REVIEW ARTICLE

ORAL MUCOSITIS –MANAGEMENT PROTOCOL BY ORAL PHYSICIAN

Dr. Suresh Ludhwani[1]

[1]Post Graduate Student, Department of Oral Medicine and Radiology, Ahmedabad Dental College and Hospital

Corresponding Author

Dr. Suresh Ludhwani
Post Graduate Student, Department of Oral Medicine and Radiology, Ahmedabad Dental College and Hospital
Email: drgeminia@gmail.com

Access this Article Online

Quick Response Code

www.idjsr.com

Use the QR Code scanner to access this article online in our database

Article Code: IDJSR 0005

Abstract

Oral mucositis also called stomatitis, is one of the most common and troublesome forms in individual undergoing cancer treatment. Oncology treatment does not distinguish between the malignant cells and normal epithelial cells of mucosa because of their high proliferative capacity. Thus, the mucosa becomes atrophic, and more susceptible to trauma, allowing the development of inflammation and installation of secondary infection, which aggravates the patient's clinical conditions and reduce the quality of life. The clinical management of mucositis includes preventive and palliative strategies. The role of the oral physician in prevention and management of chemotherapy and radiotherapy induced mucositis is critical.

Introduction

Oral mucositis may be defined as inflammation of oral mucosa with extensive ulceration and painful irritation (1).It is considered an acute inflammation caused by the necrosis of the basal layer of the oral mucosa. The more important clinical features are erythema and/or ulceration (6), which may extend from the mouth to the rectum (2). It can induce several life-threatening complications, such as intestinal obstruction and perforation (3), reducing the patient's quality of life and leading to severe infections, which may require the interruption of the antineoplasic treatment (6). Oral and throat pain caused by the mucosa ulceration, abdominal pain, vomits and diarrhea are characteristics that compromise the patient's nutritional status because of a decrease of

food intake, leading to weight loss (5). The progression of oral lesions and its impact on general conditions of the patient may require parenteral nutrition or temporary interruption of the antineoplasic treatment (7).

It is a complex biological process divided into four phases, which are interdependent and can occur due to action of cytokines on epithelium. These phases are

1. Inflammatory or vascular phase: day 0
2. Epithelial phase: days 4-5
3. Ulcerative or bacteriologic phase: days 6-12
4. Healing phase: days 12-162

Epidemiology

Mucositis has received significant attention from the physician community in the last two decades of life. It is estimated that oral mucositis affects 40% of the patients undergoing chemotherapy, 75% of the patient undergoing chemotherapy and bone marrow transplantation and more than 90% patient undergoing radiotherapy for head and neck cancer. According to *chiappelli*, 40% of the patient undergoing radiotherapy develop mucositis. (12)

Pathophysiology

Firstly, the chemotherapy drugs induce the death of the basal epithelial cells, which may occur by the generation of free radicals. These free radicals activate second messengers that transmit signals from receptors on the cellular surface to the inner cell environment, leading to up-regulation of pro-inflammatory cytokines, tissue injury, and cell death. The pro-inflammatory cytokines produced by macrophages, such as TNF-α, amplify the mucosal injury; the production of these pro-inflammatory cytokines can also be stimulated by a superimposed infection of the ulcerated areas of the mucosa. Later, epithelial proliferation and cellular differentiation occur, restoring the integrity of the mucosa (12). The anti cancer drug most commonly associated with oral mucositis include bleomycin, doxorubicin, fluorouracil and methotrexate. The cancer therapy agents vincristine and daunorubicin have a toxic effect on the mucosa [Köstler et al., 2001]. Either the use of these drugs or the cancer itself leads to neutropenia, which predisposes the mucosa to mucostitic lesions and also enables bacterial invasion of the submucosa and vascular walls, leading to bacteraemia and septicaemia [Sonis, 2004; Brown and Wingard, 2004]. The patient in the case described here initially exhibited bacteraemia, the remission of which occurred following haematological recovery associated to the use of meropenem and vancomycin.

In radiotherapy, an inflammatory response is influenced by the depth and volume of radiation, total gray delivered and the number and frequency of treatments. The onset, duration and intensity vary with the individual but most often the onset starts with second week of therapy or after a dose of about 2000cGy.radiation therapy causes loss of taste by damaging the microvilli and outer surface of taste cells, the onset is rapid and progressive with ageusia or mouth blindness occurring after 3000 cGy.

Clinical Manifestation

The first symptoms reported by patients with oral mucositis are burning mouth and color changes in the mucosa, which becomes white because of insufficient keratin desquamation. Then, this epithelium is replaced by atrophic, edematous, erythematous, and friable mucosa, allowing the development of ulcerated areas with the formation of a pseudomembrane, characterized by the presence of a fibrinopurulent, yellow, and outstanding layer (6,9). The ulcerated lesions are painful and compromise the patient nutrition and oral

hygiene, and also are considered sites for the development of local and systemic infections. In the oral mucosa, this condition involves the ventral portion of tongue, floor of the mouth and soft palate (scully et al;2004).

According to the World Health Organization, oral mucositis is classified into the following grades:

Grade 0 – absence of mucositis;

Grade I – presence of painful ulcerations and erythema;

Grade II – presence of painful, erythema, edema or ulcerations that do not affect the patient food intake;

Grade III – confluent ulcerations that affect the food intake;

Grade IV – the patient requires parenteral nutrition (13).

Oral Hygiene Assessment

Prior to cancer therapy, the patient was submitted to an assessment of the oral cavity. Dental caries or periodontal disease associated with inadequate oral hygiene may lead to a greater risk for oral complications during the course of cytotoxic therapy. Odontogenic and gingival infections are a considerable source of bacteria, which aggravate oral mucositis lesions. These risk factors underscore the importance of an inspection of the oral environment before and during treatment that has a potentially toxic effect on the mucosa, as prior assessment allows differentiating oral mucositis from other pre-existing lesions as well as the elimination of potential sources of infection and sites of chronic irritation [Stevenson-Moore, 1990; Pajari et al., 1995; Brown and Wingard, 2004]. This conduct is part of the protocol for patients at the Oncology Clinic at which the present case was treated.

Regarding the indices used for the assessment of mucositis, the first study employed the Daily Mucositis Index (DMI) [Tardieu et al., 1996], the gradation of which ranges from 0 to 3 and assesses different aspects in the lips, gums, oral mucosa and tongue. In the present case, the WHO scale [1979] was employed, which ranges from 0 to 4 and does not measure different aspects in the different sites analysed. Moreover, the aforementioned study assessed the lesions only on the first and last days of treatment, whereas the assessment was performed on a daily basis in the present case.

CATEGORY	RATING	1	2	3	4
LIPS	1 2 3 4	Smooth,pink,moist and intact	Slightly wrinkled and dry; one or more isolated reddened areas	Dry and somewhat swollen, may have one or two isolated blisters; inflammatory line or demarcation	Very dry and edematous ;entire lip inflamed; generalized blisters or ulcerations
Gingiva and oral mucosa	1 2 3 4	Smooth,pink,moist and intact	Pale and slightly dry; one or two isolated lesions, blisters or reddened areas.	Dry and somewhat swollen, generalized redness; more than two isolated lesions, blisters or reddened areas.	Very dry and edematous; thick and engorged; entire tongue very inflamed; tip very red and demarcated with coating; multiple blisters or ulcers.
Tongue	1 2 3 4	Smooth,pink,moist and intact	Slightly dry; one or two isolated reddened areas; papillae prominent , particularly at base.	Dry and somewhat swollen,; generalized redness but tip and papillae are redder; one or two isolated lesions or blisters.	Very dry and edematous; thick and engorged; entire tongue very inflamed; tip very red and demarcated with coating; multiple blisters or ulcers.
Teeth	1 2 3 4	Clean; No debris	Minimal debris; mostly between teeth	Moderate debris clinging to one-half of visible enamel	Teeth covered with debris
Saliva	1 2 3 4	Thin, watery, plenty	Increase in amount	Saliva scanty and maybe somewhat thicker than normal	Saliva thick and ropy, viscid or mucid
Oral dysfunction		No dysfunction	Mild dysfunction	Moderate dysfunction	Severe dysfunction
Score		5	6-10	11-15	16-20

Treatment modalities

Antioxidants

Antioxidants may he particularly important since cancer treatment is an oxidative process. Radiotherapy and chemotherapy generate free radical species, which require anfioxidants to be neutralized

Beta-carotene

This has been proven to be useful in chemotherapy-induced mucositis. In one trial, chemotherapy patients were given 400,000 IU per day for 3 weeks and then 125,000 IU for an additional 4 weeks.

Vitamin E in combination with vitamin C
Both act on a cellular level by protecting the cell membrane and preventing peroxidation.

Glutamine
A precursor of glutathione, this is very important for stress periods. It is the most abundant amino acid in the human body, and it is now considered a conditionally essential amino acid during periods of catabolism. Early studies show that glutamine has a positive effect through three mechanisms: *(1)* as a cellular fuel; *(2)* as a precursor for nucleotides needed for cell regeneration; and *(3)* as a source of glutathione, which is a potent antioxidant's The use of 4 grams of powdered glutamine in oral rinse in a swish and swallow suspension, twice per day, decreases the intensity and duration of the mucositis

Lysofylline
A protectant that reduces lipid peroxidation also decreases oxidative injury. It is presently being tested in chemoradiation trials of head and neck cancer

Mucosal barriers

Clobetasol (0.05% ointment 1:1 with Orábase).
As a topical corticosteroid, it plays a role in inflammation and immunosuppression. It is contraindicated in infection.

Mouthwashes

Benzydamine hydrochloride
As an oral rinse, this has been shown to be effective, safe, and well tolerated in ameliorating the symptoms of cancer treatment induced mucositis. Rinsing then expectorating 15 mL of 0.15% solution every 2 hours will help with the painful inflammation of the mouth and throat. Benzydamine base local analgesic, antimicrobial, and anti-inflammatory properties. It prevents the release of the arachidonic acid cycle, which is an initiator of the inflammatory process.

Corticosteroid mouthwashes
These may be beneficial and are contraindicated if the patient bas a bacterial or viral infection. Triamcinolone acetonide 0.2% aqueous suspension can be used as a rinse for 1 minute twice a day and expectorated.

Chamomile mouthwashes
These have been used to improve mucosal healing. With controversial results. However, rinsing with 15 drops in 10 mL of warm water, three times a day, has reduced the incidence and severity of mucositis in cancer patients.

Local anesthetic mouthwashes
These may help to relieve pain on a temporary basis.

Analgesics

Capsaicin
This is found in chili peppers and acts upon nerve endings to provide temporary pain relief. The exact mechanism of action is unknown

Morphine
A central nervous system analgesic, it depresses pain impulse transmission. It is effective for managing mucositis pain in cancer patients, but dry mouth is one of its adverse reactions. (13)It does not improve the health of the mucosa.

Fentanyl (transdermal patch)
A very potent short acting opioid, it is used primarily as an anesthetic. It is available in a sustained-release transdermal delivery system (duragesic) with a half-life of 22 hours.

Immunomodulators

Thalidomide

An immunomodulatory and antiangiogenic agent, it inhibits tumor necrosis factor-alpha (TNF-o;), which is associated with oropharyngeal ulcers. In multiple studies, the efficacy of this medication against oral and esophageal ulcers bas been demonstrated. In one trial, 92% of patients had complete healing after 4 weeks by taking 200 mg by mouth at bedtime.

Nonpharmacologic approach

Cryotherapy

This produces vasoconstriction, which reduces blood flow and diminishes the distribution of the chemotherapeutic agent to the oral mucosa. Ice swishing for 30 minutes following cancer therapy has been shown to be beneficial for these patients

Low-intensity laser therapy

This may improve wound healing and accelerate replication of the cells. Low-energy helium-neon (He-Ne) laser seems to be a safe, simple, atraumatic, and efficient method for the prevention and treatment of chemotherapy/radiotherapy- induced mucositis.

Management protocol

Grade 1

Brush with soft bristled nylon brush and floss daily
Rinse with salt and soda or 15% hydrogen peroxide
Apply a moisturizer.
Promote oral hydration and nutritional intake
Remove and clean denture

Grade 2 & 3

Increase frequency of oral hygiene to every 2-3 hours
Use foam oral wash if brushing is too painful
Use agent to protect mucosa
Apply topical agent for pain control
Supplement oral intake with enteral or parental support.
Provide proper analgesics and/or antibiotics if indicated
Cultural suspect areas

Grade 4

Continue frequent oral hygiene
I.V antibiotics
Laser therapy
Cryotherapy

Conclusion

Mucositis is a common side effect of radio and/or chemotherapy anticancer treatments, but it has a complex pathophysiology and requires management strategies that have not been standardized yet. To identify patients at high risk to develop this condition is essential to reduce the costs of the anticancer treatment and to avoid its interruption after the installation of mucositis. There are many agents used for the treatment of mucositis with different mechanisms of action. However, there are no conclusive evidences on their effectiveness to establish protocols for patients undergoing radio and/or chemotherapy

References

1. Implications for evidence-based research in alternative and complementary palliative treatments. Evid Based Complement Alternat Med 2005;2:489-94.
2. Epstein JB, Schubert MM. Oral mucositis in myelosuppressive cancer therapy. Oral

Surg Oral Med Oral Pathol Oral Radiol Endod 1999;88:273-6.
3. Gibson RJ, Bowen JM, Keef DM. Technological advances in mucositis research: new insights and new issues. Cancer Treat Rev 2008;34:476-82.
4. Rubenstein EB, Peterson DE, Schubert M, Keefe D, McGuire D, Epstein J et al. Clinical practice guidelines for the prevention and treatment of cancer therapy-induced oral and gastrointestinal mucositis. Cancer 2004;100:2026-46.
5. Volpato LE, Silva TC, Oliveira, TM, Sakai VT, Machado MA. Radiation therapy and chemotherapy-induced oral mucositis. Rev Bras Otorrinolaringol 2007;73:562-568.
6. Keefe DM, Schubert MM, Elting LS, Sonis ST, Epstein JB, Raber- Durlacher JE et al. Updated clinical practice guidelines for the prevention and treatment of mucositis. Cancer 2007;109: 820-31.
7. Arora H, Pai KM, Maiya A, Vidyasagr MS, Rajeev A. Efficacy of He- Ne Laser in the prevention and treatment of radiotherapy-induced oral mucositis in oral cancer patients. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2008;105:180

8. Lionel D, Christophe L, Marc A, Jean-Luc C. Oral mucositis induced by anticancer treatments: physiopathology and treatments. The Clin Risk Manag 2006;2:159-68.

_____End of Article_____