

# Cancer Therapy: Oral Complications And Its Management

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## **ABSTRACT-**

*Over past three decades, cancer survival rate indicates the presence of problem in life quality of cancer patients. Oral health is valuable in an individual's overall life quality. But adverse effects of cancer therapies such as surgery, chemotherapy and radiotherapy affects the oral health status severely. Prevention and treatment of these complications should be considered by the clinician. This review article gives a detailed description about oral complications first which is then followed by management of those oral complications.*

**Key words:** Oral complication, Chemotherapy, Radiotherapy

## **INTRODUCTION**

Cancer is a terrifying experience for many people and it is a course of great pressure and stress for patients and their relatives starting from its diagnosis till the treatment. Survival rates vary with stages at which cancer is diagnosed and it also differs based on the cancer types. 5- year survival rate is collected from 2002 to 2008 for all cancers, where the rate is 68% compared to 49% in 1975–1977.<sup>1</sup>Improvement in cancer diagnosis and treatment approach ensures increased opportunity for dentists to meet patients who are under or already underwent cancer treatment. Cancer treatment approaches are surgical resection, chemotherapy and radiotherapy. Soft and hard tissue of the oral structures are affected by radio- and chemotherapy directly but their systemic toxicity causes damages indirectly. Acute and chronic oral complications appear during and after cancer therapy and it often encircle mucositis, dysgeusia, and infectious diseases<sup>2</sup>. Oral health maintenance is mandatory for preserving daily activities which involves eating, communications and for preventing infectious diseases<sup>3</sup>. Though dental treatment is essential for maintaining good oral health and preventing pathological condition, priority is often given to cancer treatment since it is a life threatening condition<sup>4</sup>. Hence oral health status of cancer patients is important for all health care practitioners including dentist since it is ethical and medical/legal responsibility.

## **ORAL COMPLICATIONS**

Certain oral complications are related to cancer treatment. They are stomatitis, infection, bleeding, mucositis, pain, loss of function and xerostomia. The three anatomical sites usually affected by these complications are oral mucosa, periodontium and teeth<sup>5</sup>.

### **Surgical Complications**

The long-term complications are limitations on speech, mastication and swallowing, cranial nerves damage and the result is neurological issues, chronic fistulas, and healing problems to aesthetic considerations including severe deformity and prosthetic rehabilitation<sup>6</sup>. Complications associated with surgery is listed below

SURGERIES	COMPLICATIONS
Ablation of Tongue	Due to significant loss of tongue, mastication and transfer of bolus is difficult
Surgery in floor of mouth, maxilla, and mandible along with adjacent tissues	Difficulty in chewing

Maxillary or mandibular resection	Difficulty in grinding and diminished biting force
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## TRISMUS

It is a usually a postsurgical complaint. Postoperative healing, including fibrosis and scar contraction results in limited interocclusal opening less than 35 mm between maxillary and mandibular incisors. Maxillary surgery involving origin of medial and lateral pterygoid muscles from the pterygoid plates and mandibulectomy involving any of the muscles of mastication can cause Trismus.<sup>7</sup>

## ENUCLEATION OF PRIMARY TUMOR AND LYMPH NODES

This causes damage to cranial nerves such as spinal accessory nerve, phrenic nerve, hypoglossal nerve, lingual nerve, vagus nerve, sympathetic trunk, and marginal mandibular branch of the facial nerve.

## FISTULA

Another complication associated with oral oncological surgery. It appears within 3-4 weeks or 1 week after surgery. Post surgically chronic fistulas persist for 1 month. Prevention is best but treatment such as surgical excision and closure of the mucosa and skin are indicated .<sup>6</sup>

## Chemotherapeutic Complications

Chemotherapeutic agents affect not only the malignant cells but also the normal tissue. Depending on patient's immune status before and during chemotherapy regimen is treatment frequency and dosage, the route of administration, and tumour type. These drugs cause oral complications such as mucositis, pain, infection, haemorrhage, xerostomia, and neurologic and nutritional problems in some patients <sup>8</sup>.

## ORAL MUCOSITIS

- It is an iatrogenic condition of erythematous inflammatory changes which often appear on buccal and labial surfaces, the ventral surface of the tongue, the floor of the mouth, and the soft palate of patients who are under chemotherapy.
- Severity: Ranges from localized to generalized erythema; to frank ulceration and haemorrhage.
- Clinical features: Initially it is described as a burning sensation causing hypersensitivity. Progression of this condition causes difficulty in eating, swallowing, and talking. In severe cases, it leads to anoxia-induced brain injury and even death <sup>9</sup>.
- After the initiation of chemotherapy, mucositis usually begins with aplasia as a variant of iatrogenic stomatitis in 7–14 days.
- Clinical Signs: Leukoedema appears as a poorly defined milky white area which is often observed on the buccal mucosa, which vanishes during movement <sup>8</sup>After 1-2 weeks, epithelial loss and development of severe ulceration is observed <sup>10</sup>.
- Subjective input and clinical assessment of the patient is noted. By combining both objective and subjective elements World Health Organization (WHO) has given a grading scale

**TABLE:1 WHO Oral Mucositis Grading <sup>11</sup>**

Grade	Clinical presentation
0	Normal
1	Soreness with/without erythema
2	Ulceration and erythema
3	Ulceration and extensive erythema, patient cannot swallow solid food
4	Mucositis of such severity that feeding is not possible

## MANAGEMENT

Currently there is no medication to eradicate mucositis<sup>2</sup>. But painful symptoms are treated. For relieving pain an oral solution mixture known as “Magic Mouthwash,” is used where it is composed of diphenhydramine, viscous lidocaine, bismuth, subsalicylate and corticosteroids. It relieves acute pain and reduces inflammation thus enhancing an easier way of food consumption. Opioids are used to treat high grade mucositis pain.<sup>12</sup> Application of ice chips to the mouth every 30 minutes is a method used by the oncologists for preventing and treating oral mucositis

## ORAL INFECTIONS

Oral infections associated with chemotherapy accounts for 25–50% of infections which promotes morbidity and mortality in patients. Sensitive areas are teeth, gingiva, salivary glands, and mucosa. Oral microbial flora and opportunistic microbiome such as coagulase-negative Staphylococci and Streptococci, Klebsiella pneumonia, Pseudomonas aeruginosa, and Escherichia coli are responsible. It was explained that pathogenic microorganisms present subgingivally or in periradicular area causes acute exacerbations of existing periodontal or periradicular infections when there is a fall in granulocyte count below 1000/mm<sup>3</sup><sup>13</sup>.

### Fungal infections

- Most dangerous complication dominant among infections is fungal infection, most notably caused by Candida species.
- Mortality rate: Higher when compared to other infections and oral cavity is the most predominant site for this infection.<sup>13</sup>
- Clinical Condition: Manifest in various forms, among which erythematous or pseudomembranous candidiasis occurs frequently.
- Erythematous candidiasis: Appears as patchy or diffuse erythematous areas often affecting the palate.
- Pseudomembranous candidiasis: Clinically observed as curd-like or white patch lesions, producing bleeding and erosion below the tissue when rubbed off.
- Hyperplastic candidiasis: Appears as swollen white plaques resembling leukoplakia which cannot be scraped off.
- Chronic atrophic candidiasis: It is often troublesome which is usually accompanied by angular cheilitis (an infection at the corner of the oral cavity where it include Staphylococcus species) and denture stomatitis (caused by illfitting denture bases particularly in maxilla and it also acts as a source of chronic irritation and reservoir for Candida albicans)<sup>8</sup>.

## MANAGEMENT

According to Infectious Disease Society of America (IDSA), clotrimazole troches and nystatin pastilles are the first line drugs for mild oropharyngeal candidiasis. But in certain situation like hyposalivation and/or mucositis, it may be difficult to apply, hence an alternate solution i.e. nystatin rinse is used. IDSA also recommends systemic fluconazole (100–200 mg/day for 2 weeks) for treating moderate to severe infections. In case of fluconazole resistance, itraconazole capsules (200 mg/day for 2–4 weeks) or itraconazole oral solution (200 mg/day for 2 weeks) can be used. Posaconazole is suggested as a second line drug by IDSA<sup>14</sup>

### Viral infections

- Most commonly seen in patients under chemotherapy. Viral species such as herpes simplex virus (HSV), varicella zoster virus (VZV), and cytomegalovirus (CMV) are often involved<sup>8</sup>.
- Herpes Simplex Virus (HSV) reoccur 7–14 days after chemotherapeutic treatment and lesions are observed on lips and keratinized mucosa where they appear as small vesicles which ulcerate and coalesce rapidly. Luckily if it is self limiting, and it cures in 14 days.
- VZV infections also referred as herpes zoster/shingles occur within the trigeminal dermatome. Extraorally or intraorally lesions are observed with characteristics of halting at the midline on the side of the respective trigeminal division.
- Cytomegalovirus (CMV): Intraorally, these infections are observed as irregular pseudomembranous ulcerations along with certain clinical manifestations such as esophagitis, gastritis, colitis, hepatitis,

pneumonia, and retinitis. Moreover fever is also involved but usually cures within 3–5 days. CMV progression in immunosuppressed patients is usually fatal<sup>8</sup>.

## MANAGEMENT

- Acyclovir (200–800 mg thrice a day) or valacyclovir (500 mg twice a day).
- Intravenous dose of acyclovir 5 mg/kg for every 8 hours or perorally 200–400 mg for 3–5 times a day can also be given.
- An alternative drug is famciclovir. If patient is resistant to famciclovir, intravenous foscarnet may be used<sup>15</sup>.

## Bleeding

Another complication related to chemotherapy where bleeding can be rapid, traumatically induced, or from existing pathology<sup>16</sup>. Bleeding can also be due to thrombocytopenia secondary to hematopoietic tissues suppression. Laboratory tests are used for testing bleeding potential. Thrombocyte count and bleeding time makes dentist very clear about the platelet quantity, quality, and functions.

## Radiotherapeutic adverse effects

Due to radiotherapy certain intraoral and extraoral tissues such as salivary glands, taste buds, mucous membranes, bone and teeth, the temporomandibular joint (TMJ) and related musculatures are usually affected. Side effects of radiotherapy are classified into acute and chronic types. Acute symptoms appear early in radiotherapy period and persist 2-3 weeks after treatment, whereas chronic symptoms appear at any time after completion of treatment, ranging from weeks to years<sup>17</sup>.

## Xerostomia

- It is a most often reported oral complication in patients under radiotherapeutic treatment for head and neck cancers.
- Ionizing radiation leads to irreversible damage of glandular tissue and decreased salivary fluid secretion.
- Progressive glandular atrophy, fibrosis and decreased salivary outflow happens after early exposure to radiation and it becomes severe afterwards.
- If major salivary glands are exposed to radiation then the prevalence of xerostomia ranges from 94% to 100%.
- Clinical features: It becomes apparent since saliva appears “scant, sticky, and viscous.” Patient have complaints oral discomfort, pain, dryness of the mucosa which in turn causes difficulties in speech, chewing, and swallowing affecting their quality of life.
- Reduction in salivary outflow increases the dental caries and calms down the mucosal integrity.
- After a few months, hypertrophy of the unirradiated salivary gland occurs and lasts up to 1 year after treatment thus aggravating the condition; but if all the major salivary glands are involved in the field of radiation, salivary function is predicted to decrease 50–60% within the first week<sup>18</sup>.
- Since taste is related to salivary functions, taste loss occurs in relation to xerostomia

## MANAGEMENT

- Sips of water must be frequently taken for every 10 minutes and melt ice chips are kept in mouth for comfort.
- Artificial saliva spray (e.g., Xerotin, MoiStir, Salivart, Xero-Lube, Saliva Orthana) and mouth moisturizing gel (e.g., Biotene Oral Balance) can be used.
- Lubrication of lips can be done with petroleum jelly.
- Avoid coffee, tea, soft drinks with sugar and alcoholic mouth rinses since they can dehydrate the mouth.
- Alcohol-free mouth rinses (e.g., BioXtraalcoholfreemouthrinse, Biotene mouthwash, and OralSeven moisturising mouthwash) can be used.
- Saliva stimulating tablets and medications like pilocarpine (Salagen, 5 mg, thrice a day) can be used to increase salivary gland activity and salivary flow rate.
- For salivary flow stimulation and to avoid caries sorbitol- or xylitol-based chewing gum can be used.

### Dysgeusia

- Dysgeusia occurs at a rapid rate and gets aggravated to an accumulated dose of 30 Gy, then taste deterioration progression reduces as perception for all four tastes, that is, salty, sweet, sour, and bitter, nears zero.
- Additionally microvilli damages happens due to radiation which may result in secondary taste loss<sup>19</sup>.
- Luckily, in majority of cases taste acuity is partially or completely restored in 20–60 days and 2–4 months after radiation therapy, respectively.

### MANAGEMENT

- Supplementing diet with vitamin D
- Dietary counselling

### Radiation-Induced Mucositis

- It is the most dangerous and worrisome acute reaction for patients under radiotherapy persisting 2-3 weeks post radiotherapeutically. About 90% to 95% of patients exhibit complete resolution by the end of 4th week
- Erythema appear due to thinning of epithelium and vascular dilation, inflammation, and oedema of the submucosa<sup>20</sup>.
- As treatment continues, mucosa gets ulcerated and fibrinous exudate can be seen. Bleeding can also be observed.
- Symptoms: Intense pain, dysphagia, and odynophagia.

### Other complications due to radiotherapy:

- Dental pulp of patients under radiotherapy exhibits decreased vascularity with fibrosis and atrophy.
- Pulp responds to trauma, dental procedures, and bacterial infections can be compromised, but pain tolerance was found to be raised.
- In tooth development, tooth bud might be demolished if irradiation happens before significant calcification hence development is reduced. During later stage of development, enamel and dentine disorders can be noticed if tooth bud is exposed to radiation.
- Direct ionizing radiation affects TMJ and the muscles of mastication leading to fibrosis and contracture thus resulting in trismus<sup>21</sup>.

### CONCLUSION

Though acute oral complications of cancer therapies can be reduced, they remain unavoidable. Awareness is required for prevention. Hence every clinician involved in cancer therapy should be aware of these complications to treat and prevent the patients, by which best patient care at an appropriate time can be provided.

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