.

Refined carbohydrates should be replaced with substances such as sorbitol, xylitol, aspartame and saccharine that are not degraded into organic acids by oral bacteria.[25] Certain foods are known to have an irritating effect on dry oral mucosa – dry, acidic or spicy foods, highly flavoured foods, alcohol and alcohol-containing mouthwashes and tobacco products. The patient is advised to avoid them.

Bone Changes Exposure to high levels of ionizing radiation can markedly affect the bone matrix. Changes in bone resulting from injury to the remodelling system (osteocytes, osteoblasts, and osteoclasts), causing atrophy, osteoradionecrosis and pathological fractures.[17,26] Currently, the pathogenesis of osteoradionecrosis is thought to arise from a fibro-atrophic process rather than from vascular alterations; vascular dysfunctions help to generate the initial pre fibrotic phase.[27] Tooth extraction and dental disease in irradiated regions have long been recognized as major risk factors for the development of osteoradionecrosis.[26] The mandible bone is at high risk of osteoradionecrosis in comparison to maxilla. The non-healing bone may become secondarily infected. In addition to histologic changes in bone, children undergoing radiation therapy may experience abnormalities in the growth and maturation of craniofacial skeletal structures.[3,28] Craniofacial and dental abnormalities can cause severe cosmetic or functional sequelae, necessitating surgical or orthodontic intervention.

Management

Just over one-third of ORN occurs spontaneously with soft tissue breakdown over non-viable bone. The remaining two-thirds of cases are initiated by traumatic incidents, such as tooth extraction, biopsies, the progression of periodontal disease, subgingival scaling or ill-fitting prosthesis.[29] Due to the potential for irritation of the underlying traumatized mucosa and the development of ORN, denture-wearing should be kept to a minimum. It is recommended that 'at least one year should elapse before patients who had teeth extracted immediately before radiotherapy begin wearing dentures. This is particularly true where sharp bony spicules or ridges are present, such as at the mylohyoid line. Flexible liners may be employed in the interim, but there is the potential for supporting the growth of fungi. Pankhurst recommends 'Dentures should be avoided where possible and a shortened dental arch should be accepted where appropriate.[30]

Murray found the incidence of ORN in dentate patients is nearly double that of edentulous patients. The interplay effect of oral hygiene, alcohol and tobacco leads to rapid onset of ORN.[31] To minimize the risk of developing osteoradionecrosis, optimal precautions should be adopted. These include complete removal of the non-restorative teeth as soon as possible to maximize the healing period. When osteoradionecrosis results in small lesions of the bone, daily saline irrigations, and antibiotic coverage are recommended.

Hyperbaric oxygen (HBO) is often employed for the management of ORN, however, the precise role and guidelines for its use have not been clearly defined. HBO therapy delivers oxygen tensions between 1,500- 2,200mmHg at the arteriole level, depending on the treatment schedule used, allowing oxygen to diffuse much more deeply into tissues to overcome relative ischemia. It has been demonstrated there is an acceleration in the repair of wounds and increased bone healing following HBO therapy.[29]

Edema*:* Early in the post-radiation period scarring fibrosis and edema begins to appear. Edema is most prominent in the anterior region of tongue following irradiation of the anterior tongue and floor of mouth carcinoma occasionally severe enough to cause obstruction of tongue mobility and salivary control further impeding speech and denture placement tongue and cheek biting is another the complaint. The severity of edema varies from time to time and day to day. It is usually severe in the morning.

Management Same as of mucositis.

Candidiasis*:* Since radiation therapy lands one in a state of immunosuppression; candidiasis and viral infections like herpes simplex virus is commonly seen in these patients.

Management Frequent rinsing usually manages oral candidiasis with a hydrogen peroxide saline solution, and the use of topical antifungal medications such as nystatin (200,000-400,000IU) 2-3ml retained in the mouth for three minutes and then swallowed, four times daily). Two weeks' treatment is usually required but, for refractory cases, systemic ketoconazole 200mg daily for a minimum of two weeks is recommended.[32]

Acute viral infections: Herpes simplex virus (HSV) is the major viral pathogen encountered in immunosuppressed chemotherapy and radiation therapy patients. Fortunately, simple diagnostic Techniques such as cytology and viral culture can evaluate suspicious lesions and then safe; effective antiviral therapy can be instituted.

Acyclovir is the treatment of choice in the management of HSV infection. Inpatient populations with a high incidence of HSV reactivation in a predictable time frame (for example, seropositive bone marrow transplant and leukaemia), prophylactic cover has been suggested.[33] the issue of resistance to the drug has not been thoroughly investigated. However, there are few side effects, and neurotoxicity and nephrotoxicity are rare.

Cutaneous Changes*:* Morphologic changes of the skin in the irradiated field usually start halfway through irradiation and persist for some time afterward. An inflammatory reaction generalized in the surface, followed by desquamation of the epidermis, can lead to either the lesion healing or radio necrosis. Scarring and atrophy of the skin increase the rigidity of tissues, making them less supple and less resistant to injury.

The role of Staphylococcus aureus and its toxins has been overlooked in the pathogenesis of acute radiation dermatitis [34] When the muscles of mastication and the temporomandibular joint are included in the irradiated field; musculoskeletal fibrosis can cause trismus and mandibular dysfunction. Limited opening of the jaw interferes with adequate oral hygiene, fluoride application, speech, nutrition and dental treatment.

Because treatment of trismus can be complicated, preventive management with jaw exercises and dental prosthetics. Severe cutaneous reactions may require topical and oral antibiotic therapy in conjunction with topical corticosteroids to eradicate infection and repair the skin's barrier function.

CONCLUSION

The prevention and reduction of side effects of radiotherapy is integral part of holistic cancer care. Patient should be kept on regular follow up and should be reinforced on every visit regarding maintainence of oral hygiene.

References

1. Raney RB, Anderson JR, Kollah J *et al*;Late effects of therapy in 94 patients with localized rhabdomyosarcoma of the orbit: a report from the Intergroup Rhabdomyosarcoma Study (IRS)-III, 1984-1991. *Med Pediatr Oncol* 2000; 34(6):413–20.
2. Paulino AC, Simon JH, Zhen W *et al*;Long-term effects in children treated with radiotherapy for head and neck rhabdomyosarcoma. *Int J Radiat Oncol Biol Phys* 2000; 48(5):1489–95.
3. Denys D, Kaste SC, Kun LE *et al*; The effects of radiation on craniofacial skeletal growth: a quantitative study. *Int J Pediat Otorhinolaryngol* 1998; 45(1):7–13.
4. Dorr W, Hamilton CS, Boyd T *et al*. Radiation-induced changes in cellularity and proliferation in human oral mucosa. *Int J Radiat Oncol Biol Phys* 2002; 52(4):911–7.
5. Prott FJ, Handschel J, Micke O *et al*; Longterm alterations of oral mucosa in radiotherapy patients. *Int J Radiat Oncol Biol Phys* 2002; 54(1):203–10.
6. Sonis ST. Mucositis as a biological process: a new hypothesis for the development of chemotherapy-induced stomatotoxicity. *Oral Oncol* 1998; 34(1):39–43.
7. Kostler WJ, Hejna M, Wenzel C *et al*. Oral mucositis complicating chemotherapy and/or radiotherapy: options for prevention and treatment. *CA Cancer J Clin* 2001; 51(5):290–3158
8. Spijkervet FKL. Effective use of selective oral flora elimination on mucositis. In Spijkervet FKL ed Irradiation Mucositis, 1st edn.Copenhagen: Munksgaard 1991:84-102.
9. Moller P, Perrier M, Ozsahin M *et al*;A pros study of salivary gland function in patients undergoing RTsquamous cell carcinoma of the oropharynx. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2004; 97(2):173–89.
10. Konings AW, Coppes RP, Vissink A. On the mechanism of salivary gland radiosensitivity. *Int J Radiat Oncol Biol Phys* 2005, 62(4):1187–94.13
11. Gornitsky M, Shenouda G, Sultanem K *et al*; Doubleblind randomized, placebo-controlled study of pilocarpine to salvage salivary gland function during RTof patients of head andneck cancer. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2004; 98(1):45–52.
12. Ripamonti C, Zecca E, Brunelli C *et al*;A randomized, controlled clinical trial to evaluate the effects of zinc sulfate on cancr patients with taste alterations caused by head and neck irradiation,*Canc*.998; 82(10):1938–45.15.
13. Jensen ME, Wefel JS *et al* Human plaque pH responses to meals and the effects of chewing gum. *Br Dent J* 1989;167:204-208.
14. Manning RH, Edgar WM. pH changes in plaque after eating snacks and meals, and their modification by chewing sugared or sugar-free gum. *Br Dent J* 1993;174:241-244.
15. Edgar M, Higham SM. Saliva and the control of plaque pH. In Edgar WM, O'Mullane DM, eds. Saliva and Oral Health, 2nd edn. London: BDJ, 1996:81-94.
16. Sela M, Gedalia I, Shah L, *et al*. Enamel rehardening with cheese in irradiated patients. *Am J Dent* 1994;7:134-136.
17. Vissink A, Jansma J, Spijkervet FK*et al* ;Oralsequelae of head and neck radiotherapy. *Crit Rev Oral Biol Med* 2003; 14(3):199–212.9.
18. Ripamonti C, Zecca E, Brunelli C *et al*; A RCT to evaluate the effects of zinc sulfate on cancer patients with taste alt.caused by head and necrradiation. *Cancer* 1998; 82(10):1938–45.15
19. Hickey AJ, Toth BB, Lindquist SF *et al*. Effect of intravenous hyperalimentation and oral care on the development of oral stomatitis during cancer chemotherapy. *J Prosthet Dent*1982;47:188-193.
20. Ostchega Y. Preventing and treating cancer chemotherapy's oral complications. Nursing 1980;80:47-52.
21. Daeffler R. Oral hygiene measures for patients with cancer, III. *Cancer nursing* 1981;4:29-35.
22. Ziga SE. In Bavier AR. Nursing management of acute oral complications of cancer. NCI Monographs 1990;9:123-128.
23. Wright WE, Haller JM, Harlow SA, *et al*. An oral disease prevention program for patients receiving radiation and chemotherapy. *J Am Dent Assoc* 1985;110:43-47.
24. Bavier AR. Nursing management of acute oral complications of cancer. *NCI Monographs* 1990;9:123-128.
25. Sreebny L. Xerostomia: diagnosis, management and clinical complications. In Edgar WM, O'Mullane DM, eds. Saliva and Oral Health, 2nd edn. London: BDJ, 1996:43-66.
26. Jereczek-Fossa BA *et al*. Radiotherapy-induced mandibular bone complications. *Cancer Treat* Rev 2002; 28(1):65–74.
27. Teng MS, Futran ND. Osteoradionecrosis of the mandible. *Curr Opin Otolaryngol Head Neck Surg* 2005; 13:217–21.
28. Karsila-Tenovuo S, Jahnukainen K, Peltomaki T *et al*; Disturbances in craniofacial morphology in children treated for solid tumors. *Oral Oncol* 2001; 37(7):586–92.20

29. Myers RAM, Marx RE *et al* Hyperbaricoxygen in postradiation head and neck surgery. *NCI Monographs* 1990;9:151-157.
30. Pankhurst CL, Dunne SM, Rogers JO. Restorative dentistry: Problems and solutions. *Dental Update* 1996;4:110-114.
31. Murray CG, Daly TE, Zimmerman SO. The Late effects of therapy in 94 patients with localized https://www.ncbi.nlm.nih.gov/pubmed/10842248e relationship between dental disease and radiation necrosis of the mandible. *Oral Surg* 1980;49:99-104.
32. Fischman SL. The patient with cancer. *Dent Clin Nth America* 1983;27:235-246.
33. Saral R. Management of acute viral infections. *NCI Monographs* 1990;9:107-110.
34. Hill A, Hanson M, Bogle MA *et al*; Severe radiation dermatitis is related to staphylococcus aureus. *Am J Clin Oncol* 2004;27(4):361–3.

How to cite this article:

Jagmohan.Singh *et al* (2018) 'Management of Radiation Induced Toxicities During Treatment of Head And Neck Cancers', *International Journal of Current Advanced Research,* 07(7), pp. 14131-14135.
DOI: http://dx.doi.org/10.24327/ijcar.2018.14135.2551

****