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Review

Applications of Photobiomodulation Therapy in Oral Medicine—A Review

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ABSTRACT

Applications of photobiomodulation (PBM) in dentistry have been of great interest in the recent times. It can both stimulate and suppress biological effects. The property of PBM contributes to the analgesic, anti-inflammatory, and wound healing effects. Photobiomodulation therapy (PBMT) has a wide variety of clinical applications that include wound healing, prevention of cellular death, promotion of repair mechanisms, reduction of inflammation, pain relief, etc. Hence, it is being used effectively in the field of oral medicine and has shown promising results in the management of oral mucosal lesions, orofacial pain, and other orofacial ailments without much significant adverse effects. The purpose of this review is to discuss the applications of PBMT in the field of oral medicine.

Keywords: Lasers, mucositis, orofacial pain, photobiomodulation therapy, temporomandibular disease

INTRODUCTION

Laser (light amplification by stimulated emission of radiation) was first produced in the year 1960 by Theodore H. Maiman. Later in the late 1960s, Endre Mester developed a laser for therapeutic purposes, and he described the use of laser biostimulation for wound healing.[1] They can both stimulate and suppress biological effects; hence, it was known to produce effects of photobiomodulation (PBM). The property of PBM contributes to the analgesic, anti-inflammatory, and wound healing effects.[2,3] This noninvasive and nonthermal therapeutic properties of PBM have been used in the management of various neuromuscular, painful musculoskeletal, and trauma-related conditions.[4] The application of photobiomodulation therapy (PBMT) in dentistry has been of great interest in recent times. The purpose of this review is to discuss the applications of PBMT in the field of oral medicine.

PHOTOBIOMODULATION THERAPY

PBMT utilizes nonionizing forms of light sources, such as light-emitting diodes (LEDs), lasers, and broadband light to produce photochemical and photophysical reactions in various tissues.[5] There are evidences in the literature for PBM using monochromatic lasers, quasimonochromatic LED lights, noncoherent, and polychromatic light sources also.[6]

Laser devices used for PBM are smaller, compatible, handheld devices and are much safer when compared to the surgical lasers. PBM is based on the property of Arndt Schultz law, according to which, smaller doses have the ability to stimulate a biological response, doses at medium range can impede, and massive doses can destroy.[4] The technical specifications and considerations of these lasers differ from the surgical lasers[7,8] (Table 1). Though the therapeutic window of these lasers is broad, it is essential to calculate the required amount of dose (i.e., the energy density) before any therapeutic application.[9] The energy density can be calculated by dividing the energy of the laser with the area of the irradiated region. The calculation of required energy density depends on factors like thickness, type, area of the tissue, and pigmentation in the region being irradiated and the wavelength used. Laser waves can be transmitted more freely through fat and mucosa than muscle.[7] The PBM devices that are used commonly for various therapeutic applications in the field of oral medicine are semiconductive diode lasers. Aluminum–gallium–indium–phosphide lasers (AlGaInP) and gallium–aluminum–arsenide lasers (GaAlAs) were the most commonly used lasers for PBM in the field of oral medicine. Surgical lasers can also be used in low-energy output level for the purpose of PBM.[10]

MECHANISM OF ACTION

PBMT has a wide variety of clinical applications, which include wound healing, prevention of cellular death, promotion of repair mechanisms, reduction of inflammation, pain relief, etc. When a PBM light source is targeted on a specific site of the body, it causes the penetration of light energy into the body cells. Based on the optical properties of the tissue being

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Table 1. Technical Parameters and Considerations for Photobiomodulation Therapy

Parameter	Specification
Wavelength	600–1000 nm
Waveform	Continuous, pulsed, modulated
Spectrum	Red to infrared region
Power density	Calculated by laser output power (mW)/beam area (cm^2) 1 mW/cm^2 to 50 mW/cm^2 (average range)
Energy (expressed in Joule as J)	Calculated by mW × seconds
Dose calculation (J/cm sq units)	Calculated by energy ÷ irradiated area
Output power	1 mW up to 500 mW
Treatment interval (average)	Two to three treatments per week for several weeks depending on the nature of the application and chronicity of the disorder

irradiated, the absorption and scattering of the light in the tissue differs. Hemoglobin and melanin have high absorption ability to absorb light of wavelength shorter than 600 nm. In contrast, water absorbs light significantly at a higher wavelength of about 1150 nm.[11] Light energy gets absorbed by cytochrome c oxidase and antenna pigments, which passes it to the mitochondria. In mitochondria, the electromagnetic energy will be utilized to produce Adenosine Triphosphate (ATP). Increased ATP production stimulates the fibroblasts and promotes collagen formation. The energy produced at the site of irradiation stimulates local microcirculation, thereby promoting the process of wound healing.[4]

It also causes dissociation of nitric oxide from cytochrome c oxidase, thereby shifting the cell redox potential toward oxidation.[12] Furthermore, it causes the activation of intracellular signaling pathways and induction of transcriptional changes such as nuclear factor κB. This prevents apoptosis, cell death, promotes growth factor production, antioxidant response, and stimulates repair[13] (Figure 1).

The analgesic effect of PBMT may be due to their ability to inhibit Aδ and C fibers. They also cause inhibition of the release of mediators from injured tissues and decrease the concentration of pain mediators. They are also known to increase the acetylcholine esterase activity, thereby reducing the concentration of acetylcholine.[11]

Main Points

- Brief overview of photobiomodulation and their mechanism of action.
- Therapeutic applications of photobiomodulation in oral medicine.
- Efficiency and advantages of photobiomodulation in the management of orofacial ailments.

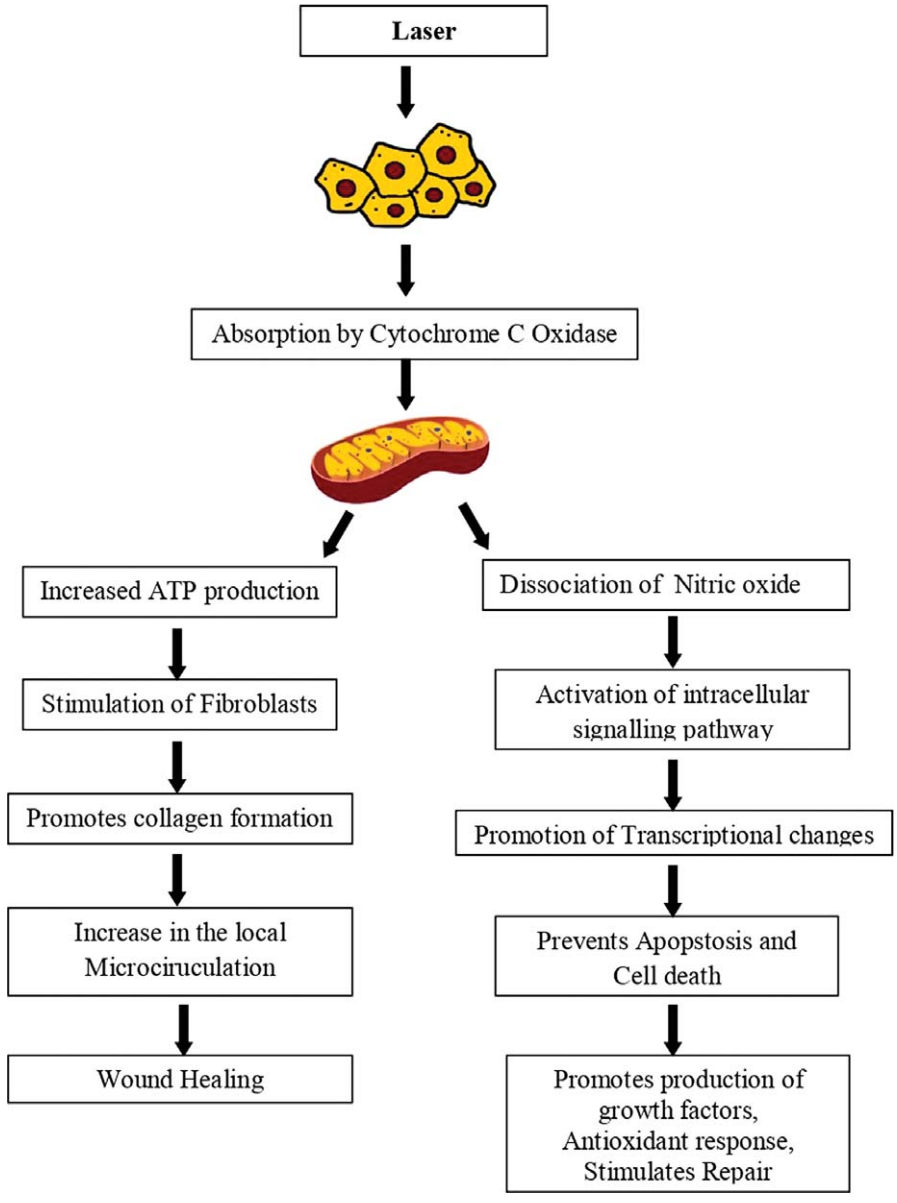
PHOTOBIOMODULATION IN ORO FACIAL AILMENTS

There are several applications of PBMT in orofacial ailments, which have been reported in the existing literature. But the dosage, methodology, and the light source used for PBM widely differ among various studies.[14] Considering their clinical usage in the field of oral medicine, the PBMT has a wide variety of applications ranging from the management of orofacial pain to the treatment of oral mucosal lesions.

Orofacial Pain

Orofacial pain can be defined as pain that is localized to the region above the neck, in front of the ears, below the oribitomeatal line, and also within the oral cavity. It includes both the pain of odontogenic origin and temporomandibular joint disorders.[15] The etiology of orofacial pain is extensive and diverse. PBMT has been used as an effective treatment option for orofacial pain. The analgesic effect of PBMT is gradual, and it requires multiple sessions with different wavelengths.[16] A systematic review by Chow et al.[17] has reported that photobiomodulating lasers can slow down the conduction and reduce the amplitude of action potentials. There have been many studies in the literature evaluating the use of PBMT for the treatment of orofacial pain. Most commonly used therapeutic wavelength for PBM in orofacial pain is 780-830 nm using GaAlAs lasers.[18] They have provided significant relief in orofacial pain. PBMT causes neural changes such as inhibition of action potential generation, inhibition of signal conduction in primary afferent neurons, and inhibition of conduction of C-fibers within the first few minutes of irradiation which causes an immediate analgesic effect.[19] In case of acute inflammatory conditions, it can aid in an early resolution of the inflammation. But most cases of orofacial pain are chronic in origin and require treatment for a longer period of time varying from two to three times per week for 3-4

Figure 1. Mechanism of action of photobiomodulation therapy in stimulation of wound healing.



weeks.[20] Patients suffering from pain might experience a mild increase in the pain immediately after the therapy. This reflects the actual improvement of the patient's condition, and the pain level usually decreases within a day.[21]

Oral Mucositis

The inflammation of the oral mucosal membrane is termed as oral mucositis. This is commonly seen in patients suffering from head and neck cancer as a side effect of chemo and radiotherapy. PBMT is being used in the preventive and therapeutic management of oral mucositis. Studies have shown lasers of 632-970 nm to be effective in treating cases of oral mucositis, achieving about 62% risk reduction and prevention of severe mucositis within a week in patients receiving chemo and radiotherapy.[22] Therapeutic wavelengths that are used in the management of oral mucositis include 670-830 nm using GaAlAs, 630-680 nm using InGAlP, and 632.8 nm using He–Ne lasers, whereas the prophylactic wavelengths include 660 nm of InGaAlP and 630 nm of GaAlAs lasers.[10] A recent study by Marin-Conde et al.[23] has demonstrated PBMT in patients undergoing chemo and radiotherapy is effective in reducing the incidence and severity of oral mucositis, without any significant side effects.

Alteration in the taste perception and dysphagia are also major side effects in patients undergoing radiotherapy for head and neck cancers (HNC). One session of PBMT with a diode laser operating at 635 nm with a dose of 3 J/cm^2 used in contact mode to irradiate different areas of the tongue has shown

significant improvement in taste perception. Similarly, cancer therapy-induced dysphagia has also been successfully managed by irradiation of various intraoral and extraoral sites. The intraoral sites that were irradiated include soft palate and oropharynx, while the extraoral irradiated sites include the midline of the neck, lateral part of the neck, ventrolateral parts of the pharynx, and larynx.[24]

North American Association for photobiomodulation therapy does not recommend PBMT directly over an active tumor to prevent the risk of transformation and stimulation of active cancer cells.[25] But recent studies on the safety of PBMT in HNC patients have proved that PBMT does not affect the overall survival, time to local recurrences, and disease-free survival of patients treated with radiotherapy with/without chemotherapy.[26]

Burning Mouth Syndrome

Burning Mouth Syndrome (BMS) has a complex etiology with diverse clinical presentation and possesses a challenge in its management. PBMT has been used as treatment option in BMS. PBMT for a period of 4-10 weeks targeting various sites like labial mucosa, tongue, and buccal mucosa has shown significant improvement in the symptoms.[27] Diode lasers comprising gallium–aluminum–arsenide (GaAlAs) in a wavelength of 830 nm, indium–gallium–aluminum–phosphide (InGaAlP) in a wavelength of 685 nm, and energy of about 2-5 J per point have been used for irradiating sites, where the pain is experienced and proved to be beneficial to the patients.[28] PBMT has shown to reduce the levels of salivary proinflammatory cytokines (tumor necrosis factor-α and interleukin-6), which can be directly related to the improvement of the condition. The reduction in pain perception may be attributed to the inhibitory action of PBMT on the neural impulse conduction and inhibition of pain mediators.[29]

Temporomandibular Disorders

Temporomandibular disorders (TMDs) can be due to arthrogenic, myogenic causes, or both. The use of PBMT for TMD is based on the type and location of the pain. In case of pain due to arthrogenic causes, irradiation is limited only to the temporomandibular joint area, while in patients with pain due to myogenic causes, specific points in the masticatory muscles are irradiated. Studies in PBMT for TMD differ in their site of application and parameters of the light source. The therapy requires multiple sessions at regular intervals for a specific period of time. Rodrigues et al.[30] have shown successful management of temporomandibular joint disorders using GaAlAs diode laser in a wavelength of 780 nm and a spot size of 0.04 cm^2 applied in contact mode. They followed different treatment protocols for myogenic and arthrogenic TMD. In case of TMD due to myogenic origin, PBM of 10 mW, 5 J/cm^2, and 0.2 J for 2 seconds per point was recommended, while for patients affected by joint problems, PBMT of 70 mW, 105 J/cm^2, 60 seconds on five points on the joint area, and 4.2 J per point was recommended. Treatment that consisted of two sessions per week for a period of 4 weeks showed significant relief among the patients. Sayed et al.[31] recommended a treatment protocol based on six sessions of PBMT (three times per week for 2 weeks) with gallium arsenide laser at 904 nm, 0.6 W, 60 seconds, and 4 J/cm^2 in the trigger points, and the patients showed significant improvement in the symptoms with increased mouth-opening ability. The disadvantage of PBMT for the management of TMD is that it requires multiple visits at different intervals and varied duration depending on the clinical presentation of the patient. Recently, Del Vecchio et al. conducted a study to overcome this limitation of multiple visits by using a laser device that emits a beam with a wavelength of 808 nm, at 5 J/min, 250 mW, and 15 kHz for 8 minutes, for irradiating the area of pain. The duration of treatment was twice daily for 1 week. The first application of laser was made by the clinician, and the patients were educated about the application and safety of the device so as to enable the patients to perform the other successive applications by themselves at home. This method showed improvement only in some patients.[32] The shortcoming of this method may be attributed to the difference in the technique of application by the different patients.

Oral Mucosal Lesions

Recurrent aphthous stomatitis (RAS) is a very common and painful ulcerative lesion of the oral cavity. PBMT has been successfully employed as a treatment modality for the management of recurrent aphthous ulcers. PBMT with a diode laser of 940 nm used in noncontact mode for 30-45 seconds with a pause for 10-20 seconds and a total of about 2 minutes in a single session has shown faster reduction of pain and healing of ulcers. Apart from providing instant pain relief with a rapid decrease in the size of the lesion, they have also shown to prevent recurrence even after 1 year of follow-up. Since no medications were required, adverse effects of using medications could be prevented. Hence, PBMT is a safe and clinically effective therapeutic modality for treating RAS.[33]

Oral lichen planus is a chronic inflammatory mucocutaneous disorder with varied forms of appearance. Various studies have reported the use of diode lasers operating in a wavelength range of 630-970 nm, duration of each session ranging from few seconds to 8 minutes, and 2-3 sessions per week may be required for complete healing of the lesion.[34] PBMT with red diode lasers has proved to reduce the pain level and sign scores in all the patients. Ultraviolet and helium–neon lasers were also used in the management of oral lichen planus; the drawback of using an ultra violet-B excimer laser is that it is potentially a carcinogen and may lead to side effects like erythema and soreness.[35] Red diode lasers are safer to use without causing any significant side effects. Hence, it is a good alternative for conventional corticosteroid therapy in treating of oral lichen planus.

Herpes labialis is a common viral illness affecting the orofacial region caused by herpes simplex virus-1. Though the primary conventional therapy includes symptomatic treatment and antivirals, PBMT has also been used effectively in the management of herpes labialis in all age groups, including pediatric patients.[36] Stona et al.[36] have shown successful management of recurrent herpes labialis in a pediatric patient with the use of an infrared diode laser operating in a wavelength of 780 nm for 80 seconds, targeting at four points over the herpetic lesion in a dose of 5 J/cm^2 for one point given for 3 consecutive days, which has shown complete relief of symptoms and scabbing

with no reported recurrence. Several studies with PBMT using lasers operating in a wavelength range between 632.8 nm and 870 nm, power of 5-80 mW, and 2.04-48 J/cm^2 have also proved to be successful in the management of the recurrent herpetic lesions.[37]

Vesiculobullous Disorders

PBMT has been employed in the management of oral lesions of vesiculobullous disorders like pemphigus and pemphigoid. Pemphigus vulgaris is a blistering disease that can affect the skin and mucous membranes. Though corticosteroids are the first line of therapy, there have been reports using PBMT in the management of oral lesions in pemphigus. PBMT with a wavelength of 660-780 nm targeted at the lesions in a dose of 8 J/cm^2 per point has shown good improvement in the symptoms and has caused regression of the lesions.[38] Mucous membrane pemphigoid (MMP) represents a group of chronic inflammatory, subepithelial blistering disease that can manifest as oral, ocular, skin, genital, nasopharyngeal, esophageal, and laryngeal lesions. Cafaro et al.[39] have successfully demonstrated PBMT in the management of MMP with a 980 nm GaAlAs diode laser in a dose of 4 J/cm^2, used in noncontact mode. All the mucosal lesions and perilesional tissues up to 0.5 cm need to be irradiated twice weekly, until the complete resolution of lesions.

Paresthesia

Paresthesia in the orofacial region may be due to a wide variety of causes. Paresthesia of the inferior alveolar nerve is the most common to occur after any surgical procedure of the mandible. PBMT has been used in the management of paresthesia both extra orally and intraorally depending on the region and the nerve affected. PBMT with lasers operating in a wavelength of about 820-830 nm targeting the affected area with an energy dose of about 4-6 J/cm^2 has been used for the management of post-operative paresthesia. PBMT for the management of paresthesia requires multiple sessions and has been proved to be effective in improving the neurosensory recovery.[40,41]

CONCLUSION

PBMT has been proved to be an effective treatment modality in the management of several orofacial disorders by enabling enhanced wound healing, reducing inflammation, and pain. There is a good number of evidence in the literature on the clinical efficacy of PBM in various medical and dental applications. Further newer applications of PBMT in dentistry and standardization of the wavelength, dosage, and treatment duration for different disorders should be explored.

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