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Chemotherapy And Its Dental Implications

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Abstract
Chemotherapy serves as a pivotal treatment for neoplasms, yet its impact on normal structures, the oral cavity for instance, can be devastating. The use of chemotherapy will invariably lead to the cessation of cell replication, resulting in numerous, systemic, and oral side effects including but not limited to: mucositis, xerostomia, infections, and an increase in bleeding tendencies. This review article focuses on the analysis of the mechanisms of chemotherapy, its systemic and oral complications, its classification as well as its dental management aspects. Of great importance in this article are the preventive measures, treatment changes, and novel methods that aim to lessen the effects of chemotherapy. Knowing how chemotherapy works and bearing in mind its dental implications provides an opportunity of taking measures that enhance the treatment outcomes and the quality of life of the patients.(1)

Keywords
Chemotherapy, mucositis, xerostomia, oral infections, systemic and oral complications

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I. Introduction

One of the leading causes of death worldwide is cancer. Chemotherapy, immunotherapy, radiation therapy, and surgery are all used to treat cancer. Chemotherapy is one of the best treatments. Chemotherapy is the treatment of cancer by using cytotoxic drugs which are capable of terminating the life of the tissues that make up a living thing like a human or animal. The drugs that usually bring the best results are devitalizing the rapidly growing neoplasms. The unfortunate side to these treatments is that, normal tissues, are also affected in some way leading to a number of other unwanted effects which are detrimental to a human being's health.

The oral cavity is the zone that suffers the most from the side effects of chemotherapy because of its high rate of cell death, microbiome, and nonstop contact with the environment. The chemotherapy induced side effects like mucositis, xerostomia, bacterial infection, and bleeding disorders will greatly hinder the patient's quality of life.

Medical practitioners in the area of dentistry need to be familiar with the consequences that arise from under going chemotherapy. Dental management plan is needed at all levels of a cancer treatment cycle before, during transition to, and after chemotherapy treatment. This Review Paper highlights the elements of chemotherapy, its mechanism, oral complications, and the best dental intervention within standard protocols for the patients who suffer.

II. Overview Of Chemotherapy

Mechanism of Action

The therapeutically intended treatment of disease is done using a cytotoxic drug which closes the mitosis and DNA copy mechanisms of the sick cell. It also imposes collateral damage on normal cells. Rapidly dividing tissues such as bone marrow, gastro-intestinal tract, and oral cavity tissues are also harmed, leading to considerable side effects. Common mechanisms of action include: (2)

1. Inhibition of DNA Synthesis – Nucleotide phosphorylation in cell division is arrested by drugs like Methotrexate and 5-Fluorouracil.

2. Disruption of Microtubule Function – Mitosis spindle formation is inhibited and halted by Paclitaxel and Vincristine, which also leads to cell division arrest.

3. Induction of DNA Damage – Apoptosis is induced by some alkylating agents such as Cyclophosphamide, due to cross-linking of DNA strands.

4. Targeted Therapy and Immunotherapy – The cancer tissues are the targets of monoclonal antibodies by using immune checkpoint inhibitors drugs like Pembrolizumab and Trastuzumab which spares other normal tissues.

Classification of Chemotherapeutic Drugs

Classification of chemotherapeutic drugs is done based on the way and mechanism in which they function, as well as their chemical composition.(3)

Alkylating Agents: These are effective for resting and dividing cells. These work by adding alkyl groups to the DNA which causes cross-linking, breaking the strands and preventing replication.(4)

Cyclophosphamide which is used in different types of cancer treatment such as Lymphoma and Breast cancer and can cause bladder lining to bleed and become inflamed known as Hemorrhagic Cystitis.

Cisplatin is often used while treating cancers of the head and neck, but it is also associated with nephrotoxicity and toxicity of the nerves.

Chlorambucil is often used in chronic lymphocytic leukemia (CLL).

Busulfan is used for chronic myeloid leukemia (CML) but it may lead to pulmonary fibrosis.

2. **Antimetabolites:** These drugs inhibit the the formational processes of a nucleotide, thus inhibiting the replication of DNA and RNA. They act like natural metabolism of the cell and worsen cell activity.

Osteosarcoma and leukemia are treated with **methotrexate**, a folate antagonist and may cause hepatotoxicity

Cancers of the colorectal and breast region are treated with **5-fluorouracil (5-FU)**, a pyrimidine analog that may lead to severe mucositis.

Ara-C (Cytarabine) is a type of cytosine analogue employed in acute myeloid leukaemia (AML) where patients suffer from cerebellar toxicity.

Gemcitabine is used to treat pancreatic tumours and non small cell lung cancer. Gemcitabine has the side effect of flu-like symptoms.

3.**Mitotic Inhibitors:** Plant Alkaloids These drugs prevent the microtubule function, stopping the formation of mitotic spindle and halting the cell division.

Vincristine is a vinca alkaloid used in pediatric leukemia and peripheral neuropathy is a major side effect.

Vinblastine is used in Hodgkin's lymphoma; associated with bone marrow suppression.

Paclitaxel is a taxane used in ovarian and breast cancer with hypersensitivity reactions and neurotoxicity. Another drug of taxane classification is **docetaxel**, predominantly used in prostate and lung cancer.

4.**Topoisomerase Inhibitors** These drugs also inhibit are topoisomerases enzymes which are essential for DNA replication and repair.

Anthracyclines such as **Doxorubicin**, which are increasingly used in breast cancer and lymphomas, have been linked to cardiac toxicity.

Acute leukemia is treated with **daunorubicin**, so cardiac failure arises with dosage.

Etoposide is a traditional podophyllotoxin topoisomerase II inhibitor used for lung cancer.

A topoisomerase I inhibitor used for colon cancer, **irinotecan** may cause severe diarrhea

Antibiotic Antitumor Agents

They are cytotoxic antibiotics that act by inhibition of DNA and RNA synthesis.

Bleomycin is an anticancer agent which is used for in both testicular cancer and Hodgkin's lymphoma; major side effect of Bleomycin has shown to be pulmonary fibrosis.

Mitomycin C is used for gastric and pancreatic cancer and may cause severe myelosuppression (decreased blood cells and platelets)

Dactinomycin (Actinomycin D) is used in Wilms' tumor and Ewing's sarcoma.

Hormonal Agents

These drugs inhibit hormone receptors or reduce hormone production, and are used to slow the growth of hormone-dependent tumors.

Tamoxifen is a selective estrogen receptor modulator (SERM) employed in estrogen receptor-positive breast cancer.

Anastrozole is an aromatase inhibitor used for postmenopausal breast cancer.

Flutamide is an androgen antagonist frequently used in prostate cancer.

Leuprolide is a gonadotropin-releasing hormone (GnRH) analog used in prostate and breast cancer.

Targeted Therapy and Monoclonal Antibodies

These drugs specifically focuses on the receptor or proteins needed by malignant cells.
Trastuzumab (Herceptin) that targets HER2 receptors in breast cancer
Rituximab, a monoclonal antibody against CD20, is used for B-cell lymphomas.
Imatinib (Gleevec), a tyrosine kinase inhibitor, is used in chronic myeloid leukaemia:
Bevacizumab is an anti-angiogenesis drug that inhibits vascular endothelial growth factor (VEGF), thus reducing angiogenesis in tumors.
Chemotherapy treatment plan commonly used.
Polyppragmasia is a type of cancer treatment which is used to increase the effect of the treatment and to reduce the resistance of the drugs. A common treatment plan with chemotherapy is:
CHOP (Cyclophosphamide, Doxorubicin, Vincristine, Prednisone) is used in lymphoma.
FOLFOX (5-Fluorouracil, Leucovorin, Oxaliplatin) is used in colorectal cancer (5)
AC-T (Adriamycin, Cyclophosphamide, Paclitaxel) is used in breast cancer

These are some of the treatment plans that affect oral health based on their cytotoxicity and duration of drug administration.

III. Systemic Side Effects Of Chemotherapy

Chemotherapy kills malignant cells as well but also causes damage to normal body tissues leading to multiple systemic side effects. The extent of these side effects is related to the treatment preventive plan, the dosage of the drug, and patient specific factors such as age, sexuality, environmental factors etc.(11)(35)

Hematological Effects
Myelosuppression caused by chemotherapy leads to decreased blood cell production.
RBCs are responsible for carrying the blood, and thus a decrease in the count of RBCs results in Anemia. Patients with a decrease in RBCs suffer from the following pallor, fatigue and breathlessness.
White Blood Cells (WBCs) Decrease in WBCs count leads to Neutropenia which increases the chances of infections like bacterial, fungal, and viral.
Platelets Thrombocytopenia is caused by decrease in the platelet count and increasing the risk of continued bleeding causing gingival bleeding, epistaxis, and petechiae.

Gastrointestinal Toxicity
Chemotherapy affects rapidly dividing cells in the gastrointestinal (GI) tract, causing:
Nausea
Vomiting
Diarrhoea
Malabsorption
Mucositis

Neurotoxicity
Peripheral Neuropathy is seen in patients which are taking drugs like paclitaxel and vincristine, causing tingling, numbness, and loss of coordination. (6)
Chemo Brain is a cognitive dysfunction characterized by memory loss and reduced concentration. (6)

Cardiotoxicity

Drugs like **doxorubicin** and **trastuzumab** cause cardiac dysfunction, like Arrhythmias, Congestive heart failure, Cardiomyopathy

Renal and Hepatic Toxicity
Acute kidney injury can be caused by Cisplatin-induced nephrotoxicity.
Liver fibrosis can occur due to Methotrexate hepatotoxicity.

IV. Oral Complications Of Chemotherapy

Chemotherapy has a major effect on the oral cavity, significantly impacting a patient's quality of life and increases the risk of secondary infections. These complications arises due to cytotoxicity, immunosuppression, and alterations in oral microbiota caused by the drugs used in chemotherapy.(7)(8)(9)(10)

Oral Mucositis

Inflammation and ulceration of the oral mucosa that leads to pain, burning sensations, and difficulty in eating and speaking. These symptoms are common with **methotrexate**, **5-fluorouracil (5-FU)**, and **doxorubicin**.

Xerostomia (Dry Mouth)

Reduced salivary secretion due to damage to the salivary glands. Common in patients which are undergoing the treatment of head and neck cancer which includes radiation therapy along with chemotherapy. Xerostomia increases the risk of dental caries, periodontal disease, and oral infections.

Dysgeusia (Altered Taste Sensation)

Patients may experience from metallic, bitter, or no taste sensation. Dysgeusia can be temporary or can be for months after chemotherapy. Dysgeusia is caused by the effects of chemotherapy drugs on taste buds and salivary glands.

Opportunistic Oral Infections

Fungal Infections like Oral candidiasis or Oral thrush can occur due to the overgrowth of Candida Albicans. Symptoms like white patches on the tongue and mucosa are observed.

Bacterial Infections increase the risk of periodontal infections and periapical abscesses due to the decrease in immunity known as immunosuppression.

Viral Infections can cause the reactivation of herpes simplex virus (HSV), causing painful ulcers in the oral cavity.

Tooth and Enamel Changes

Chemotherapy administered during the phase of growth of teeth (children) can cause enamel hypoplasia and root changes. Causing hypomineralization which makes the tooth more susceptible to decay. This was common with high-dose chemotherapy used to treat pediatric cancers.(11)

Bleeding and Gingival hyperplasia

Myelosuppression leads to thrombocytopenia, continues gingival bleeding. Drugs like methotrexate and cyclosporine can cause gingival hyperplasia.

Osteonecrosis of Jaw (ONJ)

ONJ can also occur with some chemotherapy agents, although this is more commonly associated with patients taking bisphosphonates. Slow wound healing following tooth extractions and an increased risk of osteonecrosis.(12)(13)

Oral Mucositis Induced by Chemotherapy

Pathogenesis: Triggered by direct DNA damage and oxidative stress. They release inflammatory cytokines (TNF-α, IL-6) which leads to epithelial ulceration and pain(9)(14)(15)(16)

Clinical Features: Starts as painful erythematous patches that progress to ulcers with underlying fibrinous pseudomembrane. Usually affect the buccal mucosa, dorsum of tongue, soft palate. Peaks within 7-10days of the treatment.

Grading (WHO Scale):
1. Grade 1 – Mild soreness, no ulcers
2. Grade 2 – Painful erythema, ability to eat solid food
3. Grade 3 – Ulceration, difficulty eating
4. Grade 4 – Severe ulceration, inability to eat

Management:
Topical anesthetics (e.g., lidocaine gel)
Mucosal coating agents (sucralfate, benzydamine mouthwash)
Low-level laser therapy (LLLT) – Reduces severity
Palifermin (keratinocyte growth factor) – FDA-approved for severe mucositis

Xerostomia and Salivary Gland Dysfunction

Impaired salivary gland functions can occur through Chemotherapeutic agents like cyclophosphamide and 5-fluorouracil ,leading to:

- Dry mouth
- Increased dental caries risk
- Dysphagia and altered taste perception

Management: Artificial saliva substitutes, Sialogogues (pilocarpine, cevimeline), Frequent hydration and sugar-free gum

Chemotherapy-Associated Infections
Oral Candidiasis
Bacterial Infections – Staphylococcus aureus, Streptococcus viridans causing periodontal and periapical infections
Viral Reactivation – Herpes simplex virus (HSV), Epstein-Barr virus (EBV)
Management:
Antifungals: Nystatin, Fluconazole
Antibiotics: Amoxicillin-clavulanic acid for bacterial infections
Antivirals: Acyclovir for herpes reactivation

Bleeding Tendencies
Thrombocytopenia → Increased gingival bleeding
Capillary fragility → Petechiae, ecchymosis
Impaired clotting → Prolonged post-extraction bleeding

Dental Considerations:
Platelet count >50,000/mm³ needed before invasive procedures
Tranexamic acid mouthwash for hemostasis

Osteonecrosis of the Jaw (ONJ)
Risk Factors: Bisphosphonates, high-dose chemotherapy
Clinical Features: Non-healing exposed bone, pain, secondary infections
Prevention: Avoid extractions in high-risk patients(12)

Dental Management before, during and after chemotherapy

Dental care in cancer patients require a collaborative multidisciplinary approach and strong communication between oncologists, dentists and oral medicine specialists.(14)(17)(18)(19)

Pre-chemotherapy Phase: Prophylactic Measures
Goals: To remove possible sources of infection.
Severe oral complications mitigation
Recommended Dental Protocol
Full Oral Examination
Evaluate for oral hygiene, periodontal status, and existing restorations.
Radiographs for periapical pathologies.

Periodontal & Restorative Care: Scaling and root planning for active periodontal disease. Restoration should be done to reduce the chances of emergencies during chemotherapy.

Tooth Extractions & Oral surgery: Extract all non-restorable teeth a minimum of 2 weeks before chemotherapy to allow time for healing. Elective extractions in patients receiving high-dose bisphosphonates should be avoided.
Education of the patients & Optimization of Oral Hygiene
Soft-bristled toothbrush + fluoride toothpaste.
Chlorhexidine (0.12%) mouthwash for plaque control
Do not use alcohol-based mouth rinses that could irritate the mucosa.(18)

Management of Oral Side Effects During Chemotherapy

Patients on chemotherapy tend to need alterations in oral care to prevent complications. Chemotherapy affects the oral cavity considerably due to its action on rapidly dividing cells such as those in the oral mucosa, salivary glands, and bone marrow.(20)(21)(22)

Long-Term Dental Considerations after Chemotherapy
Periodic dental follow ups (every 3–6 months).
Management of late complications (xerostomia, secondary malignancies).
Rehabilitation of patients with a high degree of edentulousness using prosthodontic procedures.(23)

Oral implications of chemotherapy in the paediatrics patients

While cancer is uncommon in children its prevalence as a pediatric illness is increasing by 1% annually. Consequently, cancer is now one of the top causes of death among children under the age of 14. Pediatric patients with various risk factors undergoing chemotherapy are at high risk for oral cavity complications. Such factors may range from the patient's age, types of malignancy, pre-treatment oral status and the quality of oral care given during anticancer therapy. Additionally, other drug-related factors as the chemotherapeutic agent's cumulative dose, timing and route of administration of the drug, and the use of other treatment modalities (i.e. the combination of chemotherapy and radiotherapy) plays important role.(4)(11)(25)

Besides the well-known problems like Oral Mucositis, Xerostomia, Opportunistic Oral Infections, enamel hypoplasia, and Gingival Hyperplasia. Paediatric patients undergoing chemotherapy can experience major effects in the development of their teeth and oral structures, resulting in a plethora of dental anomalies.

Eruption of Permanent Teeth is Delayed

Chemotherapy, causing disruption of normal odontogenesis process in children undergoing chemotherapy especially before the age of five, may result in the delayed eruption of the permanent teeth. This is due to the cytotoxic effects of the chemotherapy agent on the developing tooth structures like tooth buds, periodontal ligament, and surrounding bone.(4)

Dental anomalies

As a consequence, a wide range of dental anomalies can be observed in paediatric patients receiving chemotherapy: including microdontia (abnormally small teeth), hypodontia (missing teeth), and enamel hypoplasia.(4)

Craniofacial Growth Issues

When pediatric patients go through chemotherapy, it's not just about fighting illness ,it can really mess with how their faces and jaws develop. In most cases, the treatment slows down the build-up of bone-making cells, those known as osteoblasts, which normally help shape the jawbone. This slowdown can leave the jaw, either maxilla or mandible smaller than expected—a condition called micrognathia. The jaw growing unevenly, which often leads to bite problems, like a crossbite or an open bite situation. In many instances, these changes altered the balance of skeletal growth, so that the child might end up with a receding lower jaw (class II malocclusion) or, conversely lower jaw sticks out too far (class III malocclusion).(4)(11)

Preventive and Supportive Strategies for Chemotherapy-Induced Oral Complications

Preventive strategies include oral hygiene measures like to use a soft bristle brush and fluoride toothpaste, use of saliva substitutes and being hydrated to prevent xerostomia, cold therapy sucking of ice chips to reduce mucosal damage, antifungal and antibacterial prophylaxis and dietary modifications and avoiding spicy food. By taking these preventive measures, we can reduce chemotherapy-induced oral complications.(26)(27)

Supportive strategies includes relieving symptoms, promoting healing, and preventing secondary complications caused by chemotherapy. Pain management can be done by topical analgesia. Educating the patient about chemotherapy helps the patient to understand better. Counseling and family and friends can provide emotional support and helps the patient to fight the disease.

V. Conclusion

In conclusion, chemotherapy remarkably affects the oral health of a patient, leading to complications such as mucositis, xerostomia, increased risk of infections and bleeding tendencies. A dentist should be aware of these issues and must provide supportive as well as emotional care to patient before, during and after the chemotherapy. Knowing and understanding dental aspects and integrating oncology protocols can help to improve patient treatment and outcomes therefore improving the quality of life.

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