

Addressing the Chemotherapy Induced Oral Mucositis

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DOI: <https://doi.org/10.52403/ijshr.20240126>

ABSTRACT

A severe and common side effect of chemotherapy treatment for cancer is oral mucositis, which refers to the inflammation of the mucous membranes in the mouth. It occurs because of the cytotoxic effects of chemotherapy on the epithelial mucosa. The physical and mental well-being of patients undergoing chemotherapy can be significantly affected by this side effect, making it crucial to address oral mucositis promptly.

Oral mucositis can give rise to several challenges for patients. One of the primary issues is pain, which can range from mild discomfort to severe soreness, making it difficult for patients to eat, drink, or even speak. The discomfort can lead to a decreased appetite, resulting in nutritional deficiencies and weight loss. Additionally, the presence of open sores in the mucosa increases the risk of infection, particularly in patients with compromised immune systems. If left untreated, these issues can have a substantial impact on the overall quality of life for chemotherapy patients.

Fortunately, there are various approaches available to manage and alleviate the difficulties associated with chemotherapy-induced oral mucositis. These interventions aim to reduce pain, promote oral hygiene, and support adequate nutrition.

A literature search was conducted using different databases (PubMed, Google scholar). Through this review process, 16 articles were identified that were relevant to coping with chemotherapy induced oral mucositis. Different studies

conducted by various multidisciplinary teams are included in this article. To lessen the effects of chemotherapy-induced oral mucositis, there are several coping mechanisms. This includes a combination of pharmacological, non-pharmacological interventions and even home remedies that are part of complementary therapies. The purpose of this article is to understand the chemotherapy induced oral mucositis and its management.

Key words: Oral mucositis, chemotherapy induced oral mucositis, coping method.

INTRODUCTION

One of the most common and challenging side effects of chemotherapy is oral mucositis (OM). Studies have shown that approximately 90% of patients with head and neck cancer who undergo both chemotherapy and radiation therapy develop oral mucositis, highlighting its significant prevalence in this population¹. However, it's important to note that oral mucositis can also occur in patients receiving chemotherapy for other types of cancer.

The onset of oral mucositis typically occurs between five to fourteen days after the initiation of chemotherapy. Among individuals with solid tumours, approximately 20% to 40% will experience mucositis during their treatment course. The incidence and severity of mucositis can vary depending on several

factors, including the specific chemotherapeutic agents used, the number of chemotherapy cycles administered, the dosage of chemotherapy, and individual patient factors.

The choice of chemotherapeutic agents plays a crucial role in the development and severity of oral mucositis. Certain drugs, such as methotrexate, doxorubicin, 5-fluorouracil, and cisplatin, have been associated with a higher risk of mucositis. The cumulative effect of multiple rounds of chemotherapy can also increase the likelihood and severity of mucositis.

Moreover, the dosage of chemotherapy can impact the occurrence and intensity of oral mucositis. Higher doses of chemotherapy are generally more likely to cause mucosal damage and lead to more severe mucositis symptoms. Patient-specific factors, such as age, overall health status, nutritional status, and the presence of pre-existing oral conditions, can also influence the development and severity of oral mucositis. Individuals with compromised immune systems or pre-existing oral infections may be more susceptible to mucositis.

Mucositis is characterised by inflammation and/or ulcerative lesions located on the oral and/or gastrointestinal tract⁴. It starts seven to fourteen days following the start of the treatment. The mucosal lining of the mouth atrophies and breaks down because of oral mucositis brought on by chemotherapy,

leading to ulcers^(1,2). Oral mucositis's typical symptoms include white or red patches in the mouth, non-healing sore or blister, Pain in mouth or throat, Swelling or lumps inside the mouth.

There are five stages of oral mucositis brought on by chemotherapy include initiating, signalling, amplifying, ulcerating, and healing. First, chemotherapy can damage tissue by killing basal epithelial cells and producing reactive oxygen species in the process. The initial damage caused to cells by chemotherapy can occur directly through DNA damage or, more frequently, indirectly through reactive oxygen species. This is known as the initiation phase. This causes a cascade of enzyme and transcription factor activations that culminate in the overexpression of genes encoding inflammatory cytokines, including TNF, IL-1, and IL-6 that harm tissue by targeting the submucosa and basal epithelium. Thirdly, additional pathways, such as TNF alpha, are enhanced. The ulceration and subsequent bacterial colonisation that follow the ensuing inflammation and tissue damage feed the vicious cycle of inflammatory cytokine-mediated harm. Fourthly, further inflammation also results in mucosal ulcerations. In the final stage of the healing process, signals from the extracellular matrix cause the mucosal barrier to be restored through epithelial proliferation and epithelization^(17,28). There are different drugs that cause mucosal injury as shown in Table1.

Table1
Chemotherapeutic Agents Causing Mucositis ⁽²⁴⁾
Alkylating agents: Busulfan, Cyclophosphamide, thiotepa, procarbazine
Anthracyclines: Doxorubicin, epirubicin, daunorubicin
Antimetabolites: 5-FU, methotrexate, hydroxyurea
Antitumor agents: Actinomycin D, bleomycin, mitomycin
Texans: Paclitaxel
Vinca alkaloids: Vincristine, vinblastine

Chemotherapy induced Oral mucositis (OM) is known to have a significant impact on Quality of Life⁽¹⁹⁾. The occurrence of OM is accompanied by difficulty in chewing,

swallowing, eating, and drinking. Patients clearly feel pain related to discomfort because of the oesophagus' and oral mucosa's irritation. If neglected, the incapacitating feelings might

result in decreased appetite, which can change nutrition and increase the risk of sepsis, and if severe enough, this can result in treatment interruptions (22). Patients' sense of physical, emotional, and social comfort is negatively impacted by this. Increased mucositis symptoms also have a detrimental impact on patients' ability to adhere to the underlying disease's treatment plan and lengthen the amount of time they must stay in the hospital.

Coping with oral mucositis

Effective management of oral mucositis is crucial to alleviating discomfort and minimising its impact on overall health.

One of the simplest interventions is by maintaining good oral hygiene through gentle brushing of the teeth with a soft-bristle toothbrush and using mild, alcohol-free mouthwashes or saline rinses. These practises help keep the mouth clean and prevent the

build-up of bacteria that can exacerbate mucositis. It is important to consult with healthcare professionals for specific recommendations on suitable oral hygiene products.

In addition to oral hygiene, certain mouthwashes specifically designed for managing oral mucositis can be used. These mouthwashes often contain ingredients that help soothe oral tissues, promote healing, and provide pain relief. They can be easily administered by swishing the mouthwash for a prescribed duration before spitting it out. Healthcare providers can provide guidance on the appropriate mouthwash to use and the frequency of application.

Studies show the value and efficiency of certain mouthwashes for preventing oral mucositis brought on by chemotherapy, as shown in Table 2

Table 2

Sl.no	Study intervention	Result
1	Oral care using different mouth wash. Study design: Quasi-experimental Population: patients with mucositis undergoing chemotherapy Variable: pain and comfort Intervention: oral care using normal saline and baking soda (9).	Comparing pain and comfort before and after oral care reveals that there was a significant difference in the intervention group's pain (t=14,257, p=0,000) and comfort (t=-11,103, p=0,000) before and after oral care using regular saline and baking soda. <i>This experimental investigation showed that patients' comfort may be increased and mucositis discomfort can be decreased by gargling with a normal saline and sodium bicarbonate solution.</i>
2	Study design: Quasi-experiment pre-post-test with a control group design. Population: patients with oral mucositis undergoing chemotherapy Variable: quality of life. Intervention: effectiveness of oral care using sodium bicarbonate and zinc chloride mouthwashes on oral mucositis(10).	After the third week, there was a statistically significant difference between the three groups (p.001). Likewise, the t-test findings demonstrated that the effect of time on quality of life was significant for the groups receiving zinc chloride and sodium bicarbonate (p.001). Additionally, the zinc chloride group outperformed the sodium bicarbonate group in terms of improving the quality of life. <i>Mouthwashes with zinc chloride and sodium bicarbonate were successful in treating and lessening the severity of oral mucositis, which improved quality of life in cancer patients receiving chemotherapy. As a result, we can suggest zinc chloride and sodium bicarbonate at the beginning of chemotherapy to enhance oral health and improve these patients' quality of life.</i>
3	Study design: Randomised controlled clinical trial Population: Patients with oral mucositis undergoing chemotherapy Variable: Severity of mucositis Intervention: Impact of statin and aloe vera mouth wash (11)	The therapy outcomes of group 2 were better than those of group 3 (P=0.042) and group 1 (P=0.036), but there were no significant differences between groups 1 and 3 (P=0.674). <i>The findings reveal that aloe vera mouthwash treatments could be a helpful choice in the prevention of mucositis for chemotherapy patients. For individuals seeking to handle issues brought on by oral mucositis, these are the most practical and affordable option.</i>
4	Study design: Experimental design Population: Acute lymphatic leukaemia patients with oral mucositis grade 2 Variables: Changes in oral mucositis grade 2 Intervention: effectiveness of benzocaine gel, honey, and HOPE (a mixture of honey, olive oil–propolis extract, and beeswax) (12).	In comparison to either HOPE or controls, the honey group's recovery time from grade 2 mucositis was shorter (P.05). In grade 3 mucositis, healing times did not differ between honey and HOPE (P = 0.61), although both treatments sped up recovery relative to controls (P.01). In general, honey induced quicker healing than either HOPE or controls in both stages of mucositis (P .05). <i>According to the study, honey hastened the recovery of individuals with mucositis brought on by grade 2 or 3 chemotherapy.</i>

1. Oral care using different mouth wash.

To ensure oral health, prevent odours and dental caries, maintain the moisture of the lips and oral mucosa, and enhance overall comfort and self-esteem, it is important to prioritise mouth cleaning, tooth brushing, and gargling. Research suggests that using normal saline for oral care is recommended to promote oral hygiene. Gargling regularly with normal saline can prevent crust formation, soothe the mouth mucosa and gums, and provide moisture. Other studies suggest performing oral hygiene routines with warm water, normal saline, and baking soda up to four times a day, depending on the condition of the oral cavity. These practises have been shown to alleviate the discomfort and pain associated with mucositis (9).

Several studies have investigated the effectiveness of sodium bicarbonate (baking soda) in managing oral mucositis in cancer patients receiving chemotherapy. Medications containing a 5% sodium bicarbonate base have been found to be helpful in both preventing and treating oral mucositis. In a study conducted by Cobra et al. in 2018, the use of 5% or 10% sodium bicarbonate solutions was shown to help prevent oral mucositis in cancer patients treated with chemotherapy. Specifically, a 10% sodium bicarbonate solution in mouthwash was found to be more effective than a 5% solution in preventing oral mucositis. Furthermore, various research studies have explored the impact of zinc-based treatments on oral mucositis. Zinc, known for its wound-healing properties, has been investigated as a potential therapy for managing mucositis. Although further research is needed to establish its efficacy, some studies have shown promising results regarding the use of zinc-based treatments in reducing the severity of oral mucositis (10).

Oral care with aloe vera mouthwash: A comparison of the therapeutic benefits of atorvastatin and aloe vera mouthwash on

chemotherapy-induced oral mucositis was carried out in 120 patients with large intestine and gastric cancer who were treated with 5-fluorouracil. Three groups were chosen at random, and Group 1 got placebo mouthwash in addition to 10 mg of atorvastatin pills daily until two weeks after chemotherapy treatments. Group 3 received placebo mouthwash and placebo pills until two weeks following chemotherapy treatments, while Group 2 received aloe vera mouthwash plus placebo tabs. According to patient data on mucositis incidence, 50% of patients in the placebo group had mucositis ranging in severity from grade 2 to 4. Grade 2 mucositis affected 9 patients (22.5%) in group 1, grade 3 mucositis affected 6 patients (15%), and grade 4 mucositis affected 4 patients (10%). Only one patient (or 2.5%) in group 2 had grade 2 mucositis, according to the diagnosis. The therapy outcomes of group 2 were better than those of group 3 ($P=0.042$) and group 1 ($P=0.036$), but there were no significant differences between groups 1 and 3 ($P=0.674$). As a result, these studies suggest that aloe vera mouthwash treatments could be a useful option in the prevention of mucositis for individuals receiving chemotherapy. These are the most effective and economical options for patients to manage challenges caused by oral mucositis (11).

2. Local application of honey

Findings have demonstrated that honey promoted quicker healing in patients with grade 2/3 chemotherapy-induced mucositis. It has been observed that honeybee products have anti-inflammatory and wound healing actions. A randomised control clinical trial was conducted on 90 patients with acute leukaemia who had grade 2 and grade 3 oral mucositis. Three equal treatment groups—Honey, HOPE (a concoction of Honey, Olive Oil, Propolis Extract, and Beeswax), and Control—were divided up among the patients. For the honey,

HOPE, and control groups, respectively, the topical treatments given to each patient were benzocaine gel, honey, and HOPE, respectively. In comparison to either HOPE or controls, the honey group's recovery time from grade 2 mucositis was shorter (P.05). In grade 3 mucositis, healing times were not different between honey and HOPE (P = 0.61), although both treatments sped up recovery relative to controls (P.01). In general, honey induced quicker healing than either HOPE or controls in both stages of mucositis (P.05). In individuals with grade 2/3 chemotherapy-induced mucositis, honey accelerated healing (12).

3. Cryotherapy

To reduce the risk of developing chemotherapy-induced oral mucositis, a technique called oral cryotherapy (OC) can be employed. This involves cooling the patient's mouth during chemotherapy administration using methods such as ice cubes, cold water, popsicles, or ice cream. Applying ice chips topically to the oral cavity while receiving chemotherapy can help decrease the distribution of chemotherapeutic agents to the oral mucosa. This effect is likely achieved through local vasoconstriction and reduced blood flow (12).

Studies have shown that cryotherapy, both before and after the administration of chemotherapy medications, can significantly reduce the severity of oral mucositis and provide relief from its symptoms. This approach has been found to be particularly effective in minimising the occurrence of severe mucositis. In some cases, cryotherapy is specifically referred to as "ice chip therapy," where patients place ice chips in their mouths for approximately 30 minutes before receiving fluorouracil infusions (13).

It is important to note that cryotherapy should be administered under the supervision and guidance of healthcare professionals. They can provide instructions on the proper technique,

timing, and duration of cryotherapy sessions, ensuring that the approach is tailored to the individual patient's needs and treatment regimen (14).

While cryotherapy has shown promise in reducing the severity of oral mucositis, it is not universally applicable to all chemotherapy treatments or patients. The suitability of cryotherapy may depend on various factors, including the specific chemotherapeutic agents being used, the patient's overall health condition, and any contraindications or precautions associated with the treatment.

4. Mechanical cleaning

Patients should be urged to improve their routine mechanical cleaning techniques, such as brushing their teeth more frequently, using a soft gentle toothbrush, changing it out frequently, floss once per day, and cleaning between their teeth and rinse at least four times per day with plain solutions such as regular saline, sodium bicarbonate, or water (15).

5. Dietary support

The pain caused by severe oral mucositis can seriously interfere with food intake. Additionally, chemotherapy can potentially cause alterations in taste. A dietician or other expert, working with family carers, must keep an eye on nutritional intake and weight. When oral mucositis is present, a soft diet and liquid diet supplements are easier to stomach than a conventional diet (17). Some of the home remedies are utilised by the patient who has oral mucositis to manage the condition, which is brought on by chemotherapy. According to studies (Penn State College of Medicine), these home treatments for oral mucositis have been successful in terms of dietary habits. The patients' dietary intake has improved because of their use of various techniques, namely.

- Suck on frozen fruit pops, fruit ice, or ice chips by freezing fruits.
- Devour creamy, mushy meals.

- Dry or solid foods should be blended and moistened. Add them to sauces, casseroles, gravies, and soups.
- To make food simpler to swallow, puree or liquefy it in a blender.
- Foods that are calming should be lukewarm or cold.
- To avoid mouth sores, sip through a straw.
- Consume foods high in protein and calories to hasten healing.
- Using a straw will not only make drinking simpler, but it will also prevent contact with the injured area.
- It is best to avoid acidic foods like tomatoes, grapes, apple fruits or juices, alcohol, and cigarettes, as well as spicy meals.

6. Pain management

- NSAIDs and acetaminophen
At the time of the initial pain evaluation, most patients were routinely taking paracetamol, which the oncologists had recommended. Continued paracetamol was advised as a first step. NSAIDs are useful as a second step. NSAIDs and opioid medications are recommended in cases of extreme pain. Transdermal fentanyl and oral or enteral morphine were favoured. However, several studies showed that the pain and discomfort associated with chemotherapy-induced oral mucositis can be reduced with simple oral care and topical treatments (9,10,1).
- Anti-inflammatory agents.
Benzidamine has been used to treat and prevent oral mucositis because of its anti-inflammatory, analgesic, anaesthetic, and antibacterial characteristics. Misoprostol rinses, histamine in gel form, and the intravenous or intramuscular infusion of immunoglobulins are further anti-inflammatory medications used to prevent oral mucositis brought on by chemotherapy (22,23). However, the study published by Duenas-Gonzalez et al (23).

Similarly, to another recent investigation by Lalla et al. found no positive benefit with the administration of misoprostol rinses (200 g in 15 ml of water) (22). Both mesalazine in gel form and diphenhydramine rinses have also been researched, and the findings of the various papers indicate that both products could be useful (23).

- Topical application of medications
Nystatin, diphenhydramine, tetracycline, and hydrocortisone may be used topically to lessen the likelihood of chemotherapy-induced mucositis. Topical morphine and xylocaine jelly applied topically to individuals with head and neck cancer have also been shown to significantly lessen the severity of OM (25,26,27,28).

7. Lip care

Dryness in the lips and mouth is the first indication of oral mucositis. People may ignore these warning signs because they believe the weather has changed or for another reason, or occasionally because they never bothered to notice the dryness. Only in those situations did it progress to oral mucositis. To help the patient comprehend the implications of the side effects and how they affect quality of life, sufficient health education about chemotherapy and its side effects is required. We can moisturise lips with these various methods to lower the occurrence of oral mucositis.

- To keep your lips moist, consume plenty of water.
- Suck on ice chips while receiving chemotherapy to help minimise inflammation. Use a lip moisturiser that does not include petroleum jelly or glycerine.
- Aloe vera and honey are used to treat mouth dryness because they possess anti-inflammatory and antioxidant properties (1,28).

CONCLUSION

It is important to understand appropriate nursing interventions to cope with symptoms experienced due to chemotherapy induced oral mucositis. The symptoms of oral mucositis brought on by chemotherapy vary from patient to patient. To cope with the symptoms and lessen their intensity, a nurse assists the patient in choosing a suitable, cost-effective remedy. Regular mouth and lip care and dietary modifications are some of the preventative strategies that nurses frequently advise. The patient needs to receive appropriate psychotherapy and health education to manage the challenges. It is crucial for patients to discuss their symptoms and management strategies with healthcare professionals. They can provide personalised recommendations based on the individual's condition and the specific chemotherapy regimen being administered. By employing a combination of oral hygiene practises, specialised mouthwashes, pain management, dietary modifications, and supportive care, patients can better cope with the discomfort and challenges brought on by oral mucositis.

To lessen the effects of chemotherapy-induced oral mucositis, there are several coping mechanisms. According to studies, gargling with baking soda prevents people from developing oral mucositis. The incidence of chemotherapy-induced OM is up to 80% among patients receiving high-dose chemotherapy treatments ⁽⁵⁾. So, to accomplish early detection and prevention of oral mucositis associated with life-threatening complications, such as sepsis, which can lead to death, patients must undergo a comprehensive oral examination during and after the completion of a chemotherapy course ^(4,6). A number of agents and methods have been introduced as early preventive approaches to oral mucositis, including routine oral care, oral cryotherapy, honey, mucosal protective agents, and antimicrobial agents ⁽⁷⁾. There are many antiseptic oral rinses on the

market, but no specific, well-tolerated antiseptics have been identified as having significant efficacy. A mouthwash based on polyhexanide was tested on volunteers as a potential replacement because of its good tolerability, but its antibacterial efficacy was insufficient ⁽⁸⁾.

Declaration by Authors

Ethical Approval: Not Required

Acknowledgement: None

Source of Funding: None

Conflict of Interest: The authors declare no conflict of interest.

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How to cite this article: Amrutha C, Sherin Susan Thomas, Bindhu Mathew, Shreemayee Panda. Addressing the chemotherapy induced oral mucositis. *International Journal of Science & Healthcare Research*. 2024; 9(1): 202-210. DOI: <https://doi.org/10.52403/ijshr.20240126>
