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Management Of Chemotherapy and Radiotherapy-Induced Oral Mucositis in Head and Neck Cancer: A Review

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ABSTRACT

Background Oral mucositis (OM) is one of the most common and severe complications associated with chemotherapy and radiotherapy in head and neck cancer (HNC) patients. It significantly impairs nutritional intake, increases the risk of infection, and may lead to dose reductions or interruptions in cancer therapy.

Objective This review aims to critically evaluate current evidence regarding the pathophysiology, prevalence, risk factors, preventive strategies, and therapeutic interventions for managing OM in patients undergoing treatment for HNC.

Methods A narrative review methodology was employed. A systematic literature search was conducted across PubMed, Scopus, Web of Science, and ScienceDirect. A total of 152 articles were identified, of which 45 met the inclusion criteria based on relevance, quality, and scope. Data were thematically synthesized with emphasis on clinical applicability.

Results The included studies reported OM prevalence rates approaching 100% in concurrent chemoradiotherapy settings. Key risk factors include high-dose radiation, poor oral hygiene, and specific chemotherapeutic agents. Evidence-based interventions such as oral care protocols, low-level laser therapy, cryotherapy, and palifermin have shown varying degrees of efficacy. Multidisciplinary preventive strategies were consistently associated with better outcomes.

Conclusion Effective OM management requires a proactive, multidisciplinary approach tailored to patient-specific risk factors. While promising interventions exist, variability in outcome measures highlights the need for standardized guidelines and further clinical research.

Keywords: *Oral mucositis, Head and neck cancer, Chemoradiotherapy, Supportive care*

1. INTRODUCTION

Head and neck cancers (HNCs) comprise a varied array of malignancies originating from the oral cavity, pharynx, and larynx. These malignancies frequently require intensive multimodal therapies, encompassing high-dose radiation and chemotherapy. Although these procedures enhance survival rates, they often result in unpleasant consequences, with oral mucositis (OM) being one of the most common and debilitating [1]. Oral mucositis is defined by inflammation and ulceration of the oral mucosa, leading to pain, challenges in eating and speaking, and an elevated risk of systemic infections. In practical practice, OM frequently requires treatment interruptions or dose reductions, which may jeopardise oncological outcomes and reduce patients' quality of life [2].

The pathophysiology of oral mucositis (OM) is multifaceted and has been thoroughly delineated via a five-phase biological model: (1) initiation—direct injury to the basal epithelium caused by chemotherapy or radiation; (2) upregulation of transcription factors; (3) signal amplification via inflammatory cytokines, including tumour necrosis factor-alpha (TNF-α) and interleukin-1 beta (IL-1β); (4) ulceration with possible subsequent bacterial colonisation; and (5) healing. Dysbiosis of the oral microbiota, oxidative stress, and impaired mucosal immunity further exacerbate this intricate process [3,4]. Due to the widespread incidence of OM in patients undergoing concurrent chemoradiation, especially in the management of HNC, there is an immediate necessity for better preventive and therapeutic approaches. A variety of therapies, including pharmaceutical medicines, physical modalities, and supportive care measures, have been investigated over the past twenty years. Nonetheless, significant variability persists in clinical practice over the most effective method [5].

This review seeks to synthesise current knowledge about the aetiology, risk factors, prevalence, and, crucially, the comparative efficacy of available therapy regimens for oral mucositis in head and neck cancer patients. The objective is to direct clinicians towards evidence-based, multidisciplinary strategies that can alleviate the burden of OM and facilitate continuous cancer treatment

2. METHODOLOGY

This narrative review was conducted over a three-month period, from January to March 2025, to critically evaluate current evidence on the prevention and management of chemotherapy- and radiotherapy-induced oral mucositis (OM) in head and neck cancer (HNC) patients.

Study Design

This study employed a structured narrative review design. A systematic approach was adopted to identify, screen, and synthesize relevant literature. The review aimed to collate data on the pathophysiology, incidence, clinical implications, and therapeutic interventions related to OM in HNC patients undergoing chemoradiotherapy.

Literature Search Strategy

A comprehensive search was performed across five electronic databases:

- PubMed
- Scopus
- Web of Science
- ScienceDirect
- Google Scholar

Search terms included combinations of: *"oral mucositis"*, *"head and neck cancer"*, *"chemoradiotherapy"*, *"radiotherapy-induced mucositis"*, *"chemotherapy complications"*, *"management strategies"*, and *"preventive therapy"*. Boolean operators ("AND", "OR") were used to refine the queries.

Inclusion and Exclusion Criteria

Inclusion Criteria:

- Peer-reviewed studies published between 2000 and 2025
- English-language articles
- Randomized controlled trials, clinical trials, systematic reviews, observational studies, and consensus guidelines
- Studies focused on OM related to chemotherapy and/or radiotherapy in HNC patients

Exclusion Criteria:

- Studies not related to head and neck cancer
- Animal or in vitro studies
- Conference abstracts, editorials, and non-peer-reviewed literature

Study Selection and Screening

The initial search yielded 152 records. After removal of 32 duplicates, 120 unique articles were screened by title and abstract. A total of 87 full-text articles were assessed for eligibility, and 45 articles met the inclusion criteria for this **review [16-60].** The selection process followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.

Data Extraction and Quality Appraisal

Data were extracted using Microsoft Excel, capturing details such as author, year, study design, population, interventions, and outcomes. The CASP (Critical Appraisal Skills Programme) checklist was used for quality appraisal of qualitative and review studies, while the Cochrane Risk of Bias tool was applied to randomized trials.

Data Synthesis

Due to heterogeneity in study types and outcome measures, a narrative synthesis approach was used. Data were grouped thematically into key domains: (1) pathophysiology of OM; (2) prevalence in HNC; (3) prevention and oral care protocols; and (4) therapeutic interventions.

Software and Tools Used

- Zotero for reference management
- Rayyan QCRI for blind and collaborative article screening
- Microsoft Excel for data organization and extraction
- PRISMA 2020 flowchart tool to visualize article selection

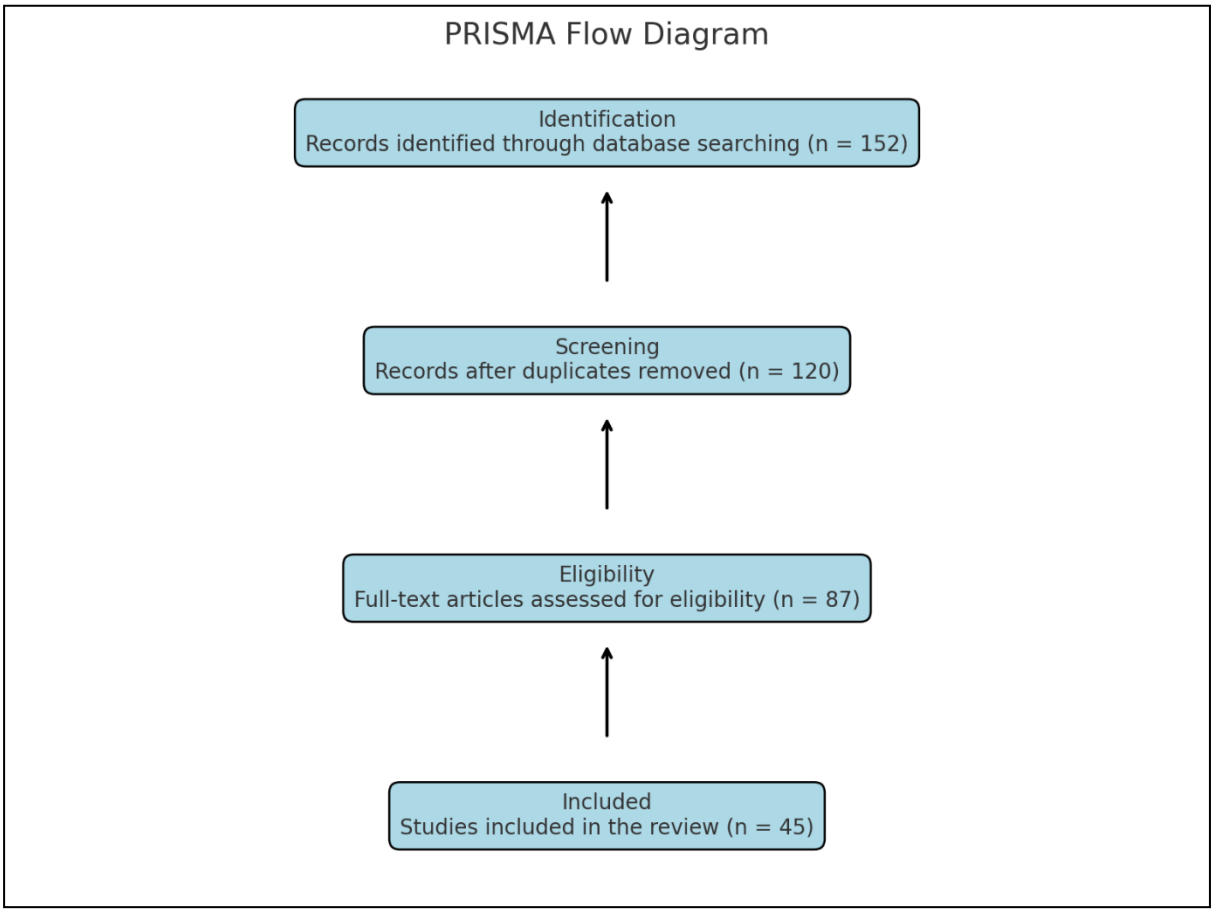

Figure: The PRISMA chart summarizing the identification, screening, eligibility assessment, and inclusion stages.

3. RESULTS

Forty-five papers fulfilled the inclusion criteria and were synthesised to assess the prevalence, risk factors, preventive measures, and therapeutic methods for oral mucositis (OM) in patients with head and neck cancer (HNC) receiving chemoradiotherapy.

Prevalence of Oral Mucositis

The incidence of OM was observed to be remarkably high, varying from 75% to 100% in individuals undergoing chemoradiotherapy. Almost all trials demonstrated that the combination of chemotherapy and radiation markedly exacerbated the severity of oral mucositis compared to monotherapy. Severe OM (Grade 3 or 4) was noted in most instances, frequently requiring alterations in treatment or temporary cessation.

Risk Factors

Key risk factors included:

1. Radiotherapy dose (>50 Gy), especially when administered over several weeks
2. Specific chemotherapeutic agents such as cisplatin and 5-fluorouracil
3. Poor oral hygiene, preexisting dental infections, smoking, and alcohol consumption
4. Low nutritional status and compromised mucosal integrity

Preventive Strategies

Literature consistently demonstrated that prevention is the most effective way to manage OM. Evidence-based strategies include:

- **Low-Level Laser Therapy (LLLT):** Identified across multiple randomized trials as the most effective single preventive modality. LLLT reduces mucosal inflammation, accelerates healing, and significantly lowers OM incidence and severity.
- **Oral Care Protocols:** Standardized oral hygiene regimens that include antimicrobial rinses (e.g., chlorhexidine), professional dental care, and patient education were strongly associated with reduced OM rates.
- **Cryotherapy:** Effective in specific chemotherapy regimens, particularly with agents like 5-fluorouracil and melphalan. This technique involves oral cooling to limit mucosal drug exposure.
- **Palifermin:** A recombinant keratinocyte growth factor that reduced OM in hematologic cancer settings. While beneficial, its routine use in solid tumors remains constrained by high cost and limited access.

Therapeutic Interventions

Once OM is established, the following interventions were used to manage symptoms:

- **Topical agents:** Benzydamine and mucosal protectants help alleviate pain and inflammation.
- **Systemic medications:** Analgesics and antimicrobials were used to control secondary infections and systemic symptoms.
- **Biologic therapies:** GM-CSF and glutamine offered mixed results and are still considered adjuncts rather than first-line therapies.

Effective Management Strategy

An extensive assessment of the analysed literature indicates that the optimal method for addressing oral mucositis (OM) in head and neck cancer (HNC) patients is a proactive, multidisciplinary strategy focused on prevention. This technique routinely demonstrates a reduction in both the incidence and severity of oral mucositis, facilitating more constant and uninterrupted oncologic treatment.

At the core of this approach are two synergistic interventions:

1. **Low-Level Laser Therapy (LLLT):**

Low-Level Laser Therapy (LLLT) is the most substantiated method for the prevention and management of Oral Mucositis (OM). Its photobiomodulatory activities enhance cellular healing, diminish pro-inflammatory cytokines, and expedite re-epithelialization. Randomised controlled trials and meta-analyses consistently indicate that low-level laser therapy (LLLT) considerably decreases the risk of severe oral mucositis (OM), shortens its duration, and diminishes the necessity for opioid analgesics and nutritional assistance. It is most efficacious when administered prophylactically before to the emergence of mucositis symptoms and maintained throughout the treatment regimen.

2. **Structured Oral Care Protocols:**

Establishing systematic oral care protocols—comprising expert dental assessments before to treatment, daily oral hygiene with non-irritating rinses (e.g., saline or chlorhexidine), soft toothbrushes, and patient education—has demonstrated a reduction in microbial load and a decrease in mucosal trauma. These methods are economical, highly scalable, and can be universally applied across many clinical environments. Their regular application correlates with enhanced mucosal integrity and reduced treatment interruptions.

3. **Adjunctive Strategies that enhance this preventive model include:**

- **Oral Cryotherapy:** Particularly beneficial in chemotherapy regimens involving short half-life agents like 5-fluorouracil and melphalan. It induces local vasoconstriction, thereby limiting mucosal exposure to cytotoxic agents.
- **Pharmacologic Agents (e.g., Palifermin):** While effective in hematological malignancies, their use in HNC is restricted due to cost and limited accessibility.

The research robustly supports a preventative, multimodal approach incorporating Low-Level Laser Therapy and systematic oral hygiene practices as the most efficacious therapeutic option for oral mucositis in head and neck cancer patients. These strategies not only alleviate the physiological effects of OM but also are essential for ensuring treatment continuation and enhancing overall patient results.

4. DISCUSSION

Oral mucositis (OM) remains one of the most challenging and debilitating complications in patients undergoing chemoradiotherapy for head and neck cancer (HNC). Its high incidence, particularly in those receiving concurrent treatment modalities, significantly compromises quality of life, treatment adherence, and nutritional status, while increasing the risk of infections and hospitalization costs [6,7]. This review highlights the multifactorial etiology of OM and underscores the evolving landscape of prevention and management strategies.

The pathophysiological framework of OM involves a five-stage biological model: initiation, upregulation, signal amplification, ulceration, and healing, as first elaborated by Sonis [8]. Damage to the basal epithelium and inflammatory cytokine cascades, particularly tumor necrosis factor-alpha and interleukin-1 beta, amplify tissue destruction, contributing to ulcerative lesions. Understanding this cascade is pivotal for the development of targeted therapies.

Preventive strategies remain the most effective approach to managing OM. Evidence supports the efficacy of structured oral care protocols in reducing both incidence and severity of mucositis [9]. Clinical practice guidelines developed by the MASCC/ISOO recommend a combination of basic oral hygiene, patient education, and topical agents such as benzydamine for head and neck cancer patients receiving radiotherapy [10].

Among the advanced interventions, low-level laser therapy (LLLT) has gained strong support due to its ability to enhance tissue repair and reduce inflammatory signaling. Several randomized trials and meta-analyses have confirmed its role in both prevention and treatment [11,12]. Similarly, cryotherapy demonstrates substantial benefit in cases involving bolus chemotherapy, especially 5-fluorouracil and melphalan [13].

Pharmacologic agents such as palifermin, a keratinocyte growth factor, have shown significant mucoprotective effects in patients undergoing hematopoietic stem cell transplantation, but their routine use in solid tumor settings remains limited by cost and access [14].

Despite these advances, the heterogeneity in grading scales (e.g., WHO, NCI-CTCAE), treatment regimens, and endpoints among clinical trials continues to challenge meta-analytical synthesis and guideline standardization. The need for uniform reporting and robust multicenter trials is critical to further improve evidence-based care [15].

5. CONCLUSION

Chemotherapy and radiotherapy for head and neck cancer patients still cause oral mucositis, which affects treatment compliance, quality of life, and healthcare expenditures. Despite the high frequency, especially with concomitant chemoradiation, breakthroughs in mucositis pathogenesis have led to tailored and evidence-based therapy methods. Rigid oral care regimens, patient education, and supportive therapies like low-level laser therapy, cryotherapy, and palifermin have reduced mucositis incidence and severity. But clinical practice, grading standards, and study standardisation vary, therefore well-designed, multicenter trials are needed to generate unified treatment guidelines. Effective oral mucositis management requires a multidisciplinary, preventive strategy tailored to patient risk profiles. Using evidence-based procedures in normal oncology care will reduce this harmful effect and ensure ongoing cancer treatment in head and neck cancer patients

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