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Case report

Pharmacological and low-level laser therapy in radiation-induced oral mucositis in patients with head and neck cancer

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ABSTRACT

Background: *Oral mucositis (OM) is common in people undergoing radiotherapy, chemotherapy, or a combination of both. Pharmacological and low-level laser therapy (LLLT) are potential treatments to reduce pain and accelerate the healing process.* ***Purpose:*** *The aim of this case report is to describe the effectiveness of combining pharmacological therapy and LLLT for OM.* ***Case:*** *A 54-year-old man with post-hemi glossectomy diagnosed with tongue cancer was referred from the radio-oncology department with complaints of painful sores all over the oral cavity after receiving radiotherapy. The canker sores worsened when eating but felt more comfortable when drinking cold water. Intraoral examination revealed erythematous lesions accompanied by fibrinous pseudomembranes and yellowish-white plaques, which could be scraped off, leaving erythematous areas with pain. These lesions were present on the upper and lower labial mucosa and the right and left buccal mucosa. The diagnosis was grade-3 OM, according to the World Health Organization (WHO) criteria.* ***Case management:*** *Pharmacological therapy included 0.025% hyaluronic acid gargles three times a day and the use of LLLT with a wavelength of 976 nm.* ***Conclusion:*** *The combination of pharmacological therapy with LLLT was effective in maintaining and improving the condition of the oral mucosa by reducing pain and ultimately improving the patient's quality of life.*

Keywords: *acute pseudomembranous candidiasis; low-level laser therapy; radiation-induced oral mucositis*
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INTRODUCTION

Head and neck cancer (HNC) management in the form of radiotherapy often causes oral mucositis (OM).[1] OM often results in difficulty chewing and swallowing, anorexia, and xerostomia, and consequently, can lead to weight loss.[1] Radiotherapy is the administration of radiation to tumor tissue, aiming to destroy tumor tissue while minimizing damage to surrounding normal tissue.

According to 2018 data from GLOBOCAN, HNC is the sixth most common type of cancer. Data from the Indonesian National Cancer Registration Agency indicates that HNC is a prevalent malignancy in men and ranks fourth among the top 10 cancers in Indonesia. Other risk factors for HNC include a history of smoking, alcohol consumption, exposure to chemicals, dietary habits, viral disorders such as Epstein–Barr virus (EBV) and human papillomavirus (HPV), and genetic variations.

Severe OM can affect the patient's food intake, weakening the body due to a lack of nutrients. This weakened condition disrupts the patient's radiation schedule, affects the intensity of anti-cancer therapy, increases the risk of infection, and raises the cost of treatment and therapy. Delaying anticancer therapy will result in cancer cells continuing to proliferate, potentially endangering the patient's life.[2]

For patients with HNC receiving chemotherapy in addition to radiation therapy, the prevalence of OM is about 90%. OM is currently measured using a variety of scales with varying criteria. The WHO OM evaluation

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scale considers objective criteria, such as the presence of erythema or ulceration, and functional criteria based on the patient's ability to eat. A quantitative scale that assesses the dimensions of ulceration is used by the Oral Mucositis Assessment Scale (OMAS). The Eastern Cooperative Oncology Group (ECOG) mucositis scale is reported in the general toxicity criteria guidelines, where the severity of mucositis is classified differently based on the anatomical site of development. Similarly, the National Cancer Institute (NCI) provides a mucositis severity measure scale in the Common Terminology Criteria for Adverse Events (CTCAE) based on the anatomical site of progression and the type of treatment, either chemotherapy or radiotherapy.[3]

OM is treated with pharmaceutical therapies for symptomatic relief and low-level laser therapy (LLLT), which is currently being researched to assist in accelerating the healing process and reducing pain.[4,5] The aim of this case report is to describe the benefits of combined pharmacological therapy and LLLT in a patient with OM triggered by radiotherapy. Early management of OM can prevent its severity and help avoid discontinuation of radiotherapy treatment. In this case, the combination of pharmacological therapy and LLLT was proven to speed up healing and reduce the pain experienced by the patient.

CASE

A 54-year-old man came to Hasan Sadikin Hospital, referred from the Radiation Oncology department, with complaints of pain due to canker sores throughout the oral cavity. The complaint started to appear after the 10th cycle of radiotherapy, which was scheduled to continue until the 30th cycle. The final diagnosis, according to histopathological anatomy, was well-differentiated squamous cell carcinoma.

The patient had received NaCl 0.9% therapy twice a day as compresses to the surface of the oral cavity as instructed by Radiation Oncology, but the canker sores remained painful. The patient was referred to the Oral Medicine department after completing the 25th cycle. Radiotherapy was scheduled five times a week, from Monday to Friday. The canker sores hurt more, especially when eating, and felt more comfortable when drinking cold water. At this time, the patient could only consume porridge and milk.

Extraoral examination showed that the patient was in good general condition, with non-anemic conjunctiva and non-icteric sclera. The upper and lower lips appeared dry and exfoliative.

Intraoral examination at the first visit showed areas of erythema accompanied by fibrinous pseudomembranes and yellowish-white plaques on the entire buccal surface, which could be scraped off, leaving areas of erythema and painful multiple red-black erosions and crusting lesions throughout the oral cavity (Figure 1). The second visit's intraoral examination showed little improvement, with the erythema areas slightly reduced (Figure 2). By the third visit, the lesions appeared to have healed (Figure 3). The diagnosis was grade-3 OM according to WHO criteria.

CASE MANAGEMENT

Instructions to maintain oral hygiene were given at the first visit by brushing the teeth and tongue using a soft toothbrush with non-detergent toothpaste at least twice a day (morning after breakfast and night before bed). The patient was

Figure 1. Clinical presentation of the patient on the first visit. The lesion on the upper and lower labial mucosa, left and right buccal mucosa, dorsal tongue, and palatum was painful, and the patient experienced difficulty eating.

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Figure 2. Clinical presentation of the patient on the second visit. The lesion on the upper and lower labial mucosa, left and right buccal mucosa, dorsal tongue, and palatum showed reduced erythema and fibrinous areas.

Figure 3. Clinical presentation of the patient on the third visit. The lesion on the upper and lower labial mucosa, left and right buccal mucosa, dorsal tongue, and palatum showed healing.

Figure 4. Laser therapy performed during the second visit targeted the erythema area of the lower labial mucosa and the right and left buccal mucosa.

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instructed to rinse the mouth using 0.025% hyaluronic acid, 10 ml, three times a day. Extraoral treatment was to apply a thin layer of Vaseline album on the upper and lower lips three times a day. The pain was evaluated using the visual analog scale (VAS) to measure the pain felt by the patient subjectively, and a score of eight was obtained.

Five days after the first visit, the patient finished the 30th cycle of radiotherapy and decided to perform LLLT with a 970 nm diode laser, with a dose of 3 J/cm^2 for ten seconds at each point, once a day, using the continuous wave method (Figure 4). The oral condition improved, but the patient still complained of pain and stinging. Pain evaluation using the VAS scale showed a subjective score of six at this second visit. The patient was still educated to maintain oral hygiene and continue using the hyaluronic acid rinse, 10 ml, three times a day.

The third visit was 15 days after the second visit, following the patient's control schedule at the radiology department. The condition had improved, and the patient had begun consuming solid food as the ulcers in the oral cavity healed. Pain evaluation using the VAS scale at this visit showed a score of two. Education was still provided to maintain oral hygiene and implement a healthy lifestyle by maintaining a proper diet, adequate water intake, and rest, as well as instructions to stop using hyaluronic acid. However, the patient was advised to continue applying a thin layer of Vaseline album on the upper and lower lips at least twice a day until the lips felt moist and normal again. LLLT therapy with a wavelength of 970 nm was given to help the healing process.

DISCUSSION

Radiotherapy for patients with tongue cancer is carried out every day from Monday to Friday, with a therapy target of 30 cycles. The patient began complaining of discomfort in his oral cavity after the 10th radiotherapy session, and the complaints worsened as the number of radiotherapy cycles increased. The patient's first visit occurred after completing 25 cycles of radiotherapy, with a diagnosis of grade-3 OM according to WHO criteria.

Assessment using the WHO scale includes the following criteria: level 0 (no OM), level 1 (erythema lesions and pain), level 2 (ulcers present but still able to eat solid food), level 3 (ulcers present, requiring liquid food due to mucositis), and level 4 (ulcers present, unable to eat due to mucositis).[3] This aligns with the patient's condition, as he had difficulty eating solid food and was only consuming porridge and milk.

Radiation exposure can cause OM. It causes DNA damage, resulting in DNA chain breaks and basal epithelial cell death. It is now recognized that the pathogenesis of OM is more complex. This involves reactive oxygen species (ROS) molecules. These molecules are unstable and contain oxygen. ROS can easily react with other molecules in the cell. ROS accumulate in cells, causing damage to DNA, RNA, and proteins, ultimately leading to cell death.[3,6,7]

The pathogenesis of OM has five phases. The initial phase is characterized by the formation of ROS induced by cytotoxic agents. The upregulation phase involves several processes occurring simultaneously. ROS, along with radiotherapy or chemotherapy stomatotoxic agents, activate the transcription factor nuclear factor-κB (NF-κB) in epithelial, endothelial, mesenchymal cells, and macrophages. NF-κB induces the regulation of various types of genes that play roles in the pathogenesis of OM, including pro-inflammatory cytokines such as tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), and interleukin-6 (IL-6).

The amplification and signaling phase sees an increase in the production of pro-inflammatory mediators, further exacerbating tissue damage. The ulceration phase is marked by lesion formation. These lesions become entry points for microorganisms, leading to secondary infections characterized by bacterial colonization, including gram-positive, gram-negative, and anaerobic bacteria. The penetration of bacterial products (endotoxins) into the submucosal layer induces tissue macrophage infiltration, activating macrophages to release TNF-α, IL-1β, and IL-6.

The healing phase begins with signals from the extracellular matrix initiating the re-epithelialization of the ulcer. Re-epithelialization is characterized by the movement of epithelial cells beneath the pseudomembrane (fibrin clot) of the ulcer, followed by proliferation, which thickens the mucosa back to normal. This process increases the expression of adhesion molecules, activating the cyclooxygenase-2 (COX-2) pathway to produce prostaglandins and promote angiogenesis.[2,3,5–9]

Patients are given pharmacological and non-pharmacological therapy management to help relieve their pain, which causes their appetite to diminish. 0.025% hyaluronic acid, which is included in the non-steroidal group, provides anti-inflammatory effects and helps the healing process. Hyaluronic acid also plays a role in biological processes, namely cell signaling, morphogenesis, matrix organization, regulation of gene expression, and cell proliferation.[6,10] Vaseline album is used on the upper and lower lips because it functions as a covering agent that maintains the outer skin, protects it from weather influences and sun exposure, and prevents natural water loss to keep the patient's lips moist.[5]

Non-pharmacological therapy includes education on oral cavity hygiene and additional LLLT therapy. LLLT is used at wavelengths between 600–980 nm because it offers three benefits. First, it helps cell proliferation and supports the angiogenesis process, which plays an important role in wound healing. LLLT also plays a role in the process of apoptosis.[4,11–14] Additionally, LLLT induces various factors related to cell growth, proliferation, differentiation, and survival, such as activation of PI3K/Akt/mTOR, NF-κB, and Src kinase. On the other hand, it suppresses the

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translocation of Bax and the activation of caspase-3, which can lead to cell death.

LLLT also increases the production of various biological mediators such as growth factors, interleukins, inflammatory cytokines, and small molecules, leading to adjustments in the inflammatory response, angiogenesis, and tissue repair. LLLT further alters nerve excitation and conduction in peripheral nerves and stimulates the release of endogenous endorphins. Laser therapy can be considered a preventive measure to manage OM.[4,13] A contraindication in dentistry is irradiation of the thyroid gland, which is located within the dental treatment area. Direct radiation to this area should be avoided, as it can stimulate hyperthyroidism at low doses or inhibit hypothyroidism at high doses.[14,15] The use of a combination of pharmacology and LLLT in our patient was shown to reduce the symptoms of OM and accelerate the healing process.

This patient responded well to the treatment given, and there was substantial improvement with the therapy provided. The patient experienced improvement within 15 days after radiotherapy treatment was completed, and the patient's complaints were no longer present. Evaluation using the VAS scale helps to measure the pain felt by patients subjectively, and in this patient, it showed a considerable change. Subjective pain reduced from a VAS score of eight during the first visit to six at the second visit and finally to two by the third visit, indicating the success of the therapy.[16] In conclusion, the combination of pharmacological therapy with LLLT was better in maintaining and improving the oral mucosa condition by reducing pain, promoting mucosal healing, and further improving quality of life.

REFERENCES

1. Prasetyo RA. Effectivity of 0.15% benzydamine on radiation-induced oral mucositis in nasopharynx carcinoma. Dent J (Majalah Kedokt Gigi). 2011; 44(2): 88–92.
2. Lorini L, Perri F, Vecchio S, Belgioia L, Vinches M, Brana I, Elad S, Bossi P. Confounding factors in the assessment of oral mucositis in head and neck cancer. Support Care Cancer. 2022; 30(10): 8455–63.
3. Pulito C, Cristaudo A, Porta C La, Zapperi S, Blandino G, Morrone A, Strano S. Oral mucositis: the hidden side of cancer therapy. J Exp Clin Cancer Res. 2020; 39(1): 210.
4. de Lima VHS, de Oliveira-Neto OB, da Hora Sales PH, da Silva Torres T, de Lima FJC. Effectiveness of low-level laser therapy for oral mucositis prevention in patients undergoing chemoradiotherapy for the treatment of head and neck cancer: A systematic review and meta-analysis. Oral Oncol. 2020; 102: 104524.
5. Brown TJ, Gupta A. Management of cancer therapy–associated oral mucositis. JCO Oncol Pract. 2020; 16(3): 103–9.
6. Kusiak A, Jereczek-Fossa BA, Cichońska D, Alterio D. Oncological-therapy related oral mucositis as an interdisciplinary problem—literature review. Int J Environ Res Public Health. 2020; 17(7): 2464.
7. Mallick S, Benson R, Rath GK. Radiation induced oral mucositis: a review of current literature on prevention and management. Eur Arch Oto-Rhino-Laryngology. 2016; 273(9): 2285–93.
8. Dewi TS, Lefaan YF, Susilawati S, Kusumadjati A, Arief EM. Correlation analysis between risk factors and mucositis oral in head and neck cancer patients undergoing radiotherapy. Padjadjaran J Dent. 2022; 34(2): 95–102.
9. Maria OM, Eliopoulos N, Muanza T. Radiation-induced oral mucositis. Front Oncol. 2017; 7: 89.
10. Semis R, Kagan S, Berdicevsky I, Polacheck I, Segal E. Mechanism of activity and toxicity of Nystatin-Intralipid. Med Mycol. 2013; 51(4): 422–31.
11. Anschau F, Webster J, Capra MEZ, de Azeredo da Silva ALF, Stein AT. Efficacy of low-level laser for treatment of cancer oral mucositis: a systematic review and meta-analysis. Lasers Med Sci. 2019; 34(6): 1053–62.
12. Sufiawati I, Christine H, Drakel FF. The effectiveness of corticosteroid and diode laser combination therapy in the treatment of severe oral lichen planus: a case report. J Int Dent Med Res. 2022; 15(1): 312–4.
13. Peng J, Shi Y, Wang J, Wang F, Dan H, Xu H, Zeng X. Low-level laser therapy in the prevention and treatment of oral mucositis: a systematic review and meta-analysis. Oral Surg Oral Med Oral Pathol Oral Radiol. 2020; 130(4): 387-397.e9.
14. Sonis ST, Hashemi S, Epstein JB, Nair RG, Raber-Durlacher JE. Could the biological robustness of low level laser therapy (Photobiomodulation) impact its use in the management of mucositis in head and neck cancer patients. Oral Oncol. 2016; 54: 7–14.
15. Tarigan RN, Wimardhani YS. Low-level laser therapy for treatment of oral mucositis. J Dent Indones. 2010; 17(3): 93–100.
16. Jaury DF, Kumaat L, Tambajong HF. Gambaran nilai VAS (visual analogue scale) pasca bedah seksio sesar pada penderita yang diberikan tramadol. e-CliniC. 2014; 2(1): 1–7.

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