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CASE SERIES

Effectiveness of Photobiomodulation in Reducing Pain of Oral Mucosal Diseases: A Case Series

Astrid Widhowaty Santoso [1], Irna Sufiawati [2]

[1]Oral Medicine Residency Program, Faculty of Dentistry, Universitas Padjadjaran, Bandung, Indonesia; [2]Oral Medicine Department, Faculty of Dentistry, Universitas Padjadjaran, Bandung, Indonesia

Correspondence: Irna Sufiawati, Oral Medicine Department, Faculty of Dentistry, Universitas Padjadjaran, Jalan Sekeloa Selatan I, Bandung, 40132, Indonesia, Email irna.sufiawati@fkg.unpad.ac.id

Introduction: Pain management becomes important in the treatment of oral mucosal diseases since it can impair the quality of life. Photobiomodulation (PBM) as an alternative therapy, has potency in reducing pain through several mechanisms targeting peripheral nerves in the target tissue.

Purpose: To discuss the effectiveness of PBM in the management of four cases of oral mucosal diseases.

Case: Four patients, two females and two males, with an age ranging from 24 to 63 years came to the Oral Medicine Department complaining of painful lesions in their oral cavity. Three cases showed ulceration of the oral mucosa and had been diagnosed with recurrent aphthous stomatitis, recalcitrant chronic ulcer, and non-specific chronic sialadenitis. One patient who complained of intense pain and swelling on the right side of the face was diagnosed with post-herpetic neuralgia (PHN).

Case Management: PBM was administered in all four cases (976 nm diode laser, three cases with spot size 0.01 cm^2, fluency 10 J/cm^2, and one case with spot size 0.5 cm^2; fluency 3 J/cm^2). Visual analog scale (VAS) control was performed before and after the PBM at each visit. The recorded VAS results show a reduction in pain that started at the post-laser time, with VAS before PBM ranging from 5 to 7 and after PBM ranging from 0 to 4. Three patients were given triamcinolone acetonide 0.1%, chlorhexidine gluconate 0.2% mouthwash, petroleum jelly, and multivitamins. One patient was given mefenamic acid and multivitamins.

Conclusion: PBM can be a useful adjunctive treatment to relieve the pain of oral mucosal diseases due to its ability to reduce pain intensity.

Keywords: low-level laser therapy, oral lesions, pain, photobiomodulation

Introduction

According to the International Association for the Study of Pain (IASP), pain is characterized as an unpleasant sensory and emotional experience due to tissue damage, or has the potential to cause tissue damage or conditions that indicate tissue damage.[1] Pain in the oral and facial region greatly affects the quality of life since it interferes with many essential functions, including decreasing food intake, inability to maintain oral hygiene, and impairing swallowing or speaking, especially if it produces severe pain in both acute and chronic lesions.[2,3] Various pathological conditions in the oral cavity can lead to acute and chronic pain. Ulcerative lesions are the most common cause of pain in the oral mucosa with recurrent aphthous stomatitis (SAR) as the most common ulcerative lesion.[3] Moreover, post-herpetic neuralgia may contribute to conditions associated with neuropathic pain in the oral mucosa (PHN).[4]

With this condition, pain management becomes paramount. Various therapeutic approaches are known to reduce pain and accelerate wound healing, including analgesics, corticosteroids, anti-inflammatory drugs, and phytotherapy.[5] However, the use of some of these drugs, such as steroid and non-steroidal anti-inflammatory drugs, is nonetheless limited when given to elderly, pediatric, and patients with impaired kidney and liver function since it contains various side effects.[6] In addition, managing cases of PHN is still considered challenging, and heretofore no treatment is thought to be effective in reducing the incidence of PHN in patients with herpes zoster.[7,8]

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Biostimulation is thought to be an appropriate alternative therapy for managing pain due to oral ulceration[9] and PHN.[7] Low-level laser therapy (LLLT) or photobiomodulation (PBM) therapy is a non-invasive, drug-free therapy that is widely used as an alternative therapy for oral ulcers. PBM uses light energy to generate biological responses from cells and restore normal cell function,[5,10] hence, it is considered effective in reducing pain intensity, reducing edema and inflammation, as well as accelerating ulcer healing.[5] The mechanism of pain reduction in PBM is related to physiological neural changes such as blockage of action potential generation and conduction of nociceptive signals in primary afferent neurons. In addition, the pain reduction effect also occurs through modulation of the release of inflammatory mediators and alteration in lymphocyte metabolism.[11,12] This report aimed to discuss the effectiveness of PBM in the pain management of oral mucosal diseases.

Case Presentation

Case 1

A 24-year-old man came to the Oral Medicine Clinic, Dental Hospital Universitas Padjadjaran, with the chief complaint of a painful ulcer in the oral cavity 1 week ago. The patient had difficulty eating and speaking. Ulcers occurred 3–5 times a year without fever. Intraoral examination revealed two rounded confluent ulcers on the right upper labial mucosa and one ulcer on the left buccal mucosa, 8–10 mm in diameter, covered by whitish pseudomembranous and surrounded by an erythematous halo with a regular border (Figure 1A and B). The patient was diagnosed with recurrent aphthous stomatitis (RAS). The patient was treated for PBM using a 976 nm diode laser (Figure 1C and D). Informed consent regarding the laser treatment and the publication of this case has been obtained from the patient. The VAS score was measured before PBM (VAS score was 7) (Table 1). The laser setting was 0.8 W in continuous wave (CW) which was the aphthous ulcer mode, suggested by the manufacturer, also in the previous work for fluence rate used was 10 J/cm^2,[12,13] spot size 0.01 cm^2, exposure time 20 seconds two times with 10–20 seconds gap on each ulcer and in non-contact mode (2–3 mm away from the lesion, moving continuously from the periphery the lesion to the center). To evaluate the patient's perception of pain, the VAS score was measured immediately (0 minute) after PBM (VAS score was 3) (Table 1). The patient was given Oral Hygiene Instruction (OHI), instructed to avoid spicy, hot, and irritating foods, and was prescribed 0.1% triamcinolone acetonide in orabase, 0.2% chlorhexidine gluconate mouthwash, petroleum jelly, multivitamins, and

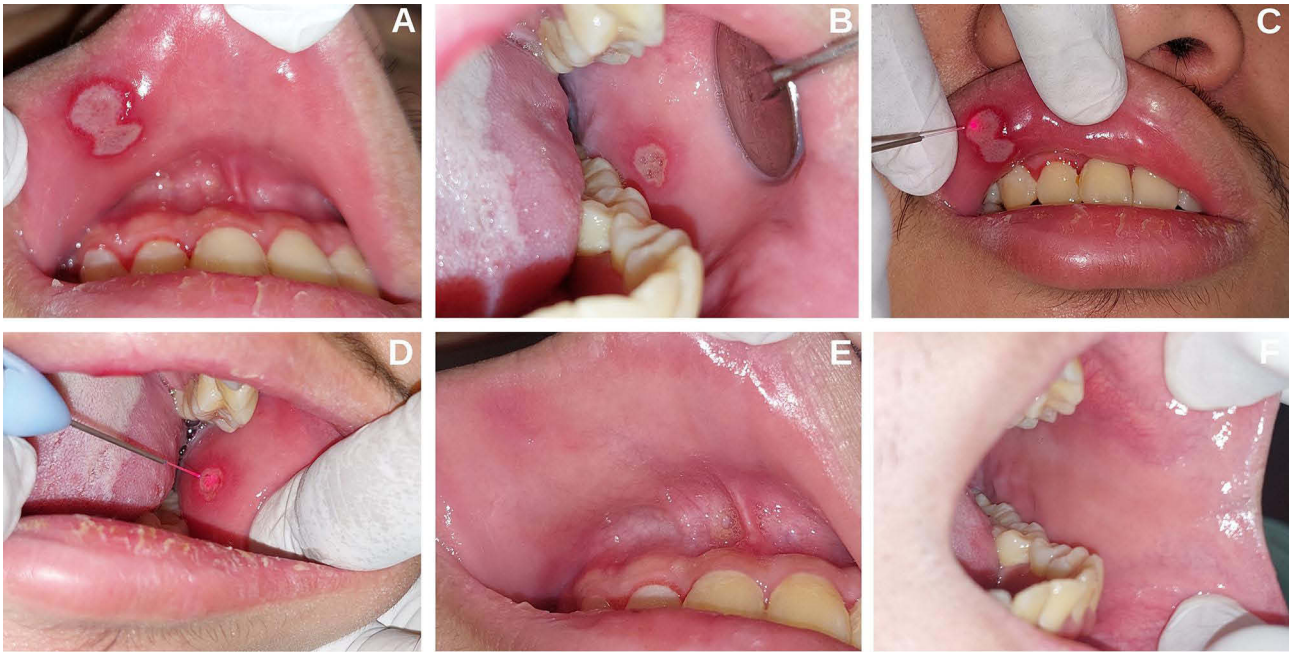

Figure 1 A 24-year-old male with RAS. (**A** and **B**) Ulcers at first visit on the right upper labial mucosa and left buccal mucosa. (**C** and **D**) Application of PBM to ulcers. (**E** and **F**) Lesion at the third visit (day 21) showed an improvement.

Table 1 VAS Score and Diameter of Lesion Measurement Result on the First Patient

		1st Visit	2nd Visit	3rd Visit	4th Visit	PBM Specification
VAS score	Before	6	0	0	–	Laser type: Diode Wavelength: 976 mm Power: 0.8 watt Tip diameter: 400 μm Settings: aphthous ulcer, continuous mode Application: no contact Location: labial and buccal mucosa
	After	3	0	0	–	
Lesion size (in mm)	Labial Buccal	12 8	6 2	–	–	
Exposure (sec) Number of cycles (times)		20" 2	10" 1	–	–	
Total energy (J)		0,8	0,8	–	–	
Total energy density (J/cm^2)		10	10			

Abbreviations: VAS, visual analog scale; sec, seconds; J/cm^2, joules per square centimeter.

consulted for a blood examination, consisting of a complete blood count, an IgG anti-HSV1 test, and testing for immunoglobulin E (IgE).

On the second visit (day 7), the patient had no complaints. The pain was reduced after 24 hours and completely relieved within 3 days after PBM. Laboratory findings showed no abnormalities, IgG anti-HSV-1 was non-reactive, and a normal level of IgE. The lesions showed a significant improvement at a follow-up of 21 days after treatment (Figure 1E and F).

Case 2

A 38-year-old woman came to the Oral Medicine Clinic of Dr Hasan Sadikin General Hospital, with chief complaints of a painful ulcer in the oral cavity for more than a month. The patient had difficulty opening her mouth. It had been examined by a previous doctor but had not improved. Intraoral examination revealed an oval, concave ulcer, 10 mm in diameter, with an irregular border, and granulation on palpation on the left labial mucosa, the ulcer on the left buccal mucosa was difficult to evaluate (Figure 2A). The VAS score measurement was 7. Toluidine blue examination did not

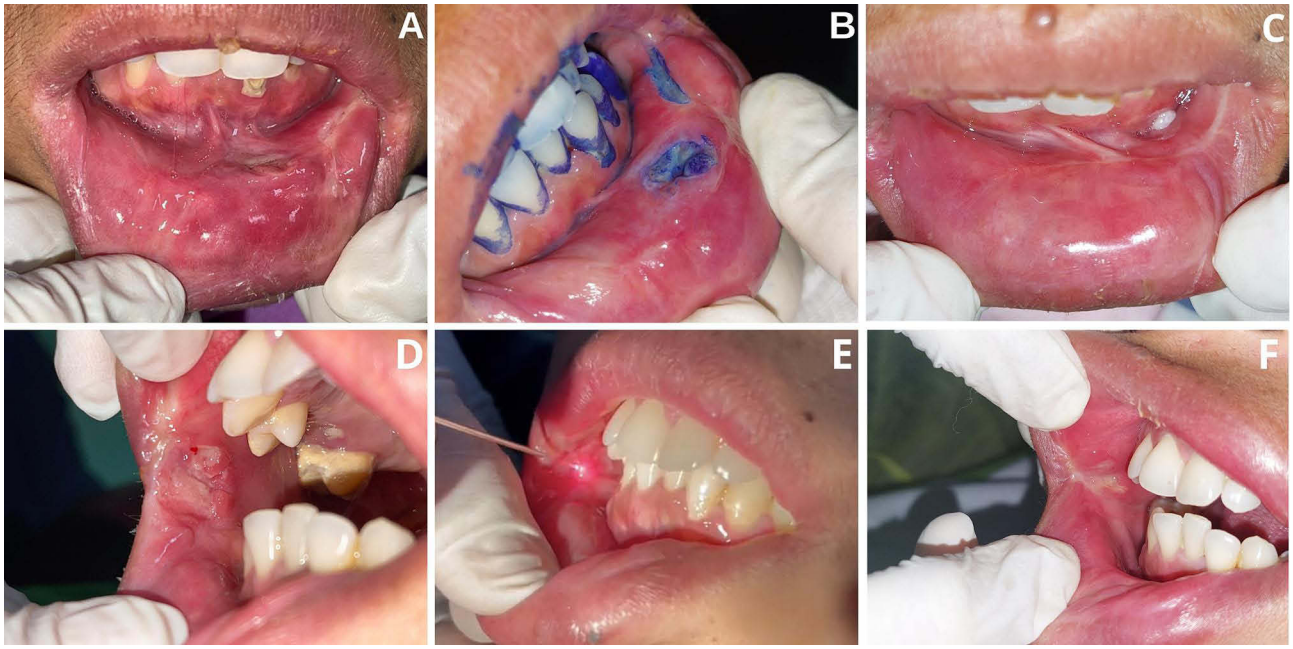

Figure 2 A 38-year-old woman with chronic oral ulcer. (**A**) Ulcer on left labial and buccal mucosa. (**B**) Toluidine blue examination: no malignancy possibilities. (**C**) On the next visit (2 months), ulcer condition after histopathological biopsy along with stricture release procedure. (**D**) Ulcer on the right buccal mucosa. (**E**) Application of PBM to ulcers. (**F**) Lesion condition in the fourth visit (day 28) showed cicatricial/fibrotic tissue formation.

indicate malignancy (Figure 2B). The patient was diagnosed with a chronic ulcer with a differential diagnosis consisting of traumatic ulcer granulomatous with stromal eosinophilia (TUGSE) and oral squamous cell carcinoma (OSCC). The patient was given Oral Hygiene Instruction (OHI), instructed to avoid spicy, hot, and irritating food, and was prescribed 0.1% triamcinolone acetonide, 0.2% chlorhexidine gluconate mouthwash, multivitamins, and was consulted for histopathological biopsy to the Oral and Maxillofacial Surgery Clinic, a complete blood count, thyroid ultrasonography (USG), and a head CT-scan examination.

On the next visit (2 months later), a painful ulcer appeared on the right buccal mucosa for 7 days. The patient had no difficulty in mouth opening. The laboratory findings' (complete blood count) result showed a decrease in mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC) value, and an increase in erythrocytes value. The thyroid ultrasonography and head CT-scan showed no abnormalities and no possibility of metastasis (Figure 3D-F). Panoramic radiograph findings showed root radix 15, 16, 38, 45 and root radix with periapical abscess 48 (Figure 3C). The histopathological examination of the previous ulcer did not indicate malignancy, and the condition leads to non-specific chronic sialadenitis at the inferior of labial mucosa and the buccal mucosa sinistra (Figure 3A and B). The patient not only received the procedure of histopathological biopsy but also

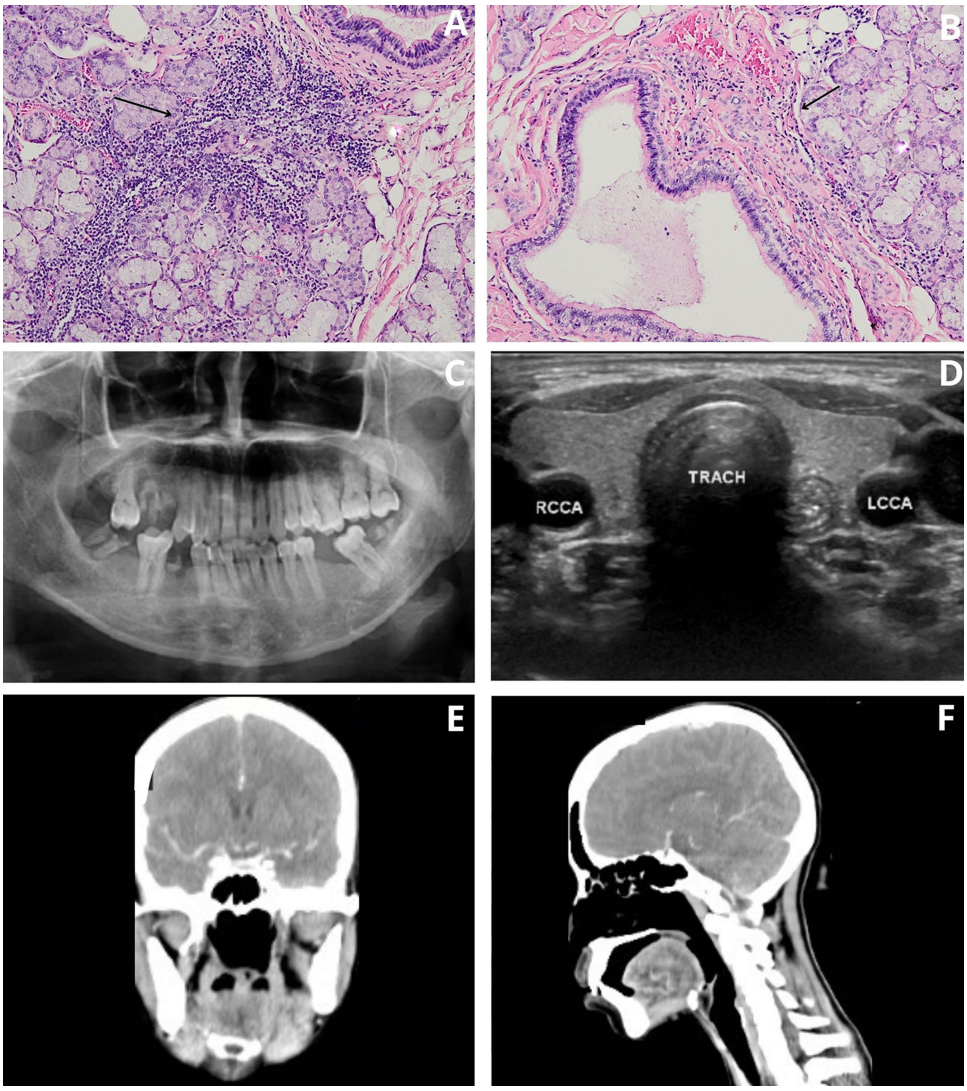

Figure 3 (**A** and **B**) Histopathological examination results: PMN inflammatory cells and lymphocyte inflammatory cells (indicated by a black arrow on (**A**), plasma cells, accompanied by proliferation and dilatation of blood vessels, salivary gland acini, and tubular ductile (with 100× magnification) (indicated by a black arrow on (**B**). (**C**) Panoramic radiograph: no abnormalities. (**D**) USG Thyroid: within normal range, lymph node enlargement as high as level IIb colli dextra (**E** and **F**) head CT-scan (with contrast): did not show bone destruction, mass, and intracranial lesion, lymph node enlargement as high as level IIb colli dextra.

stricture release to overcome the mouth opening difficulty. There was cicatricial/fibrotic tissue formation on the healed lesion (Figure 2C). Intraoral examination revealed an oval, concave ulcer, 11 mm in diameter, with an irregular border, and granulation on palpation on the right buccal mucosa (Figure 2D). The patient has signed an informed consent regarding the treatment would be given by diode laser and the publication of the case. The patient was treated for PBM using 976 nm diode laser (Figure 2E). The VAS score was measured before PBM (VAS score was 7) (Table 2). The laser setting was 0.8 W in continues wave which was the aphthous ulcer mode, suggested by the manufacturer, also in the previous work for fluence rate used was 10 J/cm^2,[12,13] spot size 0.01 cm^2, exposure time 20 seconds two times with 10–20 seconds gap on each ulcer and in non-contact mode (2–3 mm away from the lesion, moving continuously from the periphery the lesion to the center). To evaluate the patient's perception of pain, the VAS score was measured immediately (0 minute) after PBM. The patient felt immediate pain reduction after the PBM procedure, with VAS score recorded was 4 (Table 2). The patient was given Oral Hygiene Instruction (OHI), instructed to avoid spicy, hot, and irritating food, and was prescribed 0.1% triamcinolone acetonide, 1% povidone-iodine mouthwash, petroleum jelly, and multivitamins. The PBM was given in four sessions, in each session was done every 7 days. There was significant improvement of the lesions and pain reduction after the fourth visit (day 28) (Figure 2F).

Case 3

A 16-year-old man came to the Oral Medicine Clinic of Dental Hospital Universitas Padjadjaran, complaining of a painful ulcer in the right lower lip for 1 month. Ulcer appeared every 2–3 months. No history of fever. Intraoral examination revealed an oval, concave ulcer, 10 mm in diameter, with an irregular border, and granulation on palpation (Figure 4A). The VAS recorded was 6 (Table 3). The patient was diagnosed with chronic traumatic ulcer with a differential diagnosis consisting of traumatic ulcer granuloma with stromal eosinophilia (TUGSE) and oral squamous cell carcinoma (OSCC). The patient was given Oral Hygiene Instruction (OHI), instructed for avoiding spicy, hot, and irritating food, and was prescribed 0.1% triamcinolone acetonide, 0.2% chlorhexidine gluconate mouthwash, petroleum jelly, multivitamins, and was consulted for complete blood examination and IgE test.

On the second visit (day 7), the patient stated that the lesion was still painful and only slightly improved. The VAS score recorded before treatment was 3. Intraoral findings revealed an oval, concave ulcer, 8 mm in diameter, with an irregular border, and granulation on palpation (Figure 4B). The complete blood count result showed no abnormalities, and a normal level of IgE. The patient's parent agreed to the laser treatment would be performed to the patient and for the publication of this case including the photographs by signing the informed consent. The patient was treated with PBM using a 976 nm diode laser (Figure 4C). The laser setting was 0.8 W in continues wave which was the aphthous ulcer mode, suggested by the manufacturer, also in the previous work for fluence rate used was 10 J/cm^2,[12,13] spot size 0.01 cm^2, exposure time 20 seconds two times with 10–20 seconds gap on each ulcer and in non-contact mode (2–3 mm away from the lesion, moving continuously from the periphery the lesion to the center). To evaluate the patient's

Table 2 VAS Score and Diameter of Lesion Measurement Result on the Second Patient

		1st Visit	2nd Visit	3rd Visit	4th Visit	PBM Specification
VAS score	Before	7	6	3	1	Laser type: Diode Wavelength: 976 mm Energy: 0.8 watt Tip diameter: 400 μm Settings: aphtous ulcer, continuous mode Application: no contact Location: labial and buccal mucosa
	After	–	4	1	1	
Lesion size (in mm)		11	7	3	2	
Exposure (sec) Number of cycles (times)		–	20" 2	20" 2	10" 1	
Energy (J)		–	0,8	0,8	0,8	
Energy density (J/cm^2)		–	10	10	6	

Abbreviations: VAS, visual analog scale; sec, seconds; J/cm^2, joules per square centimeter.

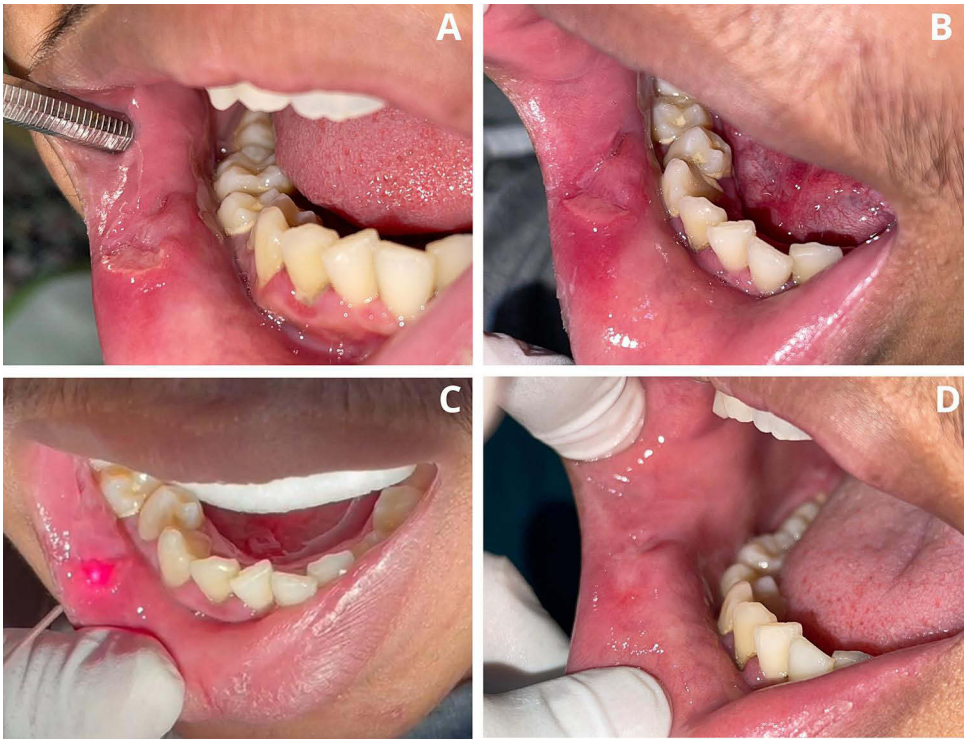

Figure 4 A 16-year-old man with TUGSE. (**A**) Ulcer on the right labial mucosa (**B**) Ulcer condition at the second visit (day 7) (**C**) Application of PBM to ulcers. (**D**) The fourth visit (day 21): ulcer lesion showed an improvement.

perception of pain, the VAS score was measured immediately (0 minute) after PBM. The patient felt immediate pain reduction with the VAS score after PBM was 1 (Table 3). The lesion was improved after three sessions of PBM (day 21) (Figure 4D; Table 3).

Case 4

A 63-year-old woman came to the Oral Medicine Clinic of Dental Hospital Universitas Padjadjaran, with a chief complaint of intense pain and burning sensation on the right face for 1 week. Two weeks before, it had been preceded by multiple vesicles, redness, and lump on the right face accompanied with painful multiple ulcers on the right side of the oral cavity (the patient gave us the clinical picture that was taken by herself; Figure 5A and C). The patient had previously checked this condition with a doctor and received acyclovir 5-gram cream and mupirocin calcium. The vesicles on the face had disappeared and left black patches. Extraoral findings revealed multiple blackish-brown patches, varying in size from 3

Table 3 VAS Score and Diameter of Lesion Measurement Result on the Third Patient

		1st Visit	2nd Visit	3rd Visit	4th Visit	PBM Specification
VAS score	Before	6	3	0	0	Laser type: Diode Wavelength: 976 mm Energy: 0.8 watt Tip diameter: 400 μm Settings: aphtous ulcer, continuous mode Application: no contact Location: right buccal mucosa
	After	–	0	0	0	
Lesion size (in mm)		10	8	7	4	
Exposure (sec) Number of cycles (times)		–	20” 2	20” 1	10” 1	
Energy (J)		–	0,8	0,8	0,8	
Energy density (J/cm^2)		–	10	10	6	

Abbreviations: VAS, visual analog scale; sec, seconds; J/cm^2, joules per square centimeter.

Figure 5 A 63-year-old woman with PHN. (**A**) Dry crusts on the right portion of the face, preceded by multiple vesicles with an erythematous area (picture taken by the patient). (**B**) The condition on the first visit: extraoral findings showed multiple blackish-brown patches. (**C**) Intraoral findings showed multiple ulcers on the right portion of labial mucosa (picture taken by the patient). (**D**)The condition on the first visit: intraoral findings showed no lesion.

to 10 mm, with a diffuse and irregular border on the right side of the face (Figure 5B). Intraoral findings showed no abnormalities on the mucosal surface, root radix on 15, 14, 12, 11, 22, and edentulous area from 35 to 37, 45 to 47 (Figure 5D). The VAS score recorded before PBM was 6. The patient then was diagnosed with post herpetic neuralgia (PHN). Informed consent regarding the laser treatment and the publication of this case was taken from the patient. The patient was treated with PBM using 976 nm diode laser with biostimulation tip. The laser setting was 3 W in pulse wave which was the biostimulation mode, suggested by the manufacturer, also in the previous work for fluence rate used was 3 J/cm^2,[14] spot size 0.5 cm^2; exposure time 20 seconds two times with 10–20 seconds gap on each area and in non-contact mode (2–3 mm away from the lesion). To evaluate the patient's perception of pain, the VAS score was measured immediately (0 minute) after PBM (Table 4). The patient felt immediate pain reduction with the VAS score after PBM was 4 (Figure 6). The patient was given Oral Hygiene Instruction (OHI), instructed to avoid direct sun exposure and apply sunscreen, and was prescribed 500 mg mefenamic acid, petroleum jelly, and multivitamins.

On the second visit (day 3), the patient complained of an intense pain on the right face, but the pain intensity was decreased. The VAS score recorded was 3. The patient was treated with PBM, and the VAS score before and after were measured (Table 4). In this session, pain and discomfort felt by patient was reduced; with VAS score recorded 15 minutes after PBM was 1. The pain was relief after four treatment sessions (day 28).

A summary of visual analogue scale (VAS) score and lesion measurement results of all cases are presented in Table 5.

Table 4 VAS Score and Diameter of Lesion Measurement Result on the Fourth Patient

		1st Visit	2nd Visit	3rd Visit	4th Visit	PBM Specification
VAS score	Before	6	3	2	1	Laser type: Diode Wavelength: 976 mm Energy: 3.0 watt Average energy: 0.5 watt Duration: 30 μs Interval: 100 μs Tip: Biostimulation tip Option: Biostimulation, pulse mode Application: no contact Location: at several points parallel to the trigeminal nerve.
	After	4	1	1	1	
Lesion size (in mm)		–	–	–	–	
Exposure (sec) Number of cycles (times)		20" 2	20" 2	10" 1	10" 1	
Energy (J)		3	3	3	3	
Energy density (J/cm^2)		3	3	3	3	

Abbreviations: VAS, visual analog scale; sec, seconds; J/cm^2, joules per square centimeter.

Discussion

According to the North American Association for Photobiomodulation Therapy (NAALT) and the World Association for Laser Therapy (WALT), photobiomodulation is the application of light for therapeutic purposes that is absorbed by endogenous chromophores and causes physiological changes through photochemical or photophysical events that are not thermal and cytotoxic.[15] Photobiomodulation (PBM) or previously known as low-level laser therapy (LLLT), also known as biomodulation or cold laser, is an alternative therapy for oral mucosal ulcers.[13] In addition, PBM is also considered effective in managing PHN cases.[7] PBM produces non-ionizing light of a single wavelength or dual-wavelength (the use of combinations of different radiation or different wavelengths to generate distinct effects on tissue compared to a single radiation),[16] through a non-thermal photochemical cell reaction known as a biostimulation reaction.[17–19] When target cells absorb photons, a cascade of biochemical events occurs and triggers rapid wound healing.[19] Over the past few

Figure 6 The PBM procedure. Laser irradiation following the dermatomal pattern (**A**) nearby trigeminal ganglion, (**B**) along with ophthalmic nerve (V1), (**C**) along with maxillary nerve (V2), and (**D**) along with mandibular nerve (V3).

Table 5 A Visual Analogue Scale (VAS) Score and Lesion Measurement Results of the Four Cases

Patients			The 1st Visit	The 2nd Visit	The 3rd Visit	PBM Specification
1	VAS	Before	6	0	0	Laser type: Diode Wavelength: 976 nm Energy: 0.8-watt Tip diameter: 400 μm Settings: Aphthous ulcer, continuous mode Application: no contact Location: on each ulcer
		After	3	0	0	
	Lesion size (mm)		Labial: 12 Buccal: 8	Labial: 6 Buccal: 2	Labial: 0 Buccal: 0	
	Exposure (sec) Number of cycles (times)		20” 2	10” 1	– –	
	Energy (J)		0,8	0,8	–	
	Energy density (J/cm^2)		10	6		
2	VAS	Before	7	6	3	
		After	–	4	1	
	Lesion size (mm)		11	7	3	
	Exposure (sec) Number of cycles (times)		–	20” 2	20” 2	
	Energy (J)		–	0,8	0,8	
	Energy density (J/cm^2)			10	10	
3	VAS	Before	6	3	0	
		After	–	0	0	
	Lesion size (mm)		10	8	7	
	Exposure (sec) Number of cycles (times)			20” 2	20” 1	
	Energy (J)		–	0,8	0,8	
	Energy density (J/cm^2)			10	6	
4	VAS	Before	6	3	2	Laser type: Diode Wavelength: 976 nm Energy: 3.0-watt Duration: 30μs Interval: 100μs Settings: Biostimulation, pulse mode Application: no contact Location: at several points parallel to the trigeminal nerve
		After	4	1	1	
	Lesion size (mm)		–	–	–	
	Exposure (sec) Number of cycles (times)		20” 2	20” 2	10” 1	
	Energy (J)		3	3	3	
	Energy density (J/cm^2)		3	3	3	

Abbreviations: VAS, visual analog scale; sec, seconds; J/cm^2, joules per square centimeter.

years, PBM has been widely used in the medical field for its beneficial therapeutic effects, such as analgesic, anti-inflammatory, and wound healing.[20]

In all four cases, the patients were treated using a diode laser-type PBM. Compared to other types of lasers, low-power diode laser therapy has many advantages, including not causing thermal injury to tissue (no thermal ablation associated with administration of laser at low-level doses and shorter duration with gap between each application to prevent excess temperature increase to the tissue so that the tissue damage does not occur),[11] being easy to handle with excellent electrical and optical efficiency,[21] having a small size, a wide spectrum, and transmission via optical fiber.

Previous studies stated diode lasers are known to stimulate aphthous ulcer pain reduction and re-epithelialization at very low power settings.[22]

After therapy using PBM, the three patients with oral mucosal ulcers and one patient with PHN felt pain reduction from the first session of treatment. The mechanism of pain reduction after laser therapy is related to the modulation of pain perception by modification of nerve conduction through (1) the release of neuropharmacological substances including endogenous endorphins (endorphins-β), encelaphalin,[23] and serotonine[7] and (2) increased synthesis of ATP in the mitochondria of neurons, resulting in hyperpolarization. The upregulation, immediate, and significant increase in mitochondrial function, as well as the increase in ATP production, are highly related to the mitochondrial cytochrome c oxidase (Cox) within the therapeutic window of a wavelength ranging from 650 to 1200 nm.[24] Increased in ATP synthesis also result in an increase of mitotic activity which can cause increase in protein synthesis by mitochondria, producing extensive tissue remodeling in the wound healing process;[25] (3) obstruction of stimuli resulting in decreased induction of pain stimuli. The conduction of these nerve fibers can be inhibited by using a low-power laser.[23] Increased pain threshold is also associated with the stabilization of cell membranes and regulation of resting cell potential. PBM limits the production of pro-inflammatory mediators, including tumor necrosis factor-α (TNF- α), Interleukin-1 (IL-1), IL-1β, and IL-6 in damaged neurons, inhibits prostaglandins E2 and increases the production of plasminogen, as well as stimulates post-traumatic maturation and regeneration.[19,22,26–28] In addition, PBM can increase tissue microcirculation/oxygenation and stimulate the growth of epithelial, endothelial, and mesenchymal cells.[29] Enhanced tissue microcirculation can lead to an increase in the delivery of nutritional substances related to the elevated mitosis rate, resulting in neoangiogenesis.[25]

The use of PBM in PHN cases has a significant effect on reducing the pain associated with neuralgia. PBM removes NO from cytochrome c-oxidase, thereby allowing the return of oxygen and then restoring ATP production. When the mitochondrial function returns to normal, cell metabolism increases, and patients feel that their complaints are improving more quickly. In another study, it was also stated that the early use of PBM can reduce the incidence of PHN. According to Cotler et al, specifically in wounded or hypoxic cells, nitric oxide (NO), which is generated in mitochondria, can displace oxygen and suppress respiration by binding to COX. The hypothesis is that PBM can photo-dissociate NO from COX and reverse the mitochondrial respiration inhibition induced by excessive NO binding.[30]

Conclusion

Due to its ability to modulate pain and regenerate wound healing, PBM can be used as an effective and non-invasive adjunctive therapy to reduce pain in chronic or recalcitrant oral ulcers as well as PHN.

Consent Statements

The patients have approved and written informed consent for the publication of this case series including the images. The institution has also approved for the publication of this report.

Acknowledgments

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Disclosure

The authors declare no conflicts of interest in this work.

References

1. Raja SN, Carr DB, Cohen M, et al. The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises. *Pain*. 2020;161(9):1976–1982. doi:10.1097/j.pain.0000000000001939
2. Radwan-Oczko M, Sokół I, Babuśka K, Owczarek-Drabińska JE. Prevalence and characteristic of oral mucosa lesions. *Symmetry*. 2022;14(2):1–14. doi:10.3390/sym14020307
3. Chung M-K, Wang S, S-L O, Kim YS. Acute and chronic pain from facial skin and oral mucosa: unique neurobiology and challenging treatment. *Int J Mol Sci*. 2021;22(11). doi:10.3390/ijms22115810

4. Lynge Pedersen AM, Forssell H, Grinde B. Orofacial pain conditions - pain and oral mucosa. *Den Nor Tann Tid*. 2016;126(2). doi:10.56373/2016-2-3
5. Chinam N, Vaidya A, John T. Photobiomodulation therapy in the treatment of a palatal ulcer. *J Oral Res Rev*. 2021;13(2):125. doi:10.4103/jorr.jorr_43_20
6. Lee HS, Lee Y, Jeong U, Oh S, Hwang CW, Kang HW. Transoral low-level laser therapy via a cylindrical device to treat oral ulcers in a rodent model. *Lasers Surg Med*. 2020;52(7):647–652. doi:10.1002/lsm.23203
7. Chen YT, Wang HH, Wang TJ, Li YC, Chen TJ. Early application of low-level laser may reduce the incidence of postherpetic neuralgia (PHN). *J Am Acad Dermatol*. 2016;75(3):572–577. doi:10.1016/j.jaad.2016.03.050
8. Portella AVT, Souza LC. Herpes-zóster e neuralgia pós-herpética. *Rev Dor*. 2013;14(3):210–215. doi:10.1590/s1806-00132013000300012
9. Dhillon JK, Kalra G. Laser biostimulation of oral ulcers in children. *Int J Laser Dent*. 2012;2(2):59–62. doi:10.5005/jp-journals-10022-1020
10. Seyyedi SA, Olyaee P, Fekrazad R, Partovi S, Fini MB, Fini MB. The effect of carbon dioxide laser on aphthous stomatitis treatment: a double-blind randomized clinical trial. *J Lasers Med Sci*. 2020;11(4):S67–S72. doi:10.34172/JLMS.2020.S11
11. Amorim Dos Santos J, Normando AGC, De toledo IP, et al. Laser therapy for recurrent aphthous stomatitis: an overview. *Clin Oral Investig*. 2020;24(1):37–45. doi:10.1007/s00784-019-03144-z
12. Pandeshwar P, Roa MD, Das R, Shastry SP, Kaul R, Srinivasreddy MB. Photobiomodulation in oral medicine: a review. *J Investig Clin Dent*. 2016;7(2):114–126. doi:10.1111/jicd.12148
13. Balakrishnan B, Naik V, Gaurav S, Sangeetha A. Photobiomodulation on oral mucosal lesions- a systematic review. *Acta Sci Dent Scienecs*. 2022;6(12):122–128. doi:10.31080/asds.2022.06.1522
14. Gomes RNS, Viana LVM, Ramos J. Effects of photobiostimulation in the treatment of post-herpetic neuralgia: a case report. *Rev Bras Geriatr e Gerontol*. 2018;21(1):102–107. doi:10.1590/1981-22562018021.170116
15. Zecha JAEM, Raber-Durlacher JE, Nair RG, et al. Low-level laser therapy/photobiomodulation in the management of side effects of chemoradiation therapy in head and neck cancer: part 1: mechanisms of action, dosimetric, and safety considerations. *Support Care Cancer*. 2016;24(6):2781–2792. doi:10.1007/s00520-016-3152-z
16. Lima A, Sergio LP, Fonseca A. Photobiomodulation via multiple-wavelength radiations. *Lasers Med Sci*. 2020;35. doi:10.1007/s10103-019-02879-1
17. Suter VGA, Sjölund S, Bornstein MM. Effect of laser on pain relief and wound healing of recurrent aphthous stomatitis: a systematic review. *Lasers Med Sci*. 2017;32(4):953–963. doi:10.1007/s10103-017-2184-z
18. Yilmaz HG, Albaba MR, Caygur A, Cengiz E, Boke-Karacaoglu F, Tumer H. Treatment of recurrent aphthous stomatitis with Er, Cr:YSGG laser irradiation: a randomized controlled split mouth clinical study. *J Photochem Photobiol B Biol*. 2017;170:1–5. doi:10.1016/j.jphotobiol.2017.03.011
19. Soliman HA, Mostafaa D. Clinical evaluation of 660 nm diode laser therapy on the pain, size and functional disorders of recurrent aphthous stomatitis. *Open Access Maced J Med Sci*. 2019;7(9):1516–1522. doi:10.3889/oamjms.2019.268
20. Akerzoul N, Chbicheb S. Low laser therapy as an effective treatment of recurrent aphthous ulcers: a clinical case reporting two locations. *Pan Afr Med J*. 2018;30:1–8. doi:10.11604/pamj.2018.30.205.15779
21. Nasry SA, El Shenawy HM, Mostafa D, Ammar NM. Different modalities for treatment of recurrent aphthous stomatitis. A Randomized clinical trial. *J Clin Exp Dent*. 2016;8(5):e517–e522. doi:10.4317/jced.52877
22. Hussein H, Zaky A, Nadim M, Elbarbary A. Low-level diode laser therapy (LLLT) versus topical corticosteroids in the management of recurrent aphthous stomatitis patients. a randomized controlled trial. *Adv Dent J*. 2021;3(4):200–210. doi:10.21608/adjc.2021.90071.1109
23. Aggarwal H, Pal Singh M, Nahar P, Mathur H, Sowmya GV. Efficacy of low-level laser therapy in treatment of recurrent aphthous ulcers - A sham controlled, split mouth follow-up study. *J Clin Diagnostic Res*. 2014;8(2):218–221. doi:10.7860/JCDR/2014/7639.4064
24. Rola P, Włodarczak S, Lesiak M, Doroszko A, Włodarczak A. Changes in cell biology under the influence of low-level laser therapy. *Photonics*. 2022;9(7). doi:10.3390/photonics9070502
25. Babu B, Uppada UK, Tarakji B, Hussain KA, Azzeghaibi SN, Alzoghaibi I. Versatility of diode lasers in low-level laser therapy for the management of recurrent aphthous stomatitis. *J Orofac Sci*. 2015;7(1):49–53. doi:10.4103/0975-8844.157392
26. Kang JW, Ryu HS, Abueva C, Chung P-S, Woo SH. Stability and effectiveness of laser and liquiband treatments in the rat model of oral ulcer. *Med Lasers*. 2021;10(4):207–213. doi:10.25289/mL.2021.10.4.207
27. Ślebioda Z, Dorocka-Bobkowska B. Low-level laser therapy in the treatment of recurrent aphthous stomatitis and oral lichen planus: a literature review. *Postep dermatologii i Alergol*. 2020;37(4):475–481. doi:10.5114/ada.2020.98258
28. Olejnik M, Ślebioda Z, Dorocka-Bobkowska B. Low-level laser therapy (LLLT) in the treatment of recurrent aphthous stomatitis (RAS) - a promising treatment option: a report of two cases. *Dent Med Probl*. 2019;56(3):317–321. doi:10.17219/dmp/108632
29. Maya R, Costa Ladeira LL, Maya JEP, Gonçalves LM, Bussadori SK, Paschoal MAB. The combination of antimicrobial photodynamic therapy and photobiomodulation therapy for the treatment of palatal ulcers: a case report. *J Lasers Med Sci*. 2020;11(2):228–233. doi:10.34172/JLMS.2020.38
30. Cotler B. The Use of Low-Level Laser Therapy (LLLT) For Musculoskeletal pain. *MOJ Orthop Rheumatol*. 2015;2(5):188–194. doi:10.15406/mojor.2015.02.00068