

## Management of Oral Complications in Patients with Head and Neck Cancer Undergoing Radiotherapy

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### ABSTRACT

Ionizing radiation causes damage in normal tissues located in the radiation portals. Oral complications of radiotherapy in the head and neck region are the result of the deleterious effects of radiation on, e.g., salivary glands, oral mucosa, bone, dentition, masticatory musculature, and temporomandibular joints. The clinical consequences of radiotherapy include mucositis, hyposalivation, taste loss, osteoradionecrosis, radiation caries, and trismus. Mucositis and taste loss are reversible consequences that usually subside early post-irradiation, while hyposalivation is normally irreversible. Furthermore, the risk of developing radiation caries and osteoradionecrosis is a life-long threat. Present study is an attempt to take a review of the management of oral lesions caused in patients undergoing radiation therapy for head and neck carcinoma and to bring out all the possible precautions before the therapy and the management of all the consequences that form as a heavy burden for the patients and have a tremendous impact on their quality of life during and after radiotherapy.

**KEYWORDS:** Oral complications, Management, Radiotherapy.

### INTRODUCTION

Radiotherapy also known as radiation therapy is used in cancer treatment. It uses ionizing radiation, which controls or kills the malignant cells. In case of a localized tumor it remains to be as a curative therapy and as an adjuvant therapy in case of preventing the recurrences of tumor after surgery. Radiotherapy also lies to be interactive with chemotherapy and also after chemotherapy.

The ionizing radiations destroy the DNA of the cancerous cells. In order to spare the normal tissues, the beams are directed from many angles of exposure to intersect with the tumor. The destruction of the DNA occurs by photons or charged particle.

Radiotherapy commonly denoted as RT, RTx or XRT. Radiotherapy can be curative, palliative, therapeutic, adjuvant or neo-adjuvant, where its intention depends upon the size, location, stage of the tumor as well the patient's health. Radiotherapy is also used in treating nonmalignant conditions like trigeminal neuralgia, keloid scar vascular restenosis, hypertrophic ossification, thyroid eye disease, early stages of Dupuytren's disease and Ledderhose disease etc.

### ORAL COMPLICATIONS DUE TO RADIOTHERAPY

Radiotherapy in one side offers as a source of treating cancers and on the other side has a number of complications that occur. Those can be acute, late or cumulative complications. As the topic interests on head and neck cancers, the management of oral complications are concentrated here.

The complications caused during radiotherapy depends on the area of tissue irradiated, size of the tumor, age of the patient, clinical condition of the patient, dosage and the associated treatments. Even a minute increase in the dosage leads to a significant complication. A complication that occurs at the time of therapy is said to be acute and it is reversible. Late complications are that worsens the quality of life, and irreversible, classified into mild, moderate and severe.

### MUCOSITIS

Mucositis is the inflammation of the mucous membrane where oral cavity is the most common site as it is one of the most sensitive parts of the body and is most vulnerable.

It has four stages,

1. Vascular/Inflammatory,
2. Epithelial,
3. Ulcerative/bacteriologic,
4. Healing.

WHO has categorized a scale to measure oral mucositis:

Degree 0 has no signs and symptoms,

Degree 1 erythematous and painful,

Degree 2 ulcer is present but can eat normally,

Degree 3 ulcer is present and can drink only fluids,

Degree 4 patient cannot eat or drink.

The condition worsens when chemotherapy is given in combination with radiotherapy. The worsened condition is called as the confluent mucositis. The mucous membrane of the entire oral cavity and tongue can get coated with a white mucus coating.

Signs and symptoms of this includes redness, shiny or swollen gums and mouth, blood in mouth, dryness, mild burning, difficulty in swallowing or talking, soreness or pain, soft, whitish patch or pus in mouth and increased mucous or thickened saliva in the mouth. Oral mucositis is the debilitating complication of radiotherapy.

The management of oral mucositis is divided into following aspects:

#### **Oral debridement**

Patients with oral mucositis brush with caution as they are neutropenic and thrombocytopenic. Brushing sometimes might cause bleeding gums and there can also result in bacteremia. There can be dried secretions can get staged on the mucosa especially the palate. The Mucolytic agents like Alkalol help to overcome by softening and dislodging the secretion.

#### **Oral decontamination**

Chlorhexidine, Anti-bacterial mouth rinse remains effective as such in reducing the overall bacterial count. The regimen of decontamination includes anti-fungal and anti-microbial rinses. Anti-fungal management usually includes nystatin or clotrimazole troches. But troches cannot dissolve in patients with very dry mouth and so cannot be used. Amphotericin can be used in place of nystatin. Fluconazole can be used for fungal prophylaxis or treatment of suspected cases.

#### **Topical and Systemic Pain management**

Pain is severe and are not restricted only to the oral mucosa. Local rinses and systemic analgesics are given together. Frequent rinsing of the oral cavity should be done in order to keep the oral cavity moist and provides a soothing effect to the ulcerative mucosa. Acute oral mucositis is effectively managed with an oral rinse containing doxepin an anti-depressant.

#### **Prophylaxis/Prevention**

Cryotherapy with ice chip is one of the preventive measure where the patient should suck the ice chip for 30mins prior to therapy. Palifermin a keratinocyte growth factor prevents oral mucositis. Photobiomodulation therapy which is a low-level laser

therapy helps in preventing and managing oral mucositis but its limited in usage. Laser therapy can also be used but it requires varying wavelength and intensity and specialized equipment.

#### **CANDIDIASIS**

Fungal infections are more prone in patients undergoing radiation therapy. It is a common infection in patients undergoing treatment for upper airway tract malignancies. Patients undergoing therapy have greater number of species like *Lactobacillus* sp., *Streptococcus aureus*, *Candida albicans*. Colonization is seen in oral mucosa of 93% of these patients and *Candida* infection is found in 17-29% of patients subjected to radiotherapy. Groz et al showed that the maximum colonization happens after 6 months after radiation therapy and after 12 months the values went back to be lower than normal. The treatment for *Candida* varies substantially and are based on its anatomic location of the infection. Fluconazole remains to be the first line of management for candidiasis. A comparative study of fluconazole with anidulafungin showed that anidulafungin was more effective in treating severely ill patients. The oral candidiasis can be treated either with topical antifungal agents like Nystatin, Clotrimazole, Amphotericin B Oral suspension or systemic oral azoles like Fluconazole, Itraconazole or Posaconazole. Chlorhexidine oral rinses can also be used as it benefits the control of oral thrush.

#### **DYSGEUSIA**

Dysgeusia is the loss of taste sensation. This affects the patient from 2nd or 3rd week of therapy onwards and also last for several weeks. This happens as the taste buds which are radiosensitive lose their histological features as a result of degeneration. The increase of salivary flow viscosity and the saliva biochemical alteration creates a mechanical barrier of saliva which makes it difficult the physical contact between the tongue and foodstuff. The recovery period remains to be around 60-120 days after the end of radiation. Studies show about 70% of patients submitted to radiotherapy have complaint of dysquesia. The management of dysgeusia can be pharmacologic and non-pharmacologic. The pharmacological treatment does not have any guidelines currently. Zinc supplements help in the recovery of loss of taste. Two pilot studies have shown the result with zinc supplements. But a larger phase III trial found Zinc supplementation had no effect on taste alteration. Amino acid glutamate is also one of the management. Strasser et al investigated glutamine's role in reducing taste alterations because research supports the use of glutamine in improving mucositis and recovery time in patients receiving high-dose chemotherapy. Unfortunately, glutamine has not shown to reduce taste alteration in patients receiving taxane-based chemotherapies.

### **RADIATION CARIES**

Patients who do not have caries initially, after subjected to radiotherapy also cause caries which are known as the radiation caries. The causes of this can be of 2 reasons, the teeth is subjected directly to radiation leading to caries and due to lack of salivation with altered properties of saliva.

The management of caries is comment restorations. If the caries have reached until the pulp it required RCT and if the tooth structure is grossly decayed extraction can be another option. A prophylactic measure to prevent caries to some extent, topical fluoride can be applied to prevent the calcification of the tooth structure.

### **OSTEORADIONECROSIS**

This is one the most serious complication of radiotherapy. This is the necrosis of bone due to ischemia that is caused by radiation. There occurs pain and loss of bone structure. The bone cells and the vascular supply suffer with irreversible injuries. This can occur spontaneously or due to any trauma to the site like extraction. The most common site is mandible and the patients with natural teeth are more prone to get affected. Approximately one year after the therapy bone exposure occurs and the risk of the disease is indefinite. About 60% of the patients complain of pain ranging from mild to severe pain. It also results in edema, suppurations and Pathological fracture with severe pain in about 15% of the patients.

The medical treatment includes nutritional supplements, saline irrigation in local wounds. Antibiotics for secondary infection. Pentoxifylline is one of drug that is used which has some success rate. A study done by Roger et al showed medical therapy can be indicated for patients affected with osteoradionecrosis as possible. This occurs in patients with poor health related quality of life.

The most successful treatment for ORN patients is Hyperbaric oxygen. This was proved by Marx in 1983 performing a successful resolution in 58 patients with mandibular ORN. Hyperbaric oxygen alleviates the oxygen tension in the tissues and this stimulates the fibroblast proliferation and the oxygen – dependent collagen synthesis. Anyhow this doesn't offer complete resolution for radiation injury as some degree of tissue hypoxia does persist.

The protocol for ORN given by Marx is as follows:

Stage 1: 30 dive HBO to 2.4 atmosphere for 90 minutes is given and the patient is assessed for evaluating the decreased bone exposure, the granulation tissues that covers the bone that is exposed, resorption of non-viable bone and absence of inflammation. Patients with good response continue upto 40 dive, whereas unresponsive patients get on to stage 2.

Stage 2: Transoral sequestrectomy is performed with primary wound closure which is followed with a total of

40 dive of HBO. If wound dehiscence occurs patient advances to stage 3. Even if the patient presents with orofacial fistula, pathological fracture or resorption of the mandible immediately after initial 30 dive go for stage 3.

Stage 3: It's the transcuteaneous mandibular resection, wound closure, and mandibular fixation with an external fixator or maxillomandibular fixation, followed by an additional 10 postoperative HBO dives.

Stage 3R: After the successful resolution of ORN mandibular reconstruction with wound closure is performed after ten weeks.

### **SOFT TISSUE NECROSIS**

Soft tissue necrosis is the ulcer located in the soft tissues exposed to radiation. This is related to dose, time and volume of the radiated gland. The risk is higher when brachytherapy is used. Soft tissue necrosis is associated with pain. Regular evaluations should be done until the condition subsides as it occurs in the site of primary lesion. Fibrosis can also occur in the soft tissues which may in turn cause trismus.

To manage the condition a good oral hygiene along with the use of analgesics and sometimes antibiotics is necessary.

### **XEROSTOMIA**

Xerostomia also referred to as dry mouth occurs mainly due to an adverse drug reaction. This is one of the most common complication and complaint from the radiated patients. Patients with xerostomia complaint about oral discomfort, loss of taste, difficulty in swallowing and speech. As a result of radiotherapy the properties of the saliva also get altered like decrease in the enzyme activity amylase, pH and buffering activity and electrolytes like calcium, potassium, sodium, phosphate. This leads to oral infections like caries, periodontal disease etc.

Management can be through mechanical or taste stimulants or salivary stimulators or systemic agents. Acupuncture is also one of its management. Systemic agents reduce xerostomia by increasing the salivary flow along with decreased oral problems associated with salivary gland hypofunction. So for the management of radiotherapy induces xerostomia systemic agents are the best choice of management. Systemic agents like pilocarpine and betanecol, when the drugs are used concomitantly with radiotherapy increases the salivary flow at rest as well at the time after the end of radiotherapy.

### **CONCLUSION**

For the treatment of malignancies radiotherapy is the most commonly used as there is increased survival rate. There are still a few complications that occur on going of the therapy or at the end and after a year of the

therapy. These complications affect the quality of life and also the progress of the treatment. The only way to prevent the adverse effects is by undertaking the precautionary measures. This includes the multidisciplinary treatment which includes the medical team, dentists, speech therapists, psychologists; nutritionist is also one of the methods to prevent these complications.

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