

REVIEW ARTICLE

TOPICAL AGENTS FOR THE PREVENTION AND TREATMENT OF ORAL MUCOSITIS

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ABSTRACT**The aim:** To make a narrative assessment of the agents currently in use, with a particular emphasis on the topical agents that we frequently utilize in our practice.**Materials and methods:** The main method of this work is a review of literary sources. We reviewed the literature (PubMed, Google Scholar, Web of Science, Scopus) to support and explain the interventions we use in different cases of oral mucositis patients. We decided to combine our experience with evidence-based data.**Conclusions:** Topical treatments alleviate and prevent oral mucositis. Topical medicines can assist maintain oral balance and moistness by modulating oral bacteria and replacing saliva.**KEY WORDS:** Oral Medicine, Oral mucositis, Topical agents

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INTRODUCTION

Oral mucositis is a common side effect of radiation, cytotoxic chemotherapy, and other targeted cancer treatments [1]. Patients with head and neck cancer may be more vulnerable due to radiation damage to the oral mucosa and decreased saliva production [2]. Oral mucositis is a disorder that is both inflammatory and infectious [1]. Although the exact process is unknown, the most likely scenario is that decreased turnover of the oral epithelium over time results in perforation of the mucosa, which subsequently becomes infected by bacteria that colonize the oral cavity [2]. Destruction of the oral mucosa may result in excruciating erythema, ulcers, and hemorrhagic lesions [2]. These factors make eating difficult, and protein loss and the danger of septicemia may potentially necessitate therapy discontinuation [3].

The WHO has developed a scale for categorizing oral mucositis that is used in the majority of clinical and experimental investigations (table I) the majority of patients with head and neck cancer will develop a mild or severe type of oral mucositis [4]. Radiotherapists, oral medicine specialists and Oral & Maxillofacial Surgeons are the doctors who treat patients with oral mucositis. Specialized dentists as well as oral medicine specialists, who are by definition the most qualified to treat oral mucositis may not be appointed in cancer centers worldwide.

We intend to provide relevant information to all physicians and surgeons engaged in order for them to assist patients.

THE AIM

Selective presentation of topically applied agents used in the prevention and treatment of oral mucositis

Numerous topical agents are now being used to prevent and treat oral mucositis. The majority are designed to protect the mucosa by forming a film that prevents local trauma ensuring that the sensitive oral mucosa does not develop lesions as a result of stress. The drug delivery system, a means of providing medications to the oral mucosa in an adhesive medium that prolongs medication release and improves therapeutic impact, is an important part of topical oral therapy. A mucoadhesive drug delivery system is a significant breakthrough as one of the ways for delivering the active chemical across mucosal membranes. Various gels have been produced with the goal of achieving prolonged drug release for a local therapeutic effect. Many preparations have been developed in the past, including the discovery of the active component and excipients used as a covering agent or healing agent [5]

MATERIALS AND METHODS

We reviewed the literature (PubMed, Google Scholar, Web of Science, Scopus) to support and explain the interventions we use in different cases of oral mucositis patients. We decided to combine our experience with evidence-based data.

REVIEW AND DISCUSSION**SUCRALFATE ORAL GELS**

To minimize pain and lesions of the oral mucosa, sucralfate gel is routinely used at the commencement of chemother-



Fig. 1. Ulcers in a patient treated with everolimus (mtor inhibitor).



Fig. 2. Grade 3 mucositis treated with systemic antifungals and also topical nystatin and dexamethasone mouthwash

apy and radiation [6]. Sucralfate gels are used to prevent lesions and to relieve sensitivity by hydrating the mucosa [7]. This is critical since radiotherapy for head and neck therapy is highly prone to result in xerostomia (dryness of the mouth). Few studies have been conducted to determine the efficacy, and the majority of writers advocate using the gel one (1) hour before meals and 2-4 times a day [8].

Sucralfate is recommended for usage only at the start of treatment as a preventative measure and for grade 1 mu-



Fig. 3. Grade 4 mucositis, notice also the food residues due to xerostomia, the patient is on radiotherapy for oral squamous cell carcinoma, received systemic antifungals and erythromycin, as well as lidocaine gel and dexamethasone mouthwash

cositis [9]. No serious adverse effects have been reported regarding the use of sucralfate gels, just concerns about the flavor and sensation of “sticky mouth” [10,11]

TOPICAL CHAMOMILE CONTAINING GELS

Chamomile is believed to be an useful topical antimicrobial treatment for oral mucositis [12]. It is available as an oral gel containing 3% chamomile [13]. BioM is a chamomile gel and foam sold in Greece. Additionally, the product contains Bakuchiol, an antibacterial and antifungal plant extract [14]. In comparison to chlorhexidine, bakuchiol has been presented as a less expensive mouth antiseptic. It may be utilized as an anti mucositis agent [15]

ANESTHETICS TOPICAL GELS

Lidocaine creams and gels have been used to alleviate pain associated with oral mucositis, particularly in grades 1 and 2 [16]. It's easy to see why the advantages are just temporary and why multiple more agents are required. It is not capable of healing lesions; it can only alleviate discomfort, and patients may report weird sensations. It has historically been used as a mouthwash [16].

In Greece, a novel design for oral pastes and gels is available that significantly simplifies their usage. Lidocaine may be coupled with steroids in this formulation.

Table I. World Health Organization (WHO) Scale of Oral Mucositis

The World Health Organization (WHO) scale assesses oral mucositis subjectively and objectively					
Grade	0	1	2	3	4
Feature	No oral mucositis	Erythema and soreness	Ulcers, able to eat solids	Ulcers, requires a liquid diet (due to mucositis)	Ulcers, alimentation not possible (due to mucositis)

CORTICOSTEROIDS USED TOPICALLY IN MUCOADHESIVE MEDIA

Triamcinolone is frequently used to treat oral ulcerative conditions in mucoadhesive media [17]. This formulation is widely available as an OTC medication in a number of countries [17]. It is used for the treatment of mildly painful cases of oral mucositis [18]. Such events are typical in patients treated with mTOR inhibitors for a variety of malignancies (Fig 1) [19]. These treatments are readily available, reasonably priced, and may be used topically for an extended period of time due to their ability to be delivered particularly to ulcers [17]. Patients should be made aware of the likelihood of acquiring oral candidiasis.

Clobetasol is a highly active steroid that is used topically to treat a variety of inflammatory oral and skin conditions [20].

The medication may be used with mucoadhesive paste. These formulations are frequently employed in the treatment of oral ulcerative disorders, such as oral lichen planus [21]. Clobetasol in oral gel has been recommended as a therapy for oral ulcers in grade 3 and 4 oral mucositis, according to experts (Fig 2) [22]. Clobetasol has a broad anti-inflammatory impact on the skin, and the gel form of clobetasol appears to have a rapid onset of action. [23].

They are used in conjunction with antimicrobial topical and systemic medications. Clobetasol and nystatin can be used in a single formulation effectively [24].

For many years, topical administration of fluocinolone in an adhesive base has been shown to be a safe and effective method of treating oral lichen planus and other inflammatory disorders [25]. It is utilized in aphthous conditions such as ulcerations. It may be used to alleviate discomfort associated with mild to moderate ulcers in people suffering from oral mucositis. It can be used in conjunction with orally administered systemic and topical medications. The price is not prohibitively expensive.

TOPICAL ORAL GEL ANTIMICROBIAL AGENTS

The presence of microbes has a critical role in the severity of oral mucositis. Superinfections with fungal and bacterial pathogens cause and worsen oral mucosal ulcers caused by cytotoxicity [1-3].

Chlorhexidine is a common topical antiseptic used to treat gingival infections [26]. Additionally, it has been reported that it possesses antifungal characteristics [27]. Chlorhexidine has historically been used to treat and prevent oral mucositis [28]. The results are inconsistent. According to some writers, it may be cytotoxic and exacerbate taste changes [28]. Generally, it is not advised (by the Multinational Association of Supportive Care in Cancer and International Society of Oral Oncology (MASCC=ISOO) Clinical Practice Guidelines for mucositis)

for the prevention or treatment of oral mucositis at the moment [28]. Despite the MAASCO guideline, it is not contraindicated in mild situations, such as plaque gingivitis associated with oral mucositis. Perhaps a gel administration in a small lesional site would be more useful.

Nystatin is a commonly used antifungal medication [29]. It is mostly used as an oral solution and a cream. It has been used to treat fungal infections in oral mucositis patients [30]. In mucoadhesive medium, it can be used with clobetasol. In people with oral lesions, nystatin may elicit a burning sensation but is generally safe and inexpensive [31]. Nystatin cannot be used to treat severe fungal infections [31]. Nystatin can be also combined with dexamethasone in oral solution.

Erythromycin has been suggested as an oral mucositis therapy [32]. It is antibacterial and anti-inflammatory in nature (like all macrolides). It is suitable for usage topically in mucoadhesive media [33]. Treatment of minor superficially infected lesions can be beneficial [33]. Taste alterations are a possible side effect [32].

The antibiotic metronidazole is used to treat infections caused by anaerobic bacteria [34]. Metronidazole is widely used in the treatment of necrotizing gingivitis [34]. Gingival infection of this sort is more prevalent in immunocompromised patients [34]. Topical metronidazole is used in connection with delayed release intrapocket media [35]. It is also compatible with mucoadhesive media [36]. It may be beneficial in preventing superinfection with anaerobic bacteria in cases of oral mucositis [36].

PROPOSED TOPICAL TREATMENT STRATEGY FOR PATIENTS INITIATING ANTI-CANCER THERAPY (INCLUDING HEAD AND NECK CANCER PATIENTS)

The most critical goal is to alleviate discomfort while retaining the capacity to eat.

Thus, agents that keep the mouth moist and trauma-free is the first line of defense. Gels such as camomile and sucralfate are examples. Currently, the most cost-effective treatment option in Greece is BioM Gel. The entire cost of two months of therapy is less than 60 euros.

Prophylactic systemic antimicrobials are indicated in some cases [32].

PROPOSED TREATMENT FOR GRADE 1 AND 2 ORAL MUCOSITIS

The most cost-effective treatment is a generic triamcinolone and lidocaine oral gel (about 20 euros per 100 gr). We maintain BioM's moderate antibacterial action in these

individuals and may supplement with a gel containing 2% nystatin. Prophylactic systemic medications may also be employed in some cases.

PROPOSED TREATMENT FOR GRADE 3 AND 4 ORAL MUCOSITIS

These patients require systemic antibacterial therapy to prevent septicemia and opiate therapy to alleviate severe pain [28]. Again, topical medications such as lidocaine and clobetasol gels are beneficial in relieving pain (Figures 2&3). Topical antimicrobial gels, such as erythromycin gel, may assist the inflamed gingiva and minimize gingival bleeding. Additionally, hydration treatments such as chamomile gels have a palliative effect.

CONCLUSIONS

After diagnosing, treating, and monitoring over 50 patients with head and neck cancer who had radio chemotherapy during the last five years, as well as counseling several individuals with chemotherapy-induced mucositis, we have a well-established view about the disease's management. Two are absolute benchmarks. Each situation is unique, and patients must be closely monitored. This is consistent with the most evidence-based guidance available [28]. At least once a week, modifications in the approach to oral symptoms should be assessed. We frequently deal with individuals who have serious issues and say that they were simply given a "gel" for several weeks and their mouth was not evaluated. People need to eat throughout therapy to stay strong and to feel better. Topical medications undoubtedly have a role in treating and preventing oral mucositis. By regulating the oral microbiota and replacing diminished saliva, topical medications can help maintain the oral balance and moist environment of the mouth.

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The Authors declare no conflict of interest.

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