



## The Side Effects of Chemotherapy and Radiotherapy Treatment on the Oral Tissue and Teeth, Prevention and Dental Intervention

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### Abstract:

Chemotherapy and radiotherapy treatment cause multiple oral side effects that impair the patient's quality of life. The most common oral side effect is mucositis, infections, salivary gland dysfunction, taste disturbance, osteoradionecrosis, Temporomandibular joint disorder, gingival bleeding, and generalized oral pain. This complication may be acute (short-term) occur during treatment and then resolve after treatment is stopped, or chronic (long-lasting) continue or appear months to years after treatment doses end, and may be caused by the treatment itself (directly) or by the side effects of the treatment (indirectly).

To manage the chemotherapy radiotherapy oral complications the oncologist will work closely with a dentist, if the oral complications become severe the treatment doses need to be decreased or stopped, after consultation with the oncologist.

**Keywords:** Chemotherapy, Radiotherapy, Mucositis, Osteoradionecrosis

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### Introduction:

#### Cancer patients have a high risk of oral complications for a number of reasons:

1. chemotherapy and radiotherapy slow down or stop the growth of fast-growing cells, such as cancer cells, normal cells in the lining of the mouth also grow quickly, so anticancer treatment can stop them from growing too. This slows the ability of oral tissue to repair itself by making new cells.
2. radiation therapy may directly damage and break down oral tissues, salivary glands and bone.
3. chemotherapy and radiation therapy upset the healthy balance of bacteria in the mouth; these changes may lead to mouth sores, infections and tooth decay.

#### The most common oral complications caused by either chemotherapy or radiation therapy this include the following:

1. inflammation appears in the mucous membrane in the mouth (mucositis).
2. Xerostomia (salivary gland hypo function).

3. infections in the mouth or that travel through the blood stream, these can reach and affect cells all over the body.
4. changes occur in the dental growth and developmental stages in the children.
5. The taste sensation is changes.
6. malnutrition and dehydration caused by being unable to drink or eat due to oral mucositis.
7. The incidence of occurring the tooth caries and gingival disease become high. (1)

**Aim of the study:**

The aim of this study is to isolate and describe the oral side effects arising from chemotherapy and radiotherapy treatment and focus on the dentist's contribution to their treatment and management.

**The side effects of chemotherapy and radiotherapy treatment include:**

**A) Oral mucositis:**

Oral mucositis is an inflammation of the mucous membrane that occurs secondary to standard dose of chemotherapy and its target rapidly the proliferating cells particularly in the oral mucosa, they destroy the basal cells of the mucosal layers, and their replacement or turnover is affected resulting in mucosal ulceration.

In patient at the radiation therapy, when the radiation dose of (5 Gray), Erythema is observed, followed by mucositis, atrophy and finally ulceration of the oral mucosa. (3)

OM is a therapy and rate limiting complication of cancer treatment in aggressive chemotherapy protocols associated with bone marrow transplantation and head and neck radiation therapy.

The most common reported oral areas that affected are the buccal mucosa, floor of the mouth and the soft palate but there are no areas that immune.

The first sign of OM is Erythema followed by burning sensation, edema and ulceration with ill defined outline and they covered by pseudo membrane accompanied by bacterial colonization and massive leucocytes infiltration.

When the disease is in its maximum expression Erythema transforms into deep ulceration and pain is severed.

**Risk factors of oral mucositis:**

1. chemotherapy may cause neutropenia in some patients which lead to oral mucositis.
2. the higher dose of chemotherapy and frequency increases the risk of (OM).
3. (5-Fluorouracil – methotrexate) increase the incidence of OM by up to 60%.
4. periodontal disease increases the risk of OM.
5. as well as fungi and viruses, seem to be responsible for ulceration and mucositis. (4)

**- Grade of mucositis according to the world oral health organization :( 6)**

Grade I	Grade II	Grade III	Grade IV
Soreness + or - Erythema	Erythema, ulcers, patient can swallow solid food.	Ulcers with extensive Erythema patient cannot sallow food.	Mucositis to the extent that alimentionation is possible.

Patients with oral mucositis can become extremely debilitated, and their quality of life is greatly diminished.

**Some of the most common treatments used to relieve the symptoms of oral mucositis:**

1. salt rinses have been advanced as being potentially helpful in treating oral ulcers and oral pain and improving dental health.
2. oral debridement can clear the oral mucosa of debris and devitalized tissues.
3. cryotherapy (ice chips) is an inexpensive and readily available treatment.

Relief of symptoms resulted in improved swallowing, eating, and drinking, improved appetite, a decrease in the use of oral pain medications, and improved hydration. (5)

Certain types of foods were eliminated from the Childs or adult cancer patients' diets as hard foods, nuts, spicy food, acidic juice, and foods and liquids at extreme temperatures.

In a study published in the journal of pediatric dentistry which is issued in Egypt to study the effect of (vitamin E) in the treatment of oral mucositis, 80 patients with oral mucositis were randomly distributed into "2" groups; group (A) topically applied vitamin "E" and group (B), vitamin "E" was given systemically. The "2" groups were evaluated for 5 days. Results showed that in group (A) grades of oral mucositis improved significantly while in group (B) no significant improvement was noticed. It's concluded that topical application of 100 mg of vitamin E twice daily is an effective measure for the treatment of chemotherapy-induced mucositis. (9)

#### **B) Xerostomia:**

One of the most common side effects of chemotherapy and radiotherapy is xerostomia; defined as the subjective sensation of dry mouth. It's a consequence of reduced production of saliva. Reduced salivary flow can impair basic oral functions and increase the risk of caries, periodontal disease, and opportunistic infections, in addition to playing a vital role in the protection of the oral mucosa saliva is associated with antimicrobial action and it aids in the digestive gustatory, speech process, chewing and swallowing the development of xerostomia also depends on multiple factors such as the dose and frequency of radiotherapy treatment irradiated volume, site, age, systemic conditions of the patients and associated treatments .studies have shown that glandular tissues are highly sensitive to radiation doses of (20 Gray) can cause reduction of salivary flow, while doses over ( 50 Gray) are able to generate irreversible cessation, leading to worsening compromised conditions of oral tissues.

Treatment of oral carcinomas usually requires a dose of (60 to 70 Gray), radiotherapy treatment may lead to a rapid decline in salivary flow during the first week of radiation; after five weeks of irradiation of (95 %) in the region both stimulated and resting flow are inhibited, virtually ceasing and rarely fully recover. the treatment of xerostomia is mainly palliative. It can be carried out through the use of masticatory, gustatory, or electronic stimulants, saliva substitutes, or systemic agents

Currently, methods that protect the salivary glands against radiation, such as surgical transfer of the submandibular gland, stem cell therapy, and other methods are being developed to improve the quality of life of these patients. (8)

#### **C) Opportunistic infections:**

The intraoral microbial flora during the influence of chemotherapy and radiotherapy treatment shows an increase in streptococcus mutants, lactobacilli, fungi, actinomycetes naeslunda, other bacteria such as Neisseia species, streptococcus sanguis, and fusobacteria decrease. (3)

The occurrence of infections in the mucosa may complicate oral findings, including candidiasis or reactivation of herpes viruses, most commonly the herpes simplex virus (HSV).

Oropharyngeal candidosis using topical therapies is provided. But systemic antifungals such as (Amphotericin B, Fluconazole, or nystatin) are a more common treatment. (4)

Periodontal infection (gingivitis and periodontitis) increased the risk of oral bleeding. Discontinuing dental brushing and flossing can increase the risk of gingival bleeding, therefore, is reduced by eliminating gingival infection before therapy and promoting oral healthy by using a soft toothbrush daily to remove bacterial plaque during chemotherapy and radiotherapy treatment period. Mechanical plaque control not only promotes gingival health, but it also may decrease the risk of exacerbation of oral mucositis secondary to microbial colonization of the damaged mucosal surface. (7)

#### **D) Radiation tooth caries:**

Radiotherapy to the head and neck region causes xerostomia and salivary gland dysfunction which dramatically increases the risk of dental caries and its sequelae. (RT) also affects the dental hard tissues by increasing their susceptibility to demineralization following treatment. Radiation caries is a

rapidly progressing and highly destructive type of dental caries, and usually appears within the first 3 months following RT. The PH after radiation falls from 7 to 5 which is cariogenic. As the PH and buffering capacity of saliva is low, the minerals of enamel and dentin dissolve easily. Consequently, the remineralization capacity of saliva is hampered, with an increase in acidogenic, and cariogenic microorganisms (streptococcus mutans, lactobacillus, and candida species).

The effect of radiation on vascular flow to dentition as a whole also plays a role in this multifaceted caries-promoting cycle. It was observed that minimal tooth damage occurs below 30 Gray; there was 2-3 times increased risk of tooth breakdown between 30 Gray and 60 Gray likely related to salivary gland impact; and 10 times increased risk of tooth damage when the tooth-level exposure dose is above 60 Gray indicating radiation-induced damage to the tooth in addition to salivary gland damage. Clinically, three different patterns have been identified:

**Type1:** most common pattern seen; it affects the cervical aspect of the teeth, and extends to the cemento-enamel junction.

A circumferential decay develops and crown amputation often occurs.

**Type 2:** appears as areas of demineralization on all dental surfaces. Generalized erosions and worn out occlusal and incisal surfaces are seen.

**Type 3:** least common pattern seen as color changes in the dentin. The crown becomes dark brown-black and occlusal and incisal wear can be seen.

The preventive measures prior to radiation therapy should be taken by a complete dental examination, diagnosis, and treatment should be done before the start of the RT, restoration of carious lesion, endodontic therapy, and recontouring of restorations should be done to prevent any future complications. The patient should be given preventive home care instructions that include vigorous oral hygiene such as flossing, daily self-application of topical fluoride, restricted intake of cariogenic foods, and remineralization mouth rinse solutions or artificial saliva preparations. Daily topical 1% sodium fluoride gel application by means of custom-made fluoride carriers is recommended for reducing caries occurrence. **(10)**

#### **E) Osteoradionecrosis of the jaw:**

Is a serious complication of radiation therapy in the cancer treatment, the radiated bone becomes necrosis and exposed. The patient has a sign and symptoms of pain and swelling. ORN occurs most commonly in the mouth during the treatment of head and neck cancer. The determining factor for the development of radiation osteoradionecrosis or radiation osteomyelitis are the nature and the duration of the irradiation, the expense of the jaw segment that is irradiated, the size of the tumor of the jaw, and the condition of the remaining dentition. ORN can be expected after a total dose of over 66 Gray particularly in the mandible, a fear of osseous damage is the primary incentive for detecting and dominating foci of infection before radiation therapy is instituted. **(3)**

In case of radiation therapy, the risk of necrosis of the bone following treatment necessitates life time maintenance of the teeth within the radiation field, and if it's anticipated that dental maintenance will be inadequate, precancer therapy extractions are indicated. When appropriate endodontic therapy can be provided, the most common reason for dental extraction prior to cancer therapy is periodontal disease. **(4)**

#### **F) Tast disturbance:**

Certain head and neck cancers may cause changes in the sense of taste and smell. But often times, these are side effects of cancer treatment for any type of cancer. About 75 percent of people who undergo chemotherapy have some sort of change in their taste. The Radiation therapy for cancer, especially when it's targeted to head and neck may cause damage to the taste buds and salivary glands. **(2)**

Drugs most commonly associated with taste changes include: carboplatin, cisplatin, 5- fluorouracil, levamisole and methotrexate. Tast changes may occur during therapy and last for hours, days, weeks, or even months after chemotherapy. It's managed by eat small, frequent meals and do not eat 1-2 hours

before chemotherapy and up to 3 hrs after therapy, also avoid cigarette smoking and increase fluid intake. (14)

#### **G) The effect of radiotherapy treatment on the Temporomandibular joint:**

Radiotherapy to the head and neck regions can result in serious consequences to the TMG and surrounding muscular structures. Ionizing radiation leads to tissue changes that appear as trismus. Furthermore, radiation-induced masticatory muscle fibrosis, inflammation and atrophy reduce jaw mobility and induce trismus. The severity of these effects can be related to the radiation dose received and the amount of tissues involved. It has been suggested that as the radiation dose to the TMG and pterygoid muscles is increased, the maximal jaw opening decreased linearly. Magnetic resonance imaging (M.R.I) demonstrates soft tissue alterations after radiotherapy, such as changes in muscle morphology and signal intensity. Also, fibrosis, inflammation and denervation atrophy. (11)

Trismus at early stage may only affect the speech, but in severe cases nutritional intake and oral hygiene condition may deteriorate seriously. Management of trismus is by reducing the dose delivered to the TMJ.

Other several management options for trismus, they include physiotherapy, use of pharmaceuticals, micro-current therapy and oxygen therapy. Rehabilitation training for patients with trismus can slow down the progress and improve swallowing function; this mainly focuses on the use of jaw stretchers and mouth- opening exercise. The exercises include repetitive mouth opening and closing, as well as protraction, retraction and lateral jaw movements under prescribed protocol. A report suggested cricoideotomy as alternative management if both pain control and physiotherapy are found to be ineffective. (15)

#### **H) The effect of chemotherapy treatment on the developing dentition:**

Chemotherapy and radiotherapy have deleterious effects on dentition in children and adolescents. Hypodontia (partial anodontia), microdontia, and altered eruption patterns are some of the stated complications. Developmental abnormalities resulting after malignant chemotherapy occur when the patient is treated prior to six years of age. (16)

#### **Oral care for cancer patient before chemotherapy and radiotherapy treatment:**

1. Eliminate any area of infection.
2. Remove orthodontic bands if highly stomatotoxic chemotherapy is scheduled.
3. Institute periodontal disease, control measures that induce plaque control.
4. provide oral hygiene instruction. (12)
5. Use of chlorhexidine prior to treatment can help cut down on the chance of infection.
6. Schedule dental work a few days prior to chemotherapy treatment, this is the time when the patient feels best; after treatment, they have become weak.
7. Schedule oral surgery at least 7 to 10 days before myelosuppressive therapy begins. (13)

#### **Oral care during chemotherapy and radiotherapy:**

1. Patient under intense chemotherapy is at risk for fungal and yeast as well as bacterial infections, nystatine to prevent fungal infection can be used to prevent or treat.
2. during the chemotherapy the ANC (Absolute Neutrophil Count) may drops makes it harder to fight off infection, so more dental care should be done.
3. Identify and treat existing infections and tissue injury or trauma.
4. conduct prosthodontic evaluation if indicated. If are movable prosthesis is worn, make sure that it's clean and well adapted to the tissue, instruct the patient not to wear the prosthesis during treatment, if possible, or at the least not to wear it at night. Schedule the dental treatment in consultation with the oncologist to do findings.
5. Smoking cessation, studies have shown that smoking interferes with some chemotherapy treatment. (13)

#### **Oral care for cancer patients after chemotherapy and radiotherapy treatment:**

Once all complications of chemotherapy have resolved, patients may be able to resume their normal dental care schedule. However, if the immune function continues to be compromised it determines the

patient's hematologic status before initiating any dental treatment or surgery. This is particularly important to remember for patients to have undergone stem cell transplantation. The dentist must be asking the patient if has received intravenous Bisphosphonate therapy that may causing osteonecrosis in the jaw. (13)

### **Conclusion:**

A complete dental examination (clinical examination and full mouth radiographs), diagnosis, and treatment should be done before the start of radiotherapy and chemotherapy. Also, a complete examination of the mucosa, dentition, and periodontium should be done. Teeth vitality should be assessed; restoration should be done prior to initiation of radiotherapy and chemotherapy to prevent any future complications.

The dentist has an important role in decreasing the side effects of chemotherapy and radiotherapy treatment which influence the patient's quality of life and increase the incidence of healing of cancer.

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