

# Prevention and management of antineoplastic therapy induced oral mucositis

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## ABSTRACT

With the scientific advancements in the management of malignant diseases, the treatment is expensive and bears high morbidity in term of oral mucositis. It is a debilitating condition and has been researched extensively for its pathogenesis and treatment. Various treatment options include barrier forming, mucosal protectants, mouth rinses, growth factors, lasers and midline-sparing procedures. Some agents are used locally while others are administered systemically. Despite the availability of a wide range of treatment options for mucositis, a cost-effective treatment is yet to be evolved.

**Key words:** Antineoplastic therapy, mucosal protectants, oral mucositis

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## INTRODUCTION

Treatment of cancer is increasingly more effective but is associated with short- and long-term side-effects. Oral side-effects remain a major source of illness despite the use of a variety of agents to prevent them. One of these side-effects is oral mucositis, which is a debilitating condition and results from the cytotoxic effects of chemotherapeutic drugs and radiation on the oral mucosa. Mucositis causes severe pain and distress and may limit the tolerability of chemo/radiotherapy and, hence, its effectiveness. It usually follows chemo and/or radiotherapy of the head and neck region and can be seen in 40–70% of the cases. It damages the epithelium of the oral cavity and manifests in the form of erythema, ulceration and swelling. This not only makes the swallowing and speech difficult but also affects the quality of life of the patient. Furthermore, patients with

damaged oral mucosa and reduced immunity resulting from chemotherapy and radiotherapy are prone to opportunistic infections in the mouth. The mucositis may be so severe that patients' food and fluid intake and speech are reduced, further compromising the patients' response to treatment and/or palliative care. In addition, the damaged mucosal surface provides a safe site to harbor various microorganisms and provide a portal of entry allowing the microorganisms to flow into systemic circulation. Thus, the side-effects are local and systemic. While the local effects of severe mucositis may lead to reduction of the chemotherapeutic dose in subsequent cycles, the systemic effects may lead to infection, complication and interruption of therapy. At this stage, the hospitalization becomes unavoidable and parenteral nutritional therapy with analgesics is mandatory.

Currently, a large number of interventions are available. This paper reviews the pathogenesis, classification of mucositis and range of treatment available to manage this condition.

## PATHOGENESIS

Oral mucositis secondary to the cancer therapy is the

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side-effect of treatment. Its pathogenesis was unclear until Sonis projected a hypothesis that involved four sequential events.<sup>[1]</sup> In the first phase (inflammatory/vascular phase), the chemotherapeutic insult causes the release of inflammatory cytokines (tumor necrosis factor- $\alpha$ , interleukins-1 and -6, C-reactive protein) that result in local tissue damage and increased vascularity. In the next phase (epithelial phase), the chemotherapeutic agent decreases the mitosis of the proliferating epithelial cells of the oral cavity, leading to reduced turn over of epithelial cells, atrophy and ulceration. In the third phase (ulcerative/infectious phase), discrete areas of full-thickness erosion develop due to trauma and cytokine-mediated damage. These areas are colonized by mixed microorganisms and lead to a portal of entry for infection. The fourth and final stage is healing, with epithelial proliferation and differentiation. The intermediate phases exhibit marked neutropenia and leucopenia. The healing phase is characterized by the recovery of white blood counts.

However, the oral mucositis is associated with other factors also, of which the chemotherapeutic agent, field and dose of irradiation play an important role. It is seen in patients treated with antimetabolites like 5-fluorouracil, methotrexate and purine antagonists. It is also seen in patients receiving cytostatic antibiotics (e.g. Anthracycline) and cytotoxic agents (e.g. Taxanes) and patients receiving bone marrow transplant-conditioning therapies for hematological or solid tumors.<sup>[2,3]</sup>

Now, there are evidences that suggest that radiation- or chemotherapy-induced mucositis is initiated by direct injury to the basal epithelial cells and cells in the underlying tissue. DNA-strand breaks can result in cell death or injury. Non-DNA injury is initiated through a variety of mechanisms, some of which are mediated by the generation of reactive oxygen species. Sonis characterized five phases of pathophysiologic progression of mucositis, viz. initiation, upregulation and message generation, signalling and amplification, ulceration and healing. Each phase offers a potential target for therapeutic interventions.<sup>[4]</sup> The complex pathogenesis of mucositis in fact involves dynamic interactions of all of the cell and tissue types that comprise the epithelium and the submucosa. Identification of the molecular events that lead to treatment-induced mucosal injury have given a hope for identifying the interventions that may prevent and treat mucositis.<sup>[5]</sup> However, the patient's mucosal response to antineoplastic treatment has been shown to be controlled by two factors: global factors that include gender, underlying systemic disease and race and tissue-specific factors like epithelial type, intrinsic endocrine system, local microbial environment and

function. Interaction of these specific elements plus genetic influences probably govern the phases of mucosal injury.<sup>[6]</sup>

### Prevention and pretreatment interventions of oral mucositis

The chances of mucositis are always associated cancer therapy. However, there are certain predisposing factors, which if considered properly, the mucositis may be prevented. These factors have been shown in Table 1. The patient and carers should always be told precisely these predisposing factors and to follow the advice given to help prevent/minimize the mucositis.

Because the mucositis is aggravated by dental factors and poor oral hygiene, it is in the best interest of the patient that the medical team should interact with dental specialists to discuss issues and possible complications that may develop in response to chemo-radiotherapy. In addition, the available time for onset of neutropenia should also be discussed. Considering the medical status of the cancer patient, the dental team should formulate a plan to manage the existing oral and dental disease before, during and after the chemotherapy. The overall goal should be, however, to eliminate orodental diseases and stabilize the oral health and other dental conditions that may produce complications during the phase of cancer therapy.

In patients with poor oral health, the benefits of dental treatment should be weighed against the potential disadvantages, such as incomplete healing. Simultaneously, in cases where oral disease poses an eminent danger, the cytotoxic therapy should be delayed. Intervals between the chemotherapy cycle can be utilized to complete the necessary dental treatment. For patients who received radiotherapy, the surgical treatment should be delayed by 3–6 months to lower the risk of osteoradionecrosis. Neutropenia and thrombocytopenia are the common side-effects of cancer chemotherapy. In patients with neutropenia <1,000/cubic mm, where the invasive procedure is direly needed, an aggressive broad-spectrum antibiotic therapy by the parenteral route should be given. Periodontal treatment and tooth/teeth extractions should be carried out as atraumatically as possible. Where tooth extraction is performed, primary closure of wound is recommended.<sup>[7]</sup>

### ASSESSMENT OF ORAL MUCOSITIS

Prior to institution of therapy to treat mucositis, the assessment of its extent is necessary. WHO oral mucositis index [Table 2] is an ideal means of assessing the severity of the condition. On this basis, the extent

**Table 1: Predisposing factors of mucositis**

Poor oral hygiene  
 Spicy, hard and hot food  
 Alcohol  
 Tobacco  
 Ill-fitting dentures, sharp teeth, unrestored carious teeth, improper restorations  
 Underlying diseases: hematological malignancies

**Table 2: WHO oral mucositis index**

The World Health Organization oral toxicity scale measures the anatomical, symptomatic and functional components of oral mucositis. The therapy of the condition is graded from 0 (no oral mucositis) to 4 (alimentation not possible and treatment required).  
 Grade 0: None  
 Grade 1: Soreness ± erythema  
 Grade 2: Erythema, ulcers and patient cannot swallow solid food  
 Grade 3: Ulcers with extensive erythema and patient cannot swallow food  
 Grade 4: Mucositis to the extent that alimentation is not possible (TPN)  
 (Ref: Handbook for reporting results of cancer treatment. Geneva, Switzerland: World Health Organization; 1979: 15-22.)

**Table 3: Treatment options of chemo/radiotherapy-induced oral mucositis**

- A. Chemotherapeutic agents
  - Barrier oremers: Sucralfate, Gelclair
  - Antimicrobial agents: Chlorhexidine, Povidine-iodide
  - Polymyxin E, Amphotricin B, Tobramycin
  - Antiinflammatory agents: Indomethacin, Benzydamine
  - Antihistamines: Diphenhydramine, Azelastine
  - Astringent: Silver nitrate, hydrogen peroxide
  - Corticosteroids: Betamethasone
- B. Biological agents
  - Growth factors: G-CSF, GM-CSF, KGF, TGF B 3
  - Cytokines: Interleukin-11
  - Anticytokines: Pentoxiphyllin, Amifostine, Lysophyllin
  - Immunoglobulin: Human IgG
  - Amino acid: Glutamin
  - Antioxidants: Beta carotene, Vit E, Vit C
  - Enzymes: PGE1, PGE2
- C. Physical agents
  - Low lasers
  - Cryotherapy
- D. Specialized techniques
  - Midline-sparing technique of radiation
- E. Miscellaneous
  - Dental and oral hygiene care
  - Mouth rinses and topical anesthetics

of mucositis should be graded and, accordingly, medications should be decided if there is no existing treatment administration protocol that may directly correlate with the index.

Patients and their attendants should be informed about the various complications of cancer therapy, significance of oral hygiene and avoiding oral trauma during brushing of teeth and eating, etc. A soft brush is more suitable in such situations and, every time before use, it should be rinsed properly and dried to avoid any bacterial overgrowth. If the patient is a denture wearer, the prosthesis should be withdrawn until the mucositis

subsides. Continuation of use of denture may traumatize the mucosa, aggravate the inflammation and delay the healing. Further ulceration thus caused become areas of colonization for microorganisms, from where they can get an easy entry into the systemic circulation.

**Interventions during cancer therapy**

During the active phase of cancer therapy, the measures taken are aimed to prevent or to relieve the side-effects of chemo and/or radiotherapy. This involves maintenance of oral hygiene, prevention of infection and trauma, management of pain associated with mucositis, xerostomia, dysgeusia and control of spontaneous oral bleeding associated with thrombocytopenia. Various traetemt options to treat mucositis have been shown in Table 3.

It is not possible to discuss these methods in detail. Here, we will review the current measures involved in practice and research to treat oral mucositis.

During cancer therapy, strong oral hygiene measures should be adopted. The nursing team of the hospital should monitor the measures taken during hospitalization. The mouth should be examined daily to detect the complications of therapy as early as possible. In ambulant patients, where the patient condition does not allow the examination of the oral cavity, antimicrobial rinses should be given. Chlorhexidine is an effective, broad-spectrum antiseptic and bears antiplaque activity. In addition, it has got an antifungal action too. In place of chlorhexidine, povidine iodine rinse is a better alternative.<sup>[8,9]</sup> In herpes simplex seropositive patients, prophylactic oral administration of acyclovir reduces the incidence of clinical herpes simplex viral lesion.<sup>[10]</sup>

The mucositis causes severe soreness and pain in the oral cavity and makes swallowing and speech very difficult. Thus, pain management at this stage is essential. As the severity of mucositis increases, the typical pain management strategies become less effective. Their usefulness is limited to mild to moderate mucositis pain. In severe mucositis, non-steroidal antiinflammatory drugs (NSAIDs) with opioid can make the patient comfortable. However, analgesic treatment starts with NSAIDs and, as the pain increases, they are combined with opioid. NSAIDs are titrated to effective pain relief. Systemic analgesics are given by clock to achieve the maximum therapeutic effect. Adjuvant medication may be required to potentiate analgesia and manage the side-effects of NSAIDs and opioid.

Sucralfate, a complex of sucrosulfate and aluminum hydroxide, has been used as a mucosal protectant and its role has been thoroughly evaluated for the

prevention of mucositis. Its suspension is another choice for managing mucositis. It provides significant pain relief and resolution of mucositis.<sup>[11]</sup> This agent stimulates the production of prostaglandin E2, resulting in increased mucosal blood flow, higher mitotic activity and migration of epithelial cells. Prostaglandin E2 possesses cytoprotective activity and thus its effect can be anticipated. Sucralfate may also prevent the colonization of microorganisms on the mucous membrane. However, the results of studies are conflicting and do not favor adoption of this medication as standard therapy.

Epstein *et al.*, in their study, found that prophylactic oral rinsing with sucralfate did not prevent oral ulcerative mucositis. However, it may reduce the experience of pain during radiation therapy.<sup>[12]</sup> On the other hand, Cengiz *et al.* have shown that sucralfate decreases the intensity of radiation<sup>[10]</sup>-induced mucositis and oral discomfort. It is cheap, easy to administer with no serious side-effects and may be routinely used in patients receiving head and neck radiotherapy.<sup>[13]</sup> The beneficial effects of sucralfate have been established by histopathological demonstration.<sup>[14]</sup>

Gelclair is another mucosal protectant and it helps in the management of pain associated with oral mucositis. Chemically, it contains polyvinylpyrrolidone and sodium hyaluronate in a liquid gel. It forms a bioprotective coating that provides almost instant comfort and effective pain relief.<sup>[15]</sup> Benzydamine is a non-steroidal drug that has shown to possess antiinflammatory, analgesic, anesthetic and antimicrobial activities. It is an effective inhibitor of TN- $\alpha$  production, which explains its antiinflammatory effect.<sup>[15]</sup> A multicenter, randomized, double-blind study was performed to evaluate the role of benzydamine HCl as prophylaxis for radiation-induced oral mucositis in patients with head and neck cancer.<sup>[16]</sup> Benzydamine 0.15% oral rinse was found to be effective, safe and well tolerated for the prophylactic treatment of radiation-induced mucositis with head and neck carcinoma receiving a variety of radiotherapy regimen.<sup>[17,18]</sup>

The oral rinse reduced the pain associated with mucositis also. Fewer patients using benzydamine rinse required systemic analgesics.<sup>[19]</sup> Corticosteroids – hydrocortisone and betamethasone – have also been reported to reduce the radiation-induced mucositis.

Prophylactic cryotherapy in the form of ice chips sucking has been found to be effective in patents on 5-fluorouracil chemotherapy to prevent mucositis. It has been proposed that if blood flow to the cheek mucosa is diminished, less drug will reach the oral mucosa, thereby reducing the ill effects. This can be

achieved by sucking the ice chips (cryotherapy). Few studies have shown that oral cryotherapy is effective in preventing 5 FU-induced mucositis.<sup>[20]</sup> Cryotherapy has also been found to reduce mucositis in patients receiving combination chemotherapy.<sup>[21]</sup> It also reduces the requirement of narcotic analgesics to manage pain relief and parenteral nutrition.<sup>[22]</sup>

In a randomized study in 225 patients, Sorensen *et al.* found that the frequency and duration of oral mucositis may be significantly improved by either prophylactic chlorhexidine or by cryotherapy.<sup>[23]</sup> The latter is easy and inexpensive but is drug- and schedule-dependent as it cannot be used with infusional 5-FU or with chemotherapy with substantially longer half-lives than 5-FU.

The results of three randomized trials have also shown a significantly lower incidence and severity of oral mucositis compared with the controlled groups.<sup>[24,25]</sup> Cryotherapy is also effective in the prophylaxis of mucositis.<sup>[26,27]</sup> Libelly *et al.* reported that 6 h of exposure to oral ice chips significantly decreased the incidence of grade 3 and grade 4 mucositis in patients receiving melphalan.<sup>[28]</sup> Cryotherapy is an alternative method of preventing mucositis associated with chemotherapy agents that have a short life in blood.

In addition, low-level laser therapy (LLLT) may also be effective in preventing and suppressing mucositis in patients receiving high-dose chemotherapy. LLLT refers to the use of red-beam or near-infrared lasers with a wavelength between 600 and 1000 nm and power from 5 to 500 milliwatts. These lasers are non-thermal. Because of low absorption by human skin, the laser light can penetrate deeply into the tissues where it produces a photo-biostimulation effect. These types of lasers have been advocated for use in a range of medical conditions like delayed wound healing and tuberculosis and in a variety of musculoskeletal conditions like rheumatoid arthritis.

Nes and Posso investigated the effect of low-intensity lasers in chemotherapy-induced oral mucositis. They found that there was a statistically significant decrease in the daily average experience of pain felt before and after each treatment and confirmed that low-intensity laser therapy can relieve pain among patients who develop chemotherapy-induced mucositis.<sup>[29]</sup>

Sandoval *et al.* also noticed the beneficial effect of low-intensity lasers in chemotherapy- and/or radiotherapy-induced mucositis. They established that a low-energy laser was well tolerated by patients and produced beneficial effects on the management of oral mucositis, improving the quality of life during the oncologic treatment.<sup>[30]</sup>

Genot reviewed the role of LLLT in radiation- and chemotherapy-induced mucositis. On the basis of the literature data, he concluded that there is substantial evidence to suggest that LLLT may be used in decreasing the severity of chemotherapy-associated or radiotherapy-associated mucositis.<sup>[31]</sup>

The midline-sparing block technique is the method that has been used to protect the mucosa of the aerodigestive tract in the low-neck field during head and neck irradiation in treating oropharyngeal and nasopharyngeal cancers. The technique lacks wide acceptance and documentation of its efficacy. However, it has been shown to cause less weight loss and nutritional supplementation, leading to unplanned treatment interruption.<sup>[32]</sup>

### Current trends in management of Oral Mucositis

Current trends in the management of oral mucositis are more toward the search of a suitable biological agent. Various agents have been tried and tested, but with varied results. Growth factors have attracted much attention. They are naturally occurring proteins capable of stimulating cellular proliferation, differentiation and maturation. They are important for a variety of cellular processes and, typically, act as signalling molecules between cells, binding to specific receptors on the surface of their target cells. The growth factors can be applied locally or administered systemically.

Epidermal growth factor (EGF) binds to specific high-affinity, low-capacity receptors on the surface of responsive cells. It exerts a proliferative effect on cells of ectodermal and mesodermal origin. It also exhibits negative growth effects on certain carcinoma. They have been proved to be helpful for the prevention of oral mucositis in autologous stem cell transplant recipients. The study performed by Stiff *et al.* concluded that patients receiving Kepivance (EGF) reported a significant improvement in the daily functioning activities of swallowing, drinking, eating, etc. compared with the control group. The same study also documents the effectiveness of Kepivance in preventing oral mucositis in stem cell transplanting.<sup>[33]</sup> Lee *et al.* performed their study on rat models using human recombinant epidermal growth factor (rhEGF). They found that the survival and oral intake was significantly increased and concluded that orally administered rhEGF decreased the radiation-induced oral mucositis in rats.<sup>[34]</sup>

Keratinocyte growth factor is a normal cytokine that is present in many tissues and is produced in response to tissue injury.<sup>[33]</sup> KGF stimulates growth epithelial cells in tissues that have receptors for this cytosine.<sup>[35]</sup> A clinical study was performed on randomly selected

patients with colorectal cancer who were being treated with 5 FU and leucovorin to receive KGF or placebo. The KGF at a dose of 40 µg/kg/d for 3 days produced meaningful biological effects. There was a lower rate of mucositis in contrast to placebo.<sup>[36]</sup>

Plifermin, a recombinant human keratinocyte growth factor, is effective for treating mucositis resulting from chemotherapy or radiotherapy. This cytokine significantly reduced the duration of mucositis after extensive therapy. Speilberger *et al.* found that patients receiving palifermin used significantly lower cumulative doses of morphine equivalents and for fewer days than did placebo recipients and had minor adverse effects, such as rash.<sup>[37]</sup>

Palifermin has also produced a beneficial effect on mucositis in human recipients of hemopoietic stem cell transplantation who received etoposide, cytarabine and melanphan. In these patients, pre-treatment with keratinocyte growth factor reduced the mucosal atrophy and weight loss, accelerated mucosal regeneration, decreased ulceration and improved survival through gene-mediated effects on growth and differentiation.<sup>[38]</sup>

Granulocyte macrophage colony stimulating factor (GM-CSF) has been used topically to prevent chemo/radiotherapy-induced mucositis; however, the results are not encouraging. Sprinzle *et al.* demonstrated that its topical use as such cannot be recommended as its superiority could not be statistically proved over the conventional mouth washes and due to its tremendous cost.<sup>[39]</sup> The studies performed by Dazzi *et al.* reveal that it neither reduces the frequency nor duration of severe oral mucositis induced by high-dose chemotherapy given to recipients of an autologous peripheral blood hemopoietic stem cell transplant to treat solid tumors.<sup>[40]</sup>

Results of studies performed by Lieschke *et al.* indicate that patients receiving granulocyte-colony stimulating factor (G-CSF) suffered less-severe mucositis than patients who did not receive this cytokine.<sup>[41]</sup>

Interleukin-11 is believed to increase the proliferation and suppress the apoptosis of mucosal cells. However, the safety and efficacy of this cytokine in the oral mucositis has yet to be thoroughly evaluated.<sup>[42]</sup>

L-glutamine is an essential amino acid involved in cellular repair and has also been used as a supplement in parenteral nutrition preparation, with some evidence that it prevents infection in debilitated patients. It is combined with a vehicle that enhances its availability to cells of the mucous membrane. This combination favorably affects the course of the chemotherapy-induced mucositis. In a double-blind study, the control

group had severe mucositis in comparison with the L-glutamine group.<sup>[43]</sup>

Kuhrer *et al.* reported the pain relief and healing of the oral lesion using prostaglandin PGE<sub>2</sub>. Some other studies have also indicated a cytoprotective activity of PGE<sub>2</sub>. However, others disapprove this effect.<sup>[44,45]</sup>

Wadleigh *et al.* have shown that Vit. E, an antioxidant, ameliorates oral mucositis. Beta carotene also has been proved to prevent the development of several mucosal lesions.<sup>[46]</sup>

### Transforming Growth Factor $\beta 3$

Transforming Growth Factor  $\beta 3$  (TGF  $\beta 3$ ) is an inhibitor of a variety of normal epithelial cell proliferation and hemopoietic stem cells and preventing the cell cycle progression and accumulating cells during the phase of chemotherapy. It protects the stem cells from radiation-induced cytotoxic damage and initiates the regeneration of clonogenic stem cells thus causing the reduction of mucositis.<sup>[47,48]</sup>

The tumor cells are less responsive to inhibiting the effects of TGF  $\beta 3$ . The ability of TGF  $\beta 3$  to reversibly inhibit cycling of normal epithelial and hemopoietic stem cells allows it to be used as a chemoprotectant of normal tissue during cytotoxic chemotherapy. It is preferably administered topically; however, the administration may be systemic also.<sup>[49]</sup>

Azelastine is a mast cell inhibitor and is known to suppress the neutrophil-reactive oxygen production and cytokine release from the lymphocyte. Osaki *et al.* established the role of prophylactic azelastine hydrochloride, with other antioxidants reducing oral mucositis in patients receiving concomitant chemo/radiotherapy. However, a thorough study is still needed to understand its potential role.<sup>[50]</sup>

### Effect of the antifibrotic protein serum amyloid-P

Murray *et al.*<sup>[51]</sup> studied the effect of the antifibrotic protein Serum Amyloid-P (SAP) on radiation-induced oral mucositis and fibrosis in a hamster cheek-pouch model. They found that its administration, in general, significantly attenuated the radiation-induced injury and, in particular, attenuated the severity of oral mucositis and inhibited the pathogenic remodelling. They concluded that SAP may be a useful therapy for the palliation of the side-effects observed during the treatment for head and neck cancer.

### Associated problems: Xerostomia, candidiasis and degeusia

Besides mucositis, the radiation patients suffer from poor salivary flow lead to xerostomia and taste disorders.

The use of sialogogues, such as pilocarpine, has been proposed. But, the results of studies are inconsistent. In a study, 214 patients undergoing radiation therapy for head and neck cancer were allocated to receive placebo and pilocarpine. Patients in the placebo arm felt greater pain and swallowing difficulty, but the salivary function was preserved statistically significant in the pilocarpine receiving group. There was no apparent effect on mucositis.<sup>[52]</sup> Similar effects were observed in another study in which the parotid salivary flow was compared with the placebo.<sup>[53]</sup> Amifostine is another option for use with ionizing radiation for maintaining salivary flow, but it has some significant side-effects and its effect on salivation are moderate. However, if used subcutaneously, the side-effects are minimum.<sup>[54]</sup>

Candidiasis is the most common infection seen clinically in the oral cavity in the irradiated patients and studies have demonstrated in quantitative counts and rates for clinical infection of *Candida*. It may exacerbate the symptoms of mucositis. In such cases of mucositis, typical antifungals such as nystatin and clotrimazole are primarily helpful. Compliance can be compromised secondary to oral mucositis, nausea, pain and difficulty in dissolving nystatin pastilles and clotrimazole troches. Systemic antifungals – ketoconazole and fluconazole – have proved to be effective and are advantageous over topical agents.<sup>[55]</sup>

As the oral and pharyngeal mucosa are exposed to radiation, taste receptors become damaged and taste discrimination becomes increasingly compromised.<sup>[56,57]</sup> After several weeks of radiation, it is common for patients to complain of no sense of taste. It will generally take upwards of 6–8 weeks after the end of radiation therapy for the taste receptors to recover and become functional. Zinc sulfate supplements have been reported to help with the recovery of the sense of taste.<sup>[58,59,60]</sup>

## DISCUSSION

Chemotherapy, radiotherapy and a combination of the two are the methods of treating malignant neoplastic diseases. Although these approaches have lead to a significant improvement in the survival, it has come at the cost of severe complications of which oral complications are extremely debilitating in that they affect swallowing, speech, taste and interruption of antineoplastic therapy as well. The literatures are in abundance to address these problems in general and oral mucositis in particular. But, most of the studies are performed in the experimental phase and inconsistency exists in the interventional options employed. The overall results are, however, inconclusive. Sonis<sup>[4]</sup> findings on radiation- or chemotherapy-induced

mucositis help us to think of different agents at different phases for relief of the patient. The management of oral mucositis should involve a three-point approach – prevention, enhancement of healing and emotional and psychological support, which should be administered in a stage-wise manner. There is need to perform a series of multicenter, prospective, randomized trials on this aspect. Until studies give identical results, probably, it would be difficult to arrive at an acceptable solution. However, a gold standard rule has not yet been formulated to deal with such common side-effects of chemo/radiotherapy.

Of all the agents reviewed, palifermin and low-level laser appear to be most promising. However, for administration of palifermin, a scientific approach should be developed and administration of low-level laser would need very costly equipment and well-trained professionals. Both the options are very costly. Thus, a cost-effective prophylactic and therapeutic treatment with high-dose chemotherapy are the need of the time to base the research.

## CONCLUSION

Oral complications of cancer therapy are varied and bear a high morbidity. The mouth not only acts as a mirror of the oral manifestation of antineoplastic therapy, but it is the portal of entry of life-threatening infections too. The oncologist should involve the dental team in different stages of treatment to assess the mucosal damage and to render specific oral hygiene measures. A cost-effective, perfect treatment of antineoplastic therapy-induced mucositis is yet to be evolved that could be administered and matched with different stages of the WHO oral mucositis scale.

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