

MUCOSITIS IN CANCER PATIENTS TREATMENT AND MANAGEMENT

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ABSTRACT

Purpose: The aim of this study was to update the clinical practice guidelines for the use of basic oral care, prevention and/or treatment of oral mucositis (OM). **Methods:** A literature search was made of the PubMed, Medline, Science Direct, Google, Cochrane and Scopus databases, using different combinations of the following key words: “oral mucositis”, “treatment”, “prevention”, “management”, “chemotherapy”. Unfortunately, there is not a single method which is capable of preventing or eliminating OM in an efficient way. The articles were searched from 2000 -2019. The present study offers a literature review of all the articles published over the last 19 years

referred to the prevention and/or treatment of oral mucositis. **Results:** A total of 28 papers were identified within the scope of this section, out of which 20 were analyzed with reviewed studies. A new Suggestion was made for oral glutamine for the prevention of OM in head and neck (H&N) cancer patients receiving radiotherapy with concomitant chemotherapy. In this article, we reviewed new therapeutic methods of OM including cryotherapy, honey and coffee, propolis, low-level laser therapy, growth factors, stem cell therapy, hyaluronic acid-based substances. **Conclusion:** OM is almost an inevitable negative repercussion of CT, RT, and radiochemotherapy. Proper prophylaxis and management may prevent the intensity of OM and eventually leads to a better disease control.

BACKGROUND

Oral Mucositis (OM) is among the most common and dreaded toxicities of cancer therapy. It occurs in almost all patients who receive radiation therapy in which areas of oral and oropharyngeal mucosa are included in the treatment field.^[1] Lesions of oral mucositis are

often very painful and compromise nutrition and oral hygiene as well as increase risk for local and systemic infection. Mucositis can also involve other areas of the alimentary tract i.e. gastrointestinal (GI) mucositis can manifest as diarrhea. Thus, mucositis is a highly significant and sometimes dose-limiting complication of cancer therapy.^[2,3] Not only can mucositis be debilitating for patients, but it can also lead to delays or dose reductions in life-saving treatments. In general, the more intense the chemotherapy, the greater the risk of mucositis.^[4] Preventive strategies include good oral hygiene and rinses, whereas treatment strategies focus on the amelioration of pain. A stepwise treatment approach that includes bland oral rinses, topical anesthetics, and systemic analgesic agents is suggested based on clinical guidelines.^[5]

INTRODUCTION

Cancer is the second leading cause of mortality worldwide.^[6] Oral mucositis (OM) is described as inflammation of the mucosa in the oral cavity which is caused by destruction of the oral mucosal epithelial cells and growth suppression secondary to cancer treatment in the form of radiotherapy or chemotherapeutic drug substances.^[7] Although it is less common, OM also can occur secondary to chemotherapy of various solid tumours.^[8] It is the most debilitating condition and the most common complication in cancer patients.^[9] Typical manifestations are atrophy, erythema, ulceration and swelling of the mucosa.^[10] As these tissues become thinner, ulceration eventually occurs. Potential complications include pain, increased risk of local and systemic infections, bleeding, insufficient food intake and may lead to breaks in treatment sessions.^[11] The frequency of mucositis and its severity are fundamentally dependent upon the type, duration and dose of chemotherapy used.^[12] In this sense, bone marrow-suppressing (myeloablative) chemotherapy is associated with a mucositis risk of 60-100%, while the combination of chemotherapy and radiotherapy implies a risk of almost 100%.^[13] The clinical manifestations of OM become visible 4-5 days after the start of chemotherapy, with the detection of erythematous areas in the oral cavity. After 7-10 days ulcers start to develop; these gradually grow in number and size, and tend to merge, forming large ulcerated zones.^[14] These lesions are very painful, cause swallowing problems, and take about two weeks to heal once chemotherapy has been suspended.^[15]

A number of OM classification and staging systems have been described, though the most widely used is that proposed by the World Health Organization (WHO).^[16]

Table No 1: Oral mucositis classification – staging system proposed by the World Health Organization (WHO).

Grade	Clinical manifestations
0	No subjective or objective evidence of mucositis
I	Pain with or without erythema, without ulcers
II	Erythema and ulceration. The patient can swallow solids
III	Erythema and ulceration. The patient can swallow liquids, but not solids
IV	Erythema and ulceration. The patient cannot swallow liquids or solids

MATERIAL AND METHODS

A literature search was made of the PubMed, Medline, Science Direct, Google, Cochrane and Scopus databases, using different combinations of the following key words: “oral mucositis”, “treatment”, “prevention”, “management”, “chemotherapy”. Studies were eligible only if they were published as full papers in English language. The limits established for inclusion of the articles in the study were: publications in English, studies in humans, and articles published over the last 10 years [2000-2019]. These studies focus on the effects of the different treatment options for OM. Subsequently the papers thus matched such words criteria were fully reviewed and their findings duly noted.

DISCUSSION

Mucositis is considered to be devastating non haematological complication of anticancer therapy affecting 40–80% of cancer patients receiving chemotherapy and nearly half of the patients undergoing RT of head and neck(17).

Rajesh V Lala *et al.*,(2009) conducted a study on management of mucositis in patients with cancer, in this study it was reported that 303 of 599 patients receiving chemotherapy for solid tumour or lymphoma developed oral /or GI mucositis and concluded that current clinical management of oral mucositis is largely focused on palliative measures such as pain management, nutritional support and maintenance of good oral hygiene.

Abhishek Shankar *et al.*, (2017) conducted a study on current trends in the management of oral mucositis in cancer patient, it is a prospective study involving 298 patients treated with chemotherapy for solid tumour, 120 patients(40.3%) developed WHO grade 1 OM,15 patients(5%) showed WHO grade 2, and only 3 patients (1%) had severe OM and concluded that oral mucositis represents significant burden of antineoplastic therapies and its treatment still remains a challenge. The understanding of epidemiology of oral mucositis is incomplete,

however significant progress has been made in understanding the pathogenesis of oral mucositis and some preventive measures have been identified.

Farnoosh Razmara *et al.*, (2019) conducted a study on An Investigation into the Prevalence and Treatment of Oral Mucositis After Cancer Treatment and almost 40% to 70% of patients receiving standard chemotherapy regimens are likely to develop mucositis and concluded that the present study showed that new traditional alternative medicines are promising alternatives for treating cancer-induced mucositis. It is recommended that dentists use these agents in clinical practice.

Paras Ahmad *et al.*, (2019) conducted a study on treatment and prevention of oral mucositis and concluded that oral mucositis is almost an inevitable negative repercussion of CT/RT and radiochemotherapy, proper prophylaxis and management may prevent the intensity of OM and eventually leads to a better diseases control.

Begonya Chaveli Lopez *et al.*, (2016) conducted a study on oral mucositis due to chemotherapy and observed oral mucositis induced by radiotherapy in 80%, chemotherapy in 40%-80% and bone marrow transplantation in over 75% and concluded the use of palifermin, cryotherapy and low power laser offers benefits, reducing the incidence and severity of oral mucositis.

Correa MEP *et al.*, (2019) conducted a study Systematic review of oral cryotherapy for the management of oral mucositis in cancer patients and clinical practice guidelines and concluded that evidence supports recommendations for the use of oral cryotherapy for the prevention of OM for either (i) patients undergoing autologous hematopoietic stem cell transplant with high-dose melphalan conditioning protocols or (ii) patients receiving bolus 5-fluorouracil chemotherapy.

Narges Gholizadeh *et al.*, (2016) conducted a study on New Treatment Approaches of Oral Mucositis: A Review of Literature and concluded that there are pharmacologic and non-pharmacologic methods for treating mucositis, particularly a combination of these methods together can create greater therapeutic effects, most important of which are stem cell transplantation and growth factors.

Deborah B. McGuire *et al* (2013) conducted a study on Systematic review of basic oral care for the management of oral mucositis in cancer patients and concluded that the evidence for

basic oral care interventions supports the use of oral care protocols in patient populations receiving radiation and/or chemotherapy and does not support chlorhexidine for prevention of mucositis in head and neck cancer patients receiving radiotherapy. Additional well-designed research is needed for other interventions to improve the amount and quality of evidence guiding future clinical care.

Noam Yarom *et al* (2013) conducted a study on Systematic review of natural agents for the management of oral mucositis in cancer patients and concluded that Of the various natural agents reviewed here, the available evidence supported a guideline only for two agents: a suggestion in favor of zinc and a recommendation against glutamine, in the treatment settings listed above. Well-designed studies of other natural agents are warranted.

Vitaliana DeSanctis *et al* (2016) conducted a study on Mucositis in head and neck cancer patients treated with radiotherapy and systemic therapies: Literature review and consensus statements and concluded that OM represents a very stressful situation for head and neck cancer patients submitted to chemo-radiation or exclusive radiation treatment. A multidisciplinary approach is mandatory, but there is still no gold-standard protocol that is prominently better than others.

Paras Ahmad, Usman Akhtar *et al* (2019) conducted a study on Treatment and prevention of oral mucositis: A literature review and concluded that The oral cavity is one of the major sites of the human body, where RT and CT can wreak havoc. OM is almost an inevitable negative repercussion of CT, RT, and radiochemotherapy. Oral complications of RT/CT, that is, mucositis is almost imminent, but their incidence and severity can be lessened by regularly visiting physician and dentist. The role of a dentist should never be underestimated or ignored in such instances as he/she plays a crucial role in preventing as well as management of oral disorders associated with RT/CT. Proper prophylaxis and management may prevent the intensity of OM and eventually leads to a better disease control.

Preyanate Wilairat *et al* (2018) conducted a study on Comparative efficacy and safety of interventions for preventing chemotherapy-induced oral mucositis in adult cancer patients: a systematic review and network meta-analysis and concluded that this NMA suggests that cryotherapy was the most effective intervention for preventing chemotherapy-induced OM with a safety profile similar to control, but not significantly lower than sucralfate and palifermin. Large RCTs are needed to confirm these findings.

E. Una Cidon *et al* (2018) conducted a study on Chemotherapy induced oral mucositis: prevention is possible and concluded that Our study showed a significant reduction in the rate of OM grade 2–3 in patients using the especial mouthwash. This mouthwash is currently used as standard in our institution. Further evaluation in other centres to confirm these results is needed.

Celso Neiva Campos *et al* (2014) conducted a study on Oral mucositis in cancer treatment: Natural history, prevention and treatment (Review) and concluded that Oral mucositis is a painful consequence of anticancer chemotherapy and/or radiotherapy of the head and neck, developing in ~90% of patients undergoing this type of treatment. Dentists must be familiar with the necessary interventions, in order to help the patient during the course of the treatment and avoid treatment interruption. Certain measures may help minimize the symptoms associated with oral mucositis; however, further research is required, focusing on lesion prevention prior to treatment initiation. Clinical dentists may help the patients by instructing them on oral hygiene and performing minor dental treatments prior to the initiation of chemotherapy or radiotherapy.

Varsha Manohara, *et al* (2018) conducted a study on Effectiveness of mouthrinses in prevention and treatment of radiation induced mucositis: A systematic review and concluded that the results of this systematic review revealed that use of mouthrinses showed marginal reduction in radiation mucositis, with limited evidence. Studies using herbal-based products and tissue regenerating agents revealed comparatively better effectiveness with lesser side effects. However, the number of studies to support such a claim is very limited.

CONCLUSION

The oral cavity is one of the major sites of the human body. OM is almost an inevitable negative repercussion of CT, RT, and radiochemotherapy. Oral complications of RT/CT, that is, mucositis is almost imminent, but their incidence and severity can be lessened by regularly visiting physician and dentist. The role of a dentist should never be underestimated or ignored in such instances as he/she plays a crucial role in preventing as well as management of oral disorders associated with RT/CT. Proper prophylaxis and management may prevent the intensity of OM and eventually leads to a better disease control.

Mucositis management relies on symptom management and prevention of complications, which includes pain control, nutritional support, and prophylaxis/ treatment of secondary

infections. Patients should be educated on the value of good oral health relative to cancer therapy. Oral hygiene instructions should be given, which includes tooth brushing, flossing, and rinsing with bland (saline or sodium bicarbonate) solutions. Other important components include using mouth and lip moisturizers, use of soft-bristle toothbrush, maintaining adequate intake of fluids and protein, and avoiding irritating foods, alcohol and tobacco.

Few of the recommendations for prevention and management are in Radiation Therapy - Benzylamine Hydrochloride 0.15% (Tantum) is an anti-inflammatory mouth rinse that is recommended for use to prevent and/or relieve the pain and inflammation associated with oral mucositis in patients who are receiving moderate doses of radiation therapy for head and neck cancer. Amifostine is a cytoprotectant agent that may help to reduce the incidence and severity of chronic or acute xerostomia in patients who are receiving radiation therapy for head and neck cancer. Not Recommended: Chlorhexidine, Sucralfate, antimicrobial lozenges.

In Head & Neck Cancers Patients - Brushing may not be appropriate in the area of tumor involvement, Patients should be assessed for the use of daily Fluoride tray, Consult with a dentist.

In Cryotherapy- May decrease the incidence and severity of oral mucositis, Patients should be instructed to hold ice chips in mouth five minutes prior, during, and for 30 minutes after the bolus infusion of fluorouracil (5FU). Not recommended for Infusional fluorouracil, Regimens which include Oxaliplatin due to potential exacerbation of cold-induced pharyngolaryngeal dyesthesias.

In Hematopoietic Stem Cell Transplantation (HSCT)- Palifermin (keratinocyte growth factor-1) for patients with hematological malignancies receiving high dose chemotherapy with or without radiation therapy followed by HSCT, Oral cryotherapy to prevent oral mucositis in patients receiving high dose melphalan.

In Dietary Management- Promote - Daily fluid intake of 8-12 cups (2-3 litres), unless contraindicated, to help keep oral mucosa moist (e.g. water, sugar-free popsicles, non-acidic juices, ice cubes, sports drinks, broth). Well-balanced diet that is high in protein, vitamins B and C. Avoid - Dry or coarse foods (e.g. toast, crackers, chips), Spicy or hot temperature foods, Highly acidic fluids and foods (e.g. lemon glycerin swabs, vitamin C lozenges), Fluid or foods high in sugar (e.g. pop, some fruit juices), Caffeine, alcohol, tobacco

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